Clinical trial results:
A Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Low-dose Lurasidone in Acutely Psychotic Subjects with Schizophrenia

Summary

EudraCT number	2012-005271-14
Trial protocol	SK RO
Global end of trial date	18 June 2014

Results information

Result version number	v1 (current)
This version publication date	18 September 2016
First version publication date	18 September 2016

Trial information

Trial identification

Sponsor protocol code	D1050303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01821378
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sunovion Pharmaceuticals Inc.
Sponsor organisation address	One Bridge Plaza North, Suite 510, Fort Lee, United States, 07024
Public contact	Medical Director, Sunovion Pharmaceuticals Inc., 001 8665036351, clinicaltrialdisclosure@sunovion.com
Scientific contact	Medical Director, Sunovion Pharmaceuticals Inc., 001 8665036351, 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	12 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 June 2014
Global end of trial reached?	Yes
Global end of trial date	18 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary purpose of this study is to evaluate the efficacy of lurasidone 20 mg/day in subjects with an acute exacerbation of schizophrenia.

Protection of trial subjects:

The 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	16 May 2013
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	Colombia: 19
Country: Number of subjects enrolled	Russian Federation: 99
Country: Number of subjects enrolled	Romania: 78
Country: Number of subjects enrolled	United States: 128
Country: Number of subjects enrolled	Ukraine: 60
Country: Number of subjects enrolled	Slovakia: 27
Worldwide total number of subjects	411
EEA total number of subjects	105

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)	407

From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicenter, randomized, double-blind, placebo-controlled, parallel-group study designed to evaluate the efficacy and safety of lurasidone 20 mg/day administered one daily over a 6-week period in acutely psychotic subjects with chronic schizophrenia. Enrollment started on 16May2013.

Pre-assignment

Screening details:

Screen phase (up to 14 days) followed by a double-blind phase (6 weeks) and a follow-up visit (7 days post-last dose of study drug). Following the screening phase, subjects who continued to meet entry criteria were randomly assigned to 1 of 3 treatment groups: a fixed dose of lurasidone 20mg/day. lurasidone 80mg/day or Placebo in a 1:2:1 ratio.

Pre-assignment period milestones

Number of subjects started	411
Number of subjects completed	411

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	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Lurasidone 20 mg

Arm description:

Lurasidone 20 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 20mg/once daily

Arm title	Lurasidone 80 mg - 160 mg

Arm description:

The subjects who were randomized to lurasidone 80 mg/day at baseline (received lurasidone 80 mg/day or 160 mg/day throughout the study

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 80mg/once daily and also lurasidone 160 mg/once daily after week 2 for ENR 160 subjects (who received lurasidone 80 mg/day till Week 2, are classified to ENR at Week 2, and received lurasidone 160 mg/day after rerandomization at Week 2.

Arm title	Placebo

Arm description:

Placebo Comparator once daily

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

Number of subjects in period 1	Lurasidone 20 mg	Lurasidone 80 mg - 160 mg	Placebo
Started	101	198	112
Completed	74	145	70
Not completed	27	53	42
Consent withdrawn by subject	15	24	12
Adverse event, non-fatal	2	8	8
lost to follow up	2	4	-
lack of efficacy	8	15	18
Lost to follow-up	-	-	1
administrative	-	1	2
Protocol deviation	-	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Lurasidone 20 mg
Reporting group description:	
Lurasidone 20 mg once daily	

Reporting group title	Lurasidone 80 mg - 160 mg
Reporting group description:	
The subjects who were randomized to lurasidone 80 mg/day at baseline (received lurasidone 80 mg/day or 160 mg/day throughout the study	

Reporting group title	Placebo
Reporting group description:	
Placebo Comparator once daily	

Reporting group values	Lurasidone 20 mg	Lurasidone 80 mg - 160 mg	Placebo
Number of subjects	101	198	112
Age Categorical			
Please note: the demographic information is based on safety population (excluded one subject who was randomized but did not take any study medication).			
Units: participants			
<=18 years	0	0	0
Between 18 and 65 years	99	196	112
>=65 years	2	2	0
Age Continuous			
Units: years			
arithmetic mean	41.5	40.5	40.7
standard deviation	± 10.96	± 11.44	± 11.58
Gender, Male/Female			
Units: participants			
Female	36	79	34
Male	65	119	78
Region of Enrollment			
Units: Subjects			
Colombia	3	9	7
Russian Federation	23	49	27
Romania	22	38	18
United States	31	59	38
Ukraine	16	31	13
Slovakia	6	12	9

Reporting group values	Total		
Number of subjects	411		
Age Categorical			
Please note: the demographic information is based on safety population (excluded one subject who was randomized but did not take any study medication).			
Units: participants			
<=18 years	0		
Between 18 and 65 years	407		
>=65 years	4		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female			
Units: participants			
Female	149		
Male	262		
Region of Enrollment			
Units: Subjects			
Colombia	19		
Russian Federation	99		
Romania	78		
United States	128		
Ukraine	60		
Slovakia	27		

Subject analysis sets

Subject analysis set title	ENR Lurasidone 80 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects who are non-responders on Lurasidone 80 mg/day and rerandomized to Lurasidone 80 mg/day at week 2.

Subject analysis set title	ENR Lurasidone 160 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects who are non-responders on Lurasidone 80 mg/day and rerandomized to Lurasidone 160 mg/day at week 2.

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Randomized to Placebo group at baseline

Reporting group values	ENR Lurasidone 80 mg	ENR Lurasidone 160 mg	Placebo
Number of subjects	52	43	112
Age Categorical			
Please note: the demographic information is based on safety population (excluded one subject who was randomized but did not take any study medication).			
Units: participants			
<=18 years	0	0	
Between 18 and 65 years	53	43	
>=65 years	2	0	

Age Continuous Units: years			
arithmetic mean	42.2	41.3	
standard deviation	± 11	± 9.06	±
Gender, Male/Female Units: participants			
Female	23	27	
Male	32	16	
Region of Enrollment Units: Subjects			
Colombia	3	3	
Russian Federation	18	13	
Romania	9	7	
United States	16	10	
Ukraine	4	8	
Slovakia	5	2	

End points

End points reporting groups

Reporting group title	Lurasidone 20 mg

Reporting group description:

Lurasidone 20 mg once daily

Reporting group title	Lurasidone 80 mg - 160 mg

Reporting group description:

The subjects who were randomized to lurasidone 80 mg/day at baseline (received lurasidone 80 mg/day or 160 mg/day throughout the study

Reporting group title	Placebo

Reporting group description:

Placebo Comparator once daily

Subject analysis set title	ENR Lurasidone 80 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects who are non-responders on Lurasidone 80 mg/day and rerandomized to Lurasidone 80 mg/day at week 2.

Subject analysis set title	ENR Lurasidone 160 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects who are non-responders on Lurasidone 80 mg/day and rerandomized to Lurasidone 160 mg/day at week 2.

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Randomized to Placebo group at baseline

Primary: Change from baseline in Positive and Negative Syndrome Scale (PANSS) total score at Week 6 for lurasidone 20 mg and 80-160 mg versus placebo.

End point title	Change from baseline in Positive and Negative Syndrome Scale (PANSS) total score at Week 6 for lurasidone 20 mg and 80-160 mg versus placebo.

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 6 Weeks

End point values	Lurasidone 20 mg	Lurasidone 80 mg - 160 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	101	198	112	
Units: units on a scale				
least squares mean (standard error)	-17.6 (± 1.93)	-24.9 (± 1.4)	-14.5 (± 1.89)	

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Lurasidone 20 mg v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.255
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	2.2

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Placebo v Lurasidone 80 mg - 160 mg
Number of subjects included in analysis	310
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.9
upper limit	-5.7

Secondary: Change in Clinical Global Impression-Severity of Illness (CGI-S) score at Week 6 for Lurasidone 20 mg and 80-160 mg Versus Placebo.

End point title	Change in Clinical Global Impression-Severity of Illness (CGI-S) score at Week 6 for Lurasidone 20 mg and 80-160 mg Versus Placebo.

End point description:

The CGI-S is a clinician-rated assessment of the subject's current illness state on a 7-point scale (0-7), where a higher score is associated with greater illness severity. Following a clinical interview, the CGI-S can be completed in 1-2 minutes.

End point type	Secondary

End point timeframe:

Baseline to 6 Weeks

End point values	Lurasidone 20 mg	Lurasidone 80 mg - 160 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	101	198	112	
Units: units on a scale				
least squares mean (standard error)	-0.93 (± 0.105)	-1.3 (± 0.076)	-0.73 (± 0.103)	

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Lurasidone 20 mg v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.169
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.09

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Placebo v Lurasidone 80 mg - 160 mg
Number of subjects included in analysis	310
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.57

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.83
upper limit	-0.32

Secondary: Change from baseline to Week 6 for the lurasidone 20 mg, and lurasidone 80 - 160 mg groups versus the placebo group in the Montgomery-Asberg Depression Rating Scale total score

End point title	Change from baseline to Week 6 for the lurasidone 20 mg, and lurasidone 80 - 160 mg groups versus the placebo group in the 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 6 Weeks

End point values	Lurasidone 20 mg	Lurasidone 80 mg - 160 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	178	108	
Units: units on a scale				
least squares mean (standard error)	-2 (± 0.57)	-3.7 (± 0.41)	-1.7 (± 0.53)	

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Placebo v Lurasidone 20 mg
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.706
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	1.2

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Placebo v Lurasidone 80 mg - 160 mg
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	-0.7

Secondary: Proportion of subjects who achieve a response, defined as 20% or greater improvement from baseline in Positive and Negative Syndrome Score (PANSS) total score at Week 6

End point title	Proportion of subjects who achieve a response, defined as 20% or greater improvement from baseline in Positive and Negative Syndrome Score (PANSS) total score at Week 6

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	Secondary

End point timeframe:

6 Weeks

End point values	Lurasidone 20 mg	Lurasidone 80 mg - 160 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	101	198	112	
Units: percentage of participants				
number (not applicable)	53	72	44	

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Lurasidone 20 mg v Placebo

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.173
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	2.5

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Placebo v Lurasidone 80 mg - 160 mg
Number of subjects included in analysis	310
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	5.2

Secondary: Change from Week 2 to Week 6 for the ENR (early non-responders) lurasidone 160mg group vs the ENR (early non-responders) lurasidone 80 mg group in the following: PANSS total score

End point title	Change from Week 2 to Week 6 for the ENR (early non-responders) lurasidone 160mg group vs the ENR (early non-responders) lurasidone 80 mg group in the following: PANSS total score

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	Secondary

End point timeframe:

week 2 to week 6

End point values	ENR Lurasidone 80 mg	ENR Lurasidone 160 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	52	43		
Units: units on a scale				
least squares mean (standard error)	-8.9 (± 2.2)	-16.6 (± 2.47)		

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	ENR Lurasidone 80 mg v ENR Lurasidone 160 mg
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.3
upper limit	-1.1

Secondary: Change from baseline to Week 6 for the ENR lurasidone 80mg and ENR lurasidone 160mg groups vs the placebo in the MADRS total score

End point title	Change from baseline to Week 6 for the ENR lurasidone 80mg and ENR lurasidone 160mg groups vs the placebo in the MADRS 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 6

End point values	ENR Lurasidone 80 mg	ENR Lurasidone 160 mg	Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	52	42	108	
Units: units on a scale				
least squares mean (standard error)	-2.5 (± 0.89)	-3.5 (± 0.1)	-1.7 (± 0.59)	

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	ENR Lurasidone 80 mg v Placebo
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.464
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	1.3

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Placebo v ENR Lurasidone 160 mg
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.122
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	0.5

Secondary: Change from week 2 to week 6 for ENR Lurasidone 80 mg vs. ENR lurasidone 160 mg in CGI-S score

End point title	Change from week 2 to week 6 for ENR Lurasidone 80 mg vs. ENR lurasidone 160 mg in CGI-S score

End point description:

The CGI-S is a clinician-rated assessment of the subject’s current illness state on a 7-point scale (0-7), where a higher score is associated with greater illness severity. Following a clinical interview, the CGI-S can be completed in 1-2 minutes.

End point type	Secondary

End point timeframe:

week 2 to week 6

End point values	ENR Lurasidone 80 mg	ENR Lurasidone 160 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	52	43		
Units: units on a scale				
least squares mean (standard error)	-0.61 (± 0.116)	-0.96 (± 0.134)		

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	ENR Lurasidone 80 mg v ENR Lurasidone 160 mg
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.052
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0

Secondary: Change from Baseline to Week 6 for the ENR Lurasidone 80mg and ENR Lurasidone 160mg Groups vs the Placebo in the PANSS total Score

End point title	Change from Baseline to Week 6 for the ENR Lurasidone 80mg and ENR Lurasidone 160mg Groups vs the Placebo in the PANSS total Score

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	Secondary

End point timeframe:

Baseline to week 6

End point values	ENR Lurasidone 80 mg	ENR Lurasidone 160 mg	Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	52	43	112	
Units: units on a scale				
least squares mean (standard error)	-14.4 (± 2.69)	-21.7 (± 3)	-14.4 (± 1.98)	

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	ENR Lurasidone 80 mg v Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.992
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	6.6

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	ENR Lurasidone 160 mg v Placebo
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.4
upper limit	-0.2

Secondary: Change from Baseline to Week 6 for the ENR Lurasidone 80mg and ENR Lurasidone 160mg Groups vs the Placebo in the CGI-S Score

End point title	Change from Baseline to Week 6 for the ENR Lurasidone 80mg and ENR Lurasidone 160mg Groups vs the Placebo in the CGI-S Score

End point description:

The CGI-S is a clinician-rated assessment of the subject's current illness state on a 7-point scale, where a higher score is associated with greater illness severity. Following a clinical interview, the CGI-S can be completed in 1-2 minutes.

Reason for the discrepancy of the LS mean (SE) for placebo in outcome 2 and outcome 9 is because the different MMRM model used in outcome 2 and outcome 9. The treatment groups included in the MMRM model for outcome 2 are placebo, lurasidone 20 mg, and lurasidone 80-160 mg. The treatment groups included in the MMRM model for outcome 9 are placebo, ENR lurasidone 80 mg, and ENR lurasidone 160 mg.

End point type	Secondary

End point timeframe:

baseline to week 6

End point values	ENR Lurasidone 80 mg	ENR Lurasidone 160 mg	Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	52	43	112	
Units: units on a scale				
least squares mean (standard error)	-0.83 (± 0.143)	-1.31 (± 0.16)	-0.73 (± 0.106)	

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	ENR Lurasidone 80 mg v Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.578
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	0.25

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	ENR Lurasidone 160 mg v Placebo

Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	-0.2

Other pre-specified: Change from baseline to Week 6 for the lurasidone 20 mg and lurasidone 80 - 160 mg groups compared to the placebo group in the GAF score

End point title	Change from baseline to Week 6 for the lurasidone 20 mg and lurasidone 80 - 160 mg groups compared to the placebo group in the GAF score

End point description:

The GAF is a numeric scale (0 through 100) that measures a patient's overall level of psychological, social, and occupation functioning. It is designed to guide clinicians through a methodical and comprehensive consideration of all aspects of a patient's symptoms and functioning. The scale begins at 100 - superior functioning - to 0 - inadequate information.

End point type	Other pre-specified

End point timeframe:

6 Weeks

End point values	Lurasidone 20 mg	Lurasidone 80 mg - 160 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	101	198	112	
Units: units on a scale				
least squares mean (standard error)	11.5 (± 1.43)	15.8 (± 1.04)	9.2 (± 1.4)	

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Lurasidone 20 mg v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.258
Method	Mixed models analysis
Parameter estimate	Least Square Mean Difference
Point estimate	2.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	6.2

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Placebo v Lurasidone 80 mg - 160 mg
Number of subjects included in analysis	310
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Slope
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.2
upper limit	10.1

Other pre-specified: Change from baseline to Week 6 for the lurasidone 20 mg and lurasidone 80 - 160 mg groups compared to the placebo group in the Euroqol (EQ-5D) Index score

End point title	Change from baseline to Week 6 for the lurasidone 20 mg and lurasidone 80 - 160 mg groups compared to the placebo group in the Euroqol (EQ-5D) Index score

End point description:

The EQ-5D is a standardized measure of health state consisting of two parts: a) EQ-5D measuring mobility, self-care, pain/discomfort, usual activities, and anxiety/depression on a 0 2 scale with lower scores indicating improvement, and b) a 20-cm visual analogue scale (VAS) for health status rating on a 0-100 scale with higher scores indicating improvement. EQ-5D health states, defined by the EQ-5D descriptive system, may be converted into a single summary index (i.e. the EQ-5D index score) by applying a formula that essentially attaches values (also called weights) to each of the levels in each dimension. The EQ-5D Index scores ranged from -0.429 to 1.000. Generally higher observed EQ-5D Index scores indicate a better degree of health.

End point type	Other pre-specified

End point timeframe:

6 weeks

End point values	Lurasidone 20 mg	Lurasidone 80 mg - 160 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	173	103	
Units: units on a scale				
least squares mean (standard error)	0.041 (± 0.024)	0.095 (± 0.018)	-0.042 (± 0.023)	

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Lurasidone 20 mg v Placebo
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	0.084
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.018
upper limit	0.149

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Placebo v Lurasidone 80 mg - 160 mg
Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	0.138
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.081
upper limit	0.194

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
6 Weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups	
Reporting group title	Lurasidone 20 mg
Reporting group description:	
Lurasidone: Lurasidone 20 mg once daily	
Reporting group title	Lurasidone 80-160 mg
Reporting group description:	
Lurasidone 80 mg once daily initially rerandomized either to 80 mg or 160 mg at week 2 (one subject who was randomized was not treated with study drug, therefore, excluded from the safety population).	
Reporting group title	Placebo
Reporting group description:	
Placebo: Once Daily	

Serious adverse events	Lurasidone 20 mg	Lurasidone 80-160 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 101 (2.97%)	6 / 198 (3.03%)	8 / 112 (7.14%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 101 (0.00%)	1 / 198 (0.51%)	0 / 112 (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
Fibula Fracture			
subjects affected / exposed	0 / 101 (0.00%)	1 / 198 (0.51%)	0 / 112 (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
Tibia Fracture			
subjects affected / exposed	0 / 101 (0.00%)	1 / 198 (0.51%)	0 / 112 (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

General disorders and administration site conditions			
Therapuetuc Response Delayed	Additional description: General Disorders and Administration Site conditions		
subjects affected / exposed	0 / 101 (0.00%)	0 / 198 (0.00%)	1 / 112 (0.89%)
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	3 / 101 (2.97%)	3 / 198 (1.52%)	4 / 112 (3.57%)
occurrences causally related to treatment / all	1 / 3	0 / 3	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic Disorder			
subjects affected / exposed	0 / 101 (0.00%)	2 / 198 (1.01%)	3 / 112 (2.68%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 3
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	Lurasidone 20 mg	Lurasidone 80-160 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 101 (42.57%)	92 / 198 (46.46%)	58 / 112 (51.79%)
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 101 (9.90%)	11 / 198 (5.56%)	8 / 112 (7.14%)
occurrences (all)	18	12	12
Somnolence			
subjects affected / exposed	5 / 101 (4.95%)	6 / 198 (3.03%)	6 / 112 (5.36%)
occurrences (all)	5	6	6
Akathisia			
subjects affected / exposed	5 / 101 (4.95%)	21 / 198 (10.61%)	2 / 112 (1.79%)
occurrences (all)	9	24	2
Sedation			
subjects affected / exposed	3 / 101 (2.97%)	6 / 198 (3.03%)	2 / 112 (1.79%)
occurrences (all)	3	6	2
Tremor			

subjects affected / exposed	2 / 101 (1.98%)	6 / 198 (3.03%)	2 / 112 (1.79%)
occurrences (all)	2	6	2
Dizziness			
subjects affected / exposed	1 / 101 (0.99%)	6 / 198 (3.03%)	1 / 112 (0.89%)
occurrences (all)	1	6	1
Parkinsonism			
subjects affected / exposed	1 / 101 (0.99%)	6 / 198 (3.03%)	1 / 112 (0.89%)
occurrences (all)	1	6	1
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	2 / 101 (1.98%)	5 / 198 (2.53%)	4 / 112 (3.57%)
occurrences (all)	2	5	5
Nausea			
subjects affected / exposed	2 / 101 (1.98%)	17 / 198 (8.59%)	4 / 112 (3.57%)
occurrences (all)	2	21	5
Diarrhoea			
subjects affected / exposed	2 / 101 (1.98%)	8 / 198 (4.04%)	3 / 112 (2.68%)
occurrences (all)	2	8	3
Constipation			
subjects affected / exposed	3 / 101 (2.97%)	6 / 198 (3.03%)	2 / 112 (1.79%)
occurrences (all)	4	9	2
Vomiting			
subjects affected / exposed	0 / 101 (0.00%)	11 / 198 (5.56%)	1 / 112 (0.89%)
occurrences (all)	0	12	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	16 / 101 (15.84%)	21 / 198 (10.61%)	24 / 112 (21.43%)
occurrences (all)	22	33	33
Agitation			
subjects affected / exposed	5 / 101 (4.95%)	9 / 198 (4.55%)	11 / 112 (9.82%)
occurrences (all)	5	9	14
Anxiety			
subjects affected / exposed	8 / 101 (7.92%)	8 / 198 (4.04%)	7 / 112 (6.25%)
occurrences (all)	18	9	12
Restlessness			

subjects affected / exposed	0 / 101 (0.00%)	6 / 198 (3.03%)	4 / 112 (3.57%)
occurrences (all)	0	10	9
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 101 (0.99%)	0 / 198 (0.00%)	4 / 112 (3.57%)
occurrences (all)	1	0	4
Back Pain			
subjects affected / exposed	4 / 101 (3.96%)	3 / 198 (1.52%)	1 / 112 (0.89%)
occurrences (all)	4	3	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: