Clinical trial results:
A Twelve Week, Multicenter, Open Label Extension Study in Subjects with Schizophrenia

Summary

EudraCT number	2011-004790-90
Trial protocol	SK IT
Global end of trial date	01 November 2013

Results information

Result version number	v1 (current)
This version publication date	15 October 2016
First version publication date	15 October 2016

Trial information

Trial identification

Sponsor protocol code	D1050307

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01566162
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sunovion Pharmceuticals Inc.
Sponsor organisation address	One Bridge Plaza North, Suite 510, Fort Lee, United States, 07024
Public contact	Manager, Sunovion Pharmaceuticals Inc., 001 8665036351, clinicaltrialdisclosure@sunvion.com
Scientific contact	Medical Director, Sunovion Pharmaceuticals Inc., 001 8665036351, clinicaltrialdisclosure@sunvion.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	01 November 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 November 2013
Global end of trial reached?	Yes
Global end of trial date	01 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a 12-week, multi-center, open-label extension study designed to evaluate the longer-term safety, tolerability and effectiveness of lurasidone for the treatment of subjects with schizophrenia.

Protection of trial subjects:

none

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2012
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	Serbia: 22
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	United States: 114
Country: Number of subjects enrolled	Slovakia: 15
Country: Number of subjects enrolled	Russian Federation: 19
Country: Number of subjects enrolled	South Africa: 17
Worldwide total number of subjects	191
EEA total number of subjects	19

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)	190

From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who completed the 28-week double-blind phase or who experienced a protocol-defined relapse event during the double-blind phase in Study D1050238 were eligible to participate. In addition, subjects who were participating in the open-label or double-blind phase of Study D1050238 at the point in time when the study was terminated.

Pre-assignment

Screening details:

All eligible subjects were transitioned immediately from Study D1050238. A total of up to 7 days hospitalization was permitted from the completion/termination of Study D1050238 through the first week of this extension study.

Period 1

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

Arms

Arm title	Lurasidone

Arm description:

Lurasidone 40 – 80mg flexible dose

Lurasidone: Lurasidone 40-80 mg taken orally taken once daily

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

Dosage and administration details:

lurasidone 40 - 80mg flexible dose/once daily

Number of subjects in period 1	Lurasidone
Started	191
Completed	155
Not completed	36
Consent withdrawn by subject	10
Adverse event, non-fatal	9
Lost to follow-up	7
administrative	2
Lack of efficacy	3
Protocol deviation	5

Baseline characteristics

Reporting groups	
Reporting group title	Lurasidone
Reporting group description: Lurasidone 40 – 80mg flexible dose Lurasidone: Lurasidone 40-80 mg taken orally taken once daily	

Reporting group values	Lurasidone	Total	
Number of subjects	191	191	
Age Categorical Units: participants			
<=18 years	0	0	
Between 18 and 65 years	190	190	
>=65 years	1	1	
Age Continuous Units: Years			
arithmetic mean	42.7		
standard deviation	± 12.3	-	
Gender, Male/Female Units: participants			
Female	76	76	
Male	115	115	
Region of Enrollment Units: Subjects			
Serbia	22	22	
France	4	4	
United States	114	114	
Slovakia	15	15	
Russian Federation	19	19	
South Africa	17	17	
Italy	0	0	

End points

End points reporting groups

Reporting group title	Lurasidone

Reporting group description:

Lurasidone 40 – 80mg flexible dose

Lurasidone: Lurasidone 40-80 mg taken orally taken once daily

Primary: Safety - Treatment-emergent adverse events (TEAEs), TEAEs leading to discontinuation, and serious AEs (SAEs)

End point title	Safety - Treatment-emergent adverse events (TEAEs), TEAEs leading to discontinuation, and serious AEs (SAEs)[1]

End point description:

Number of subjects with treatment-emergent adverse events (TEAEs), TEAEs leading to discontinuation, and serious AEs (SAEs)

End point type	Primary

End point timeframe:

12 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The rational with regards no statistical analyses performed for primary outcome of 307: because this is the extension study of D1050238, and every subject took lurasidone during the study, and thus only one treatment group is reported and no statistical analyses can be performed.

End point values	Lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	191			
Units: participants				
number (not applicable)				
Subjects with TEAEs	72			
TEASs leading to discontinuation	7			
Subjects with TESAEs	13			

Statistical analyses

No statistical analyses for this end point

Primary: Efficacy - Change in Positive and Negative Syndrome Scale (PANSS) total score

End point title	Efficacy - Change in Positive and Negative Syndrome Scale (PANSS) total score[2]

End point description:

The PANSS is an interview-based measure of the severity of psychopathology in adults with psychotic disorders. The measure is comprised of 30 items. An anchored Likert scale from 1-7, where values of 2 and above indicate the presence of progressively more severe symptoms, is used to score each item. The PANSS total score is the sum of all 30 items and ranges from 30 through 210. A higher score is associated with greater illness severity.

End point type	Primary

End point timeframe:

Baseline to week 12 LOCF endpoint

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: The rational with regards no statistical analyses performed for primary outcome of 307: because this is the extension study of D1050238, and every subject took lurasidone during the study, and thus only one treatment group is reported and no statistical analyses can be performed.

End point values	Lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	191			
Units: units on a scale				
arithmetic mean (standard deviation)	-8.4 (± 15.06)			

Statistical analyses

No statistical analyses for this end point

Primary: Efficacy - Change from baseline in Clinical Global Impression-Severity of Illness (CGI-S) score.

End point title	Efficacy - Change from baseline in Clinical Global Impression-Severity of Illness (CGI-S) score.[3]

End point description:

The CGI-S score is a single value, clinician-rated assessment of illness severity and ranges from 1= 'Normal, not at all ill' to 7= 'Among the most extremely ill patients'. A higher score is associated with greater illness severity.

End point type	Primary

End point timeframe:

Baseline to week 12 LOCF endpoint

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: The rational with regards no statistical analyses performed for primary outcome of 307: because this is the extension study of D1050238, and every subject took lurasidone during the study, and thus only one treatment group is reported and no statistical analyses can be performed.

End point values	Lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	191			
Units: units on a scale				
arithmetic mean (standard deviation)	-0.48 (± 1.051)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Montgomery -Asberg Depression Rating Scale total score

End point title	Change from baseline in Montgomery -Asberg Depression Rating Scale total score

End point description:

The MADRS consists of 10 items, each rated on a Likert scale, from 0=”Normal” to 6=”Most Severe”. The MADRS total score is calculated as the sum of the 10 items. The MADRS total score ranges from 0 to 60. Higher scores are associated with greater severity.

End point type	Secondary

End point timeframe:

Baseline to week 12 LOCF endpoint

End point values	Lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	182			
Units: units on a scale				
arithmetic mean (standard deviation)	-3.3 (± 7.83)			

Statistical analyses

No statistical analyses for this end point

Secondary: Short Form-12 Health Survey (SF-12)

End point title	Short Form-12 Health Survey (SF-12)

End point description:

The SF-12v2 is a self-administered, multipurpose short-form (SF) generic measure of health status. It was developed to be a shorter, yet valid, alternative to the SF-36 for use in large surveys of general and specific populations as well as in large longitudinal studies of health outcomes. The 12 items in the SF-12v2 are a subset of those in the SF-36; SF-12v2 includes one or two items from each of the eight health concepts with higher scores indicative of higher functioning and better health. The Physical Component Score is a composite of the Physical Functioning, Role Functioning, Bodily Pain and General Health scales. Physical Composite Scores (PCS) is computed using the scores of twelve questions and range from 0 to 100, where a zero score indicates the lowest level of health measured by the scales and 100 indicates the highest level of health.

End point type	Secondary

End point timeframe:

Baseline to week 12 LOCF endpoint

End point values	Lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	182			
Units: units on a scale				
arithmetic mean (standard deviation)	-0.45 (± 6.642)			

Statistical analyses

No statistical analyses for this end point

Secondary: Modified Specific Levels of Functioning (SLOF) total score.

End point title	Modified Specific Levels of Functioning (SLOF) total score.

End point description:

The modified SLOF scale is designed to measure directly observable behavioral functioning and daily living skills of patients with chronic mental illness. The modified SLOF consists of 24 items, each item is rated on a 5-point scale and mapped to 0 to 4. The total score will be the sum of all 24 items and ranges from 0 to 96. A higher score indicates worse condition.

End point type	Secondary

End point timeframe:

12 weeks

End point values	Lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	174			
Units: units on a scale				
arithmetic mean (standard deviation)	-1.8 (± 9.55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Brief Adherence Rating Scale (BARS)

End point title	Brief Adherence Rating Scale (BARS)

End point description:

The Brief Adherence Rating Scale (BARS) is a clinician-administered adherence assessment instrument that consists of four items including three questions and a visual analog rating scale (VAS) to assess the percentage (0 100%) of doses taken by the subject in the previous month.

End point type	Secondary

End point timeframe:

12 weeks

End point values	Lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	182			
Units: percentage of monthly doses taken				
arithmetic mean (standard deviation)	99 (± 3.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: Smoking questionnaire

End point title	Smoking questionnaire

End point description:

Smoking questionnaire - average number of cigarettes per day at week 12 (LOCF).

End point type	Secondary

End point timeframe:

12 weeks

End point values	Lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: number of cigarettes smoked daily				
arithmetic mean (standard deviation)	11.1 (± 9.95)			

Statistical analyses

No statistical analyses for this end point

Secondary: Intent to Attend assessment

End point title	Intent to Attend assessment

End point description:

The ITA assessment will be administered by a research staff member. The response is recorded on a 10-point scale, with 0 = "Not at all" and 9 = "Extremely". The ITA allowed the site to capture data regarding dropout risk. The following question was completed at the baseline visit: "How likely is it that you will complete the study?"

End point type	Secondary

End point timeframe:

12 weeks

End point values	Lurasidone			
Subject group type	Reporting group			
Number of subjects analysed	185			
Units: units on a scale				
arithmetic mean (standard deviation)	8.3 (± 1.14)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12 Weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Lurasidone

Reporting group description:

Lurasidone 40 – 80mg flexible dose

Lurasidone: Lurasidone 40-80 mg taken orally taken once daily

Serious adverse events	Lurasidone		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 191 (6.81%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 191 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Artrial flutter			
subjects affected / exposed	1 / 191 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	1 / 191 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Schizophrenia			

subjects affected / exposed	6 / 191 (3.14%)		
occurrences causally related to treatment / all	2 / 6		
deaths causally related to treatment / all	0 / 0		
Psychotic Disorder			
subjects affected / exposed	4 / 191 (2.09%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 191 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Lurasidone		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 191 (17.80%)		
Nervous system disorders			
Akathisia			
subjects affected / exposed	10 / 191 (5.24%)		
occurrences (all)	10		
Headache			
subjects affected / exposed	4 / 191 (2.09%)		
occurrences (all)	5		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 191 (2.09%)		
occurrences (all)	4		
Nausea			
subjects affected / exposed	4 / 191 (2.09%)		
occurrences (all)	5		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 191 (2.09%)		
occurrences (all)	9		

Schizophrenia subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	 8 / 191 (4.19%) 8 4 / 191 (2.09%) 4		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 5 / 191 (2.62%) 5		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

none

Notes: