



Clinical trial results:

A DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMIZED WITHDRAWAL STUDY OF LURASIDONE FOR THE MAINTENANCE TREATMENT OF SUBJECTS WITH SCHIZOPHRENIA

Summary

EudraCT number	2011-001711-31
Trial protocol	SK IT
Global end of trial date	06 August 2013

Results information

Result version number	v1 (current)
This version publication date	02 October 2016
First version publication date	02 October 2016

Trial information

Trial identification

Sponsor protocol code	D1050238
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01435928
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sunovion Pharmaceuticals Inc.
Sponsor organisation address	One Bridge Plaza North, Suite 510, Ft. Lee, United States, 07024
Public contact	Medical Director, CNS, Sunovion Pharmaceuticals Inc., 001 866-503-6351, clinicaltrialdisclosure@sunovion.com
Scientific contact	Medical Director, CNS, Sunovion Pharmaceuticals Inc., 001 866-503-6351, 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	20 January 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 August 2013
Global end of trial reached?	Yes
Global end of trial date	06 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of lurasidone for the maintenance treatment of subjects with schizophrenia.

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles of Good Clinical Practice, according to the ICH Harmonized Tripartite Guideline.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 October 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects**Subjects enrolled per country**

Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Serbia: 40
Country: Number of subjects enrolled	United States: 532
Country: Number of subjects enrolled	Slovakia: 35
Country: Number of subjects enrolled	Russian Federation: 24
Country: Number of subjects enrolled	South Africa: 36
Country: Number of subjects enrolled	Italy: 1
Worldwide total number of subjects	676
EEA total number of subjects	44

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)	671
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

hospitalized patients and outpatients were assessed for eligibility and upon meeting entry criteria, were tapered off their psychotropic medications in a manner consistent with labeling recommendations and usual medical practice. A total of up to 14 days within the screening/washout phase were allowed to taper as needed

Period 1

Period 1 title	Open Label Phase - up to 24 Weeks
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	All Subjects
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Arm description:

During the Open Label Phase subjects will receive Lurasidone 40 and 80 mg, once daily in the evening with a meal or 30 minutes after eating

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 and 80 mg, once daily in the evening with a meal or 30 minutes after eating

Number of subjects in period 1	All Subjects
Started	676
Completed	287
Not completed	389
Adverse event, serious fatal	1
Consent withdrawn by subject	96
did not meet stabilization criteria	44
Administrative	14
Adverse event, non-fatal	83
Lost to follow-up	60
Lack of efficacy	46
Protocol deviation	39
Terminated at study completion	6

Period 2	
Period 2 title	Double Blind Phase - 28 Weeks
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor
Arms	
Are arms mutually exclusive?	Yes
Arm title	Lurasidone
Arm description:	
During double blind phase subjects received Lurasidone flexibly dosed 40 or 80 mg 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 and 80 mg, once daily in the evening with a meal or 30 minutes after eating	
Arm title	Placebo
Arm description:	
During double blind phase subjects received matching 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 in the evening with a meal or 30 minutes after eating	

Number of subjects in period 2 ^[1]	Lurasidone	Placebo
Started	144	141
Completed	28	20
Not completed	116	121
Consent withdrawn by subject	5	12
Administrative	5	2
Adverse event, non-fatal	3	1
Relapse criteria met	43	58
Lost to follow-up	2	5

Protocol deviation	11	4
Terminated at study completion	47	39

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Of the 287 subjects who completed the open-label phase, 2 subjects were not randomized to the double-blind phase (1 subject due to not meeting the criteria for clinical stability, and 1 subject due to an AE), thus only 285 subjects were randomized to the double blind phase.

Baseline characteristics

Reporting groups

Reporting group title	All Subjects
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Reporting group description:

During the Open Label Phase subjects will receive Lurasidone 40 and 80 mg, once daily in the evening with a meal or 30 minutes after eating

Reporting group values	All Subjects	Total	
Number of subjects	676	676	
Age Categorical			
Units: participants			
<=18 years	0	0	
Between 18 and 65 years	671	671	
>=65 years	5	5	
Age Continuous			
Units: years			
arithmetic mean	40.6		
standard deviation	± 11.85	-	
Gender, Male/Female			
Units: participants			
Female	465	465	
Male	211	211	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	7	7	
Asian	4	4	
Native Hawaiian or Other Pacific Islander	2	2	
Black or African American	353	353	
White	286	286	
More than one race	0	0	
Unknown or Not Reported	24	24	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	41	41	
Not Hispanic or Latino	635	635	
Unknown or Not Reported	0	0	
Region of Enrollment			
Units: Subjects			
France	8	8	
Serbia	40	40	
United States	532	532	
Slovakia	35	35	
Russian Federation	24	24	
South Africa	36	36	
Italy	1	1	

End points

End points reporting groups

Reporting group title	All Subjects
Reporting group description: During the Open Label Phase subjects will receive Lurasidone 40 and 80 mg, once daily in the evening with a meal or 30 minutes after eating	
Reporting group title	Lurasidone
Reporting group description: During double blind phase subjects received Lurasidone flexibly dosed 40 or 80 mg once daily	
Reporting group title	Placebo
Reporting group description: During double blind phase subjects received matching placebo.	

Primary: Time to First Relapse Event During Double-blind phase

End point title	Time to First Relapse Event During Double-blind phase
End point description:	
End point type	Primary
End point timeframe: Double-blind phase -28 weeks	

End point values	Lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	141		
Units: number of relapsed subjects	43	58		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Lurasidone v Placebo
Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.039
Method	Logrank
Parameter estimate	Odds ratio (OR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	0.98

Secondary: Change from Double-blind Baseline in Positive and Negative Syndrome Scale (PANSS) Total score

End point title	Change from Double-blind Baseline in Positive and Negative Syndrome Scale (PANSS) Total score
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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 and three scales: the Positive scale contains seven questions to assess delusions, conceptual disorganization, hallucinations behavior, excitement, grandiosity, suspiciousness/persecution, and hostility; the Negative scale contains seven questions to assess blunted effect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, lack of motivation, and similar symptoms; and the General Psychopathology subscale addresses other symptoms such as anxiety, somatic concern, and disorientation. 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	Secondary
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End point timeframe:

Double-Blind phase - 28 Weeks

End point values	Lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	141		
Units: units on a scale				
least squares mean (standard error)	8.3 (± 1.33)	12.4 (± 1.33)		

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Lurasidone v Placebo
Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.029
Method	ANCOVA

Notes:

[1] - LOCF

Secondary: Change from Double-blind Baseline in Clinical Global Impression - Severity of Illness Scale (CGI-S) score

End point title	Change from Double-blind Baseline in Clinical Global Impression - Severity of Illness Scale (CGI-S) score
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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	Secondary
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End point timeframe:
Double-blind phase - 28 Weeks

End point values	Lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	141		
Units: units on a scale				
least squares mean (standard error)	0.44 (\pm 0.087)	0.74 (\pm 0.087)		

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Lurasidone v Placebo
Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	= 0.015
Method	ANCOVA

Notes:

[2] - LOCF

Secondary: Change from Double-blind Baseline in Montgomery-Asberg Depression Rating Scale (MADRS) total score

End point title	Change from Double-blind Baseline in Montgomery-Asberg Depression Rating Scale (MADRS) total score
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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
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End point timeframe:

Double-blind phase - 28 Weeks

End point values	Lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	139		
Units: units on a scale				
least squares mean (standard error)	2.5 (\pm 0.63)	3.6 (\pm 0.63)		

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Placebo v Lurasidone
Number of subjects included in analysis	279
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.218 ^[3]
Method	ANCOVA

Notes:

[3] - LOCF

Secondary: Change from Double-blind Baseline in Short Form-12v2 Health Survey (SF-12v2) Physical Component Score

End point title	Change from Double-blind Baseline in Short Form-12v2 Health Survey (SF-12v2) Physical Component Score
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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
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End point timeframe:

Double-blind phase - 28 Weeks

End point values	Lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	138		
Units: units on a scale				
least squares mean (standard error)	0.398 (± 0.5354)	-1.341 (± 0.5373)		

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Lurasidone v Placebo
Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021 ^[4]
Method	ANCOVA

Notes:

[4] - LOCF

Secondary: Change from Double-blind Baseline in Modified Specific Levels of Functioning (SLOF) total score

End point title	Change from Double-blind Baseline in Modified Specific Levels of Functioning (SLOF) total score
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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 divided into two subscales: Social functioning (comprised of 7 items from interpersonal relationships section) and Community Living Skills (comprised of 17 items from activities and work skills sections). Each item is rated on a 5-point scale and mapped to 0 to 4 with a higher score indicating worse condition. The total score will be the sum of all 24 items and ranges from 0 to 96.

End point type	Secondary
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End point timeframe:

Double-blind phase - 28 Weeks

End point values	Lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125	121		
Units: units on a scale				
least squares mean (standard error)	0.8 (\pm 0.88)	3.2 (\pm 0.89)		

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Lurasidone v Placebo
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	superiority ^[5]
P-value	= 0.056
Method	ANCOVA

Notes:

[5] - LOCF

Secondary: Brief Adherence Rating Scale

End point title	Brief Adherence Rating Scale
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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
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End point timeframe:

Double-blind phase - 28 Weeks

End point values	Lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	138	139		
Units: percentage of monthly doses taken				
arithmetic mean (standard deviation)	98.8 (\pm 4.42)	98.9 (\pm 3.66)		

Statistical analyses

No statistical analyses for this end point

Secondary: Smoking Questionnaire (Average Number of Cigarettes Per Day) at Week 28 (LOCF)

End point title	Smoking Questionnaire (Average Number of Cigarettes Per Day) at Week 28 (LOCF)
End point description:	
Smoking history and frequency were assessed during the study by a research staff member. During the study, smoked subjects were asked about the average number of cigarettes per day they smoked over the last week.	
End point type	Secondary
End point timeframe:	
28 Weeks - Double Blind Phase	

End point values	Lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	49		
Units: number of cigarettes smoked daily				
arithmetic mean (standard deviation)	10 (\pm 12.76)	8.2 (\pm 8.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Intent to Attend (ITA) Assessment at Open-label Baseline

End point title	Intent to Attend (ITA) Assessment at Open-label Baseline
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 screening visit: "How likely is it that you will complete the study?"	
End point type	Secondary

End point timeframe:

Open Label Baseline

End point values	Lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	140		
Units: units on a scale				
arithmetic mean (standard deviation)	7.9 (\pm 14.8)	8 (\pm 1.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to all-cause discontinuation

End point title	Time to all-cause discontinuation
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End point description:

End point type	Secondary
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End point timeframe:

Double-blind phase - 28 weeks

End point values	Lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	141		
Units: number of discontinued subjects	69	82		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Lurasidone
Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.07
Method	Logrank
Parameter estimate	Odds ratio (OR)
Point estimate	0.75

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.03

Other pre-specified: EuroQol (EQ-5D): EQ-VAS Score

End point title	EuroQol (EQ-5D): EQ-VAS Score
End point description:	
<p>The EQ-5D is a self-administered, standardized measure of health states consisting of two parts: EQ-5D descriptive system consisting of one question in each of five dimensions (mobility, self-care, pain, usual activities, and anxiety) with three possible response levels per question, classifying patients into one of 243 distinct health states, and a 20-cm visual analogue health status rating.</p> <p>The 20-cm visual analog scale (VAS) has endpoints labeled "best imaginable health state" and "worst imaginable health state" that are anchored at 100 and 0, respectively. Respondents are asked to indicate how they rate their own health by drawing a line from an anchor box to that point on the EQ-VAS, which best represents their own health on that day.</p>	
End point type	Other pre-specified
End point timeframe:	
Double-blind phase - 28 Weeks	

End point values	Lurasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	138		
Units: units on a scale				
arithmetic mean (standard deviation)	74.5 (± 19.87)	68.2 (± 28.59)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For the open label phase - all subjects SAEs and AEs were reported over 24 weeks.

For the double blind phase, lurasidone and placebo, SAEs and AEs were reported over 28 weeks. The study was stopped once the anticipated number of relapses were reached.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	All Subjects
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Reporting group description:

During the Open Label Phase subjects will receive Lurasidone 40 and 80 mg, once daily in the evening with a meal or 30 minutes after eating

Reporting group title	Placebo
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Reporting group description:

During double blind phase subjects received matching placebo.

Reporting group title	Lurasidone
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Reporting group description:

During double blind phase subjects received Lurasidone flexibly dosed 40 or 80 mg once daily

Serious adverse events	All Subjects	Placebo	Lurasidone
Total subjects affected by serious adverse events			
subjects affected / exposed	59 / 676 (8.73%)	11 / 141 (7.80%)	6 / 144 (4.17%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Intentional overdose			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			

subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 676 (0.00%)	0 / 141 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 676 (0.00%)	1 / 141 (0.71%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 676 (0.00%)	1 / 141 (0.71%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 676 (0.00%)	1 / 141 (0.71%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Akathisia			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 676 (0.00%)	0 / 141 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischemic attack			

subjects affected / exposed	0 / 676 (0.00%)	0 / 141 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Drug ineffective			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden cardiac death			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Therapeutic response delayed			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 676 (0.00%)	1 / 141 (0.71%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 676 (0.00%)	0 / 141 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	20 / 676 (2.96%)	4 / 141 (2.84%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	5 / 20	2 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	11 / 676 (1.63%)	2 / 141 (1.42%)	2 / 144 (1.39%)
occurrences causally related to treatment / all	2 / 11	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	3 / 676 (0.44%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	2 / 676 (0.30%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute psychosis			

subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aggression			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination, auditory			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Homicidal ideation			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hostility			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric decompensation			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Substance induced psychotic disorder			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			

subjects affected / exposed	1 / 676 (0.15%)	1 / 141 (0.71%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	2 / 676 (0.30%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pin in extremity			
subjects affected / exposed	0 / 676 (0.00%)	0 / 141 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponytrema			
subjects affected / exposed	1 / 676 (0.15%)	0 / 141 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	All Subjects	Placebo	Lurasidone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	373 / 676 (55.18%)	47 / 141 (33.33%)	46 / 144 (31.94%)
Investigations			
Weight increased			
subjects affected / exposed	14 / 676 (2.07%)	4 / 141 (2.84%)	5 / 144 (3.47%)
occurrences (all)	14	4	5
Nervous system disorders			
Headache			
subjects affected / exposed	77 / 676 (11.39%)	5 / 141 (3.55%)	4 / 144 (2.78%)
occurrences (all)	116	8	5

Akathisia subjects affected / exposed occurrences (all) Dystonia subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Sedation subjects affected / exposed occurrences (all)	94 / 676 (13.91%)	4 / 141 (2.84%)	3 / 144 (2.08%)
	104	4	3
	21 / 676 (3.11%)	1 / 141 (0.71%)	2 / 144 (1.39%)
	23	1	2
	34 / 676 (5.03%)	0 / 141 (0.00%)	0 / 144 (0.00%)
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Abdominal discomfort subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all)	38	0	0
	24 / 676 (3.55%)	0 / 141 (0.00%)	1 / 144 (0.69%)
	28	0	1
	25 / 676 (3.70%)	0 / 141 (0.00%)	1 / 144 (0.69%)
	27	0	1
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Abdominal discomfort subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all)	69 / 676 (10.21%)	1 / 141 (0.71%)	3 / 144 (2.08%)
	79	1	3
	36 / 676 (5.33%)	0 / 141 (0.00%)	1 / 144 (0.69%)
	45	0	1
	21 / 676 (3.11%)	0 / 141 (0.00%)	0 / 144 (0.00%)
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Agitation	31	0	0
	22 / 676 (3.25%)	2 / 141 (1.42%)	4 / 144 (2.78%)
	22	2	5
	62 / 676 (9.17%)	10 / 141 (7.09%)	9 / 144 (6.25%)
	82	12	10
Anxiety subjects affected / exposed occurrences (all) Agitation	35 / 676 (5.18%)	4 / 141 (2.84%)	6 / 144 (4.17%)
	43	4	7

subjects affected / exposed occurrences (all)	21 / 676 (3.11%) 22	4 / 141 (2.84%) 5	3 / 144 (2.08%) 3
Schizophrenia subjects affected / exposed occurrences (all)	4 / 676 (0.59%) 4	11 / 141 (7.80%) 11	10 / 144 (6.94%) 11
Psychotic disorder subjects affected / exposed occurrences (all)	4 / 676 (0.59%) 4	6 / 141 (4.26%) 6	4 / 144 (2.78%) 4
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	17 / 676 (2.51%) 21	3 / 141 (2.13%) 3	6 / 144 (4.17%) 7
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	28 / 676 (4.14%) 32	1 / 141 (0.71%) 1	2 / 144 (1.39%) 2
Upper respiratory tract infection subjects affected / exposed occurrences (all)	23 / 676 (3.40%) 23	1 / 141 (0.71%) 1	1 / 144 (0.69%) 1

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: