Clinical trial results:
A Prospective Study of the Clinical Outcome Following Treatment Discontinuation After Remission in First-Episode Schizophrenia

Summary

EudraCT number	2015-001221-16
Trial protocol	Outside EU/EEA
Global end of trial date	11 March 2010

Results information

Result version number	v2 (current)
This version publication date	15 July 2016
First version publication date	09 August 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	RISSCH3024

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00378092
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag Medical Affairs EMEA
Sponsor organisation address	Turnhoutseweg 30, B-2340 Beerse, Belgium,
Public contact	Janssen Research and Development, Clinical Registry Group-JB BV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Janssen Research and Development, Clinical Registry Group-JB BV, ClinicalTrialsEU@its.jnj.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 March 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 March 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the time to relapse after discontinuation of RLAI (Risperidone Long Acting Injection) in first- episode subjects successfully treated for 2 years with RLAI. The relapse rate after treatment discontinuation, the time to response after re-exposure to treatment with RLAI and the degree of clinical improvement measured by PANSS were also evaluated.

Protection of trial subjects:

Safety was evaluated based on analysis of adverse events, clinical laboratory tests (hematology, serum chemistry, prolactin), vital sign measurements, electrocardiogram (ECGs), physical examinations, extrapyramidal symptoms (EPS), body weight and body mass index (BMI), and waist/hip circumference.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 April 2006
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	South Africa: 33
Worldwide total number of subjects	33
EEA total number of subjects	0

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)	1
Adults (18-64 years)	32
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 33 subjects entered Period 1 and discontinued their existing antipsychotic treatment. None of the subjects completed the 36-month follow-up period. A total of 31 subjects entered Period 2 and restarted Risperidone Long-Acting Injection (RLAI) treatment. Overall, 14 of the 31 subjects in Period 2 completed the 24 month treatment period.

Pre-assignment

Screening details:

In Period 1, existing RLAI treatment was discontinued. Subjects who experienced a relapse during Period 1 were transferred into Period 2, at which time RLAI and oral risperidone treatment was initiated simultaneously. Risperidone LAI was initiated at a dose of 25 milligram (mg) once every 2 weeks and continued for a maximum of 2 years in Period 2.

Period 1

Period 1 title	Discontinuation
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Risperidone Period 1

Arm description:

In period 1-RLAI was tapered and discontinued over a period of up to 6 weeks.

Arm type	Experimental
Investigational medicinal product name	Risperidone
Investigational medicinal product code	
Other name	Risperidal
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

In period 1-RLAI was tapered and discontinued over a period of up to 6 weeks.

Number of subjects in period 1	Risperidone Period 1
Started	33
Completed	32
Not completed	1
Lost to follow-up	1

Period 2

Period 2 title	After Relapse
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Risperidone Period 2

Arm description:

In period 2-Risperidone RLAI was initiated at a dose of 25 mg once every 2 weeks.

Arm type	Experimental
Investigational medicinal product name	Risperidone
Investigational medicinal product code	
Other name	Risperidal
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

In period 2-Risperidone RLAI was initiated at a dose of 25 mg once every 2 weeks.

Number of subjects in period 2[1]	Risperidone Period 2
Started	31
Completed	14
Not completed	17
Consent withdrawn by subject	2
Adverse event, non-fatal	1
Other	6
Lost to follow-up	5
Lack of efficacy	3

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: Not all the enrolled subjects were treated with study drugs. As baseline only included treated subjects, the worldwide number enrolled in the trial differs with the number of subjects reported in the baseline period

Baseline characteristics

Reporting groups	
Reporting group title	Risperidone Period 1
Reporting group description:	
In period 1-RLAI was tapered and discontinued over a period of up to 6 weeks.	

Reporting group values	Risperidone Period 1	Total	
Number of subjects	33	33	
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	1	1	
Adults (18-64 years)	32	32	
From 65 to 84 years	0	0	
85 years and over	0	0	
Title for AgeContinuous			
Units: years			
arithmetic mean	27.5		
standard deviation	± 7.92	-	
Title for Gender			
Units: subjects			
Female	14	14	
Male	19	19	

End points

End points reporting groups

Reporting group title	Risperidone Period 1
Reporting group description:	
In period 1-RLAI was tapered and discontinued over a period of up to 6 weeks.	
Reporting group title	Risperidone Period 2
Reporting group description:	
In period 2-Risperidone RLAI was initiated at a dose of 25 mg once every 2 weeks.	

Primary: Time to Relapse After Discontinuation of Risperidone Long-Acting Injection (RLAI) in First-Episode Subjects Successfully Treated for 24 Months With RLAI in Previous Study (RIS-PSY-301) (Period 1)

End point title	Time to Relapse After Discontinuation of Risperidone Long-Acting Injection (RLAI) in First-Episode Subjects Successfully Treated for 24 Months With RLAI in Previous Study (RIS-PSY-301) (Period 1)[1]
End point description:	
Relapse was diagnosed if 1 or more of the following occured: a 25 percent increase in Positive and Negative Syndrome Scale (PANSS) total score ranging from 30 (absent) to 210 (extreme ill); Clinical Global Impression (CGI-C) score of 6 ('much worse'); deliberate self-injury; emergence of clinically significant suicidal or homicidal ideation; or violent behavior resulting in significant injury to another person or significant property damage (as per Adverse Event reporting). The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.	
End point type	Primary
End point timeframe:	
Month 36 or early withdrawal (EW)	

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: No statistical analysis were performed for this endpoint

End point values	Risperidone Period 1			
Subject group type	Reporting group			
Number of subjects analysed	32[2]			
Units: units on a scale				
median (full range (min-max))	154 (34 to 880)			

Notes:

[2] - Here 'N' signifies number of subjects analysed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects who Relapsed After Discontinuation of RLAI (Period 1)

End point title	Percentage of Subjects who Relapsed After Discontinuation of RLAI (Period 1)[3]
End point description:	
Relapse was diagnosed if 1 or more of the following occured: a 25 percent increase in PANSS total score	

ranging from 30 (absent) to 210 (extreme ill); CGI-C score of 6 ('much worse'); deliberate self-injury; emergence of clinically significant suicidal or homicidal ideation; or violent behavior resulting in significant injury to another person or significant property damage (as per Adverse Event reporting). The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Primary

End point timeframe:

Month 36 or EW

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: No statistical analysis were performed for this endpoint

End point values	Risperidone Period 1			
Subject group type	Reporting group			
Number of subjects analysed	32[4]			
Units: percentage of subjects				
number (not applicable)	97			

Notes:

[4] - Here 'N' signifies number of subjects analysed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Total Score After Re-Initiation of RLAI, at Month 24 or Early Withdrawal (EW)

End point title	Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Total Score After Re-Initiation of RLAI, at Month 24 or Early Withdrawal (EW)[5]

End point description:

The PANSS is a medical scale that assesses various symptoms of schizophrenia and provides a total score (sum of the scores of all 30 items) and scores for 3 subscales: positive subscale (7 items), negative subscale (7 items), and general psychopathology subscale (16 items), each rated on a scale of 1 (absent) to 7 (extreme). The total score is the sum of all 30 PANSS items, with a range of 30 (absent) to 210 (extreme ill). Higher scores indicate worsening. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Primary

End point timeframe:

Baseline and Month 24 or EW

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis were performed for this endpoint

End point values	Risperidone Period 2			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=31) Month 24 (n=30)	86.5 (± 14.4) -27.7 (± 20.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to Treatment Response After Re-Initiation of RLAI (Period 2)

End point title	Time to Treatment Response After Re-Initiation of RLAI (Period 2)[6]

End point description:

Time to treatment response after re-initiation of RLAI was the time that elapse between baseline assessment of PANSS for Period 2 and fulfillment of the response which is defined as greater than or equal to 20 percent improvement in PANSS total score. PANSS is a medical scale that assesses various symptoms of schizophrenia and provides a total score (sum of the scores of all 30 items) with a range of 30 (absent) to 210 (extreme ill). Higher scores indicate worsening. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Primary

End point timeframe:

Month 24 or EW

Notes:

[6] - 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: No statistical analysis were performed for this endpoint

End point values	Risperidone Period 2			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: days				
median (confidence interval 95%)				
Time to 20% Response	39 (27 to 43)			
Time to 30% Response	41 (29 to 44)			
Time to 40% Response	43 (41 to 56)			
Time to 50% Response	83 (44 to 112)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PANSS Total Score and Subscales of PANSS at Month 36 or Early Withdrawal (EW) (Period 1)

End point title	Change From Baseline in PANSS Total Score and Subscales of PANSS at Month 36 or Early Withdrawal (EW) (Period 1)

End point description:

The PANSS is a medical scale that assesses various symptoms of schizophrenia and provides a total score (sum of the scores of all 30 items) and scores for 3 subscales: positive subscale (7 items), negative subscale (7 items), and general psychopathology (GP) subscale (16 items), each rated on a scale of 1 (absent) to 7 (extreme). The total score is the sum of all 30 PANSS items, with a range of 30 (absent) to 210 (extreme ill). Higher scores indicate worsening. The efficacy analysis set included all

subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 36 or EW

End point values	Risperidone Period 1			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Positive subscale	7.3 (± 1.2)			
Change at Month 36: Positive subscale	13.4 (± 5.4)			
Baseline: Negative subscale	16.1 (± 4.7)			
Change at Month 36: Negative subscale	8.2 (± 6)			
Baseline: GP subscale	21.4 (± 3.4)			
Change at Month 36: GP subscale	20.2 (± 8.6)			
Baseline: Total score	44.8 (± 7.4)			
Change at Month 36: Total score	41.8 (± 15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PANSS Total Score and Subscales of PANSS at Month 24 or Early Wihdrawal (EW) (Period 2)

End point title	Change From Baseline in PANSS Total Score and Subscales of PANSS at Month 24 or Early Wihdrawal (EW) (Period 2)

End point description:

The PANSS is a medical scale that assesses various symptoms of schizophrenia and provides a total score (sum of the scores of all 30 items) and scores for 3 subscales: positive subscale (7 items), negative subscale (7 items), and general psychopathology (GP) subscale (16 items), each rated on a scale of 1 (absent) to 7 (extreme). The total score is the sum of all 30 PANSS items, with a range of 30 (absent) to 210 (extreme ill). Higher scores indicate worsening. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 24 or EW

End point values	Risperidone Period 2			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Positive subscale (n=31)	20.6 (± 3.9)			

Change at Month 24: Positive subscale (n=30)	-8.8 (± 7.1)			
Baseline: Negative subscale (n=31)	23.9 (± 6.3)			
Change at Month 24: Negative subscale (n=30)	-4.7 (± 4.9)			
Baseline: GP subscale (n=31)	41.9 (± 8)			
Change at Month 24: GP subscale (n=30)	-14.2 (± 10.8)			
Baseline: Total score (n=31)	86.5 (± 14.4)			
Change at Month 24: Total score (n=30)	-50.8 (± 35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Marder PANSS Subscales Score at Month 36 or Early Withdrawal (EW) (Period 1)

End point title	Change From Baseline in Marder PANSS Subscales Score at Month 36 or Early Withdrawal (EW) (Period 1)

End point description:

The PANSS total score consists of the sum of all 30 PANSS items and score ranges from 30 to 210. Higher scores indicate worsening. The symptoms are rated on a 7-point Marder scale from 1 (absent) to 7 (extreme psychopathology). Positive symptoms subscale consists of 8 items with total score range of 856; negative symptoms subscale and disorganized thoughts subscale, each consists of 7 items with total score range of 7-49, uncontrolled hostility (UH) or excitement subscale and anxiety/depression subscale, each consists of 4 items with total score range of 4-28. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 36 or EW

End point values	Risperidone Period 1			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Positive symptoms factor	11.6 (± 2.4)			
Change at Month 24:Positive symptoms factor	15.5 (± 5.2)			
Baseline: Negative symptoms factor	13.2 (± 4.6)			
Change at Month 24: Negative symptoms factor	7.5 (± 6.9)			
Baseline: Disorganised thoughts	11.8 (± 2)			
Change at Month 24: Disorganised thoughts	9.9 (± 4)			
Baseline: Uncontrolled hostility	4.1 (± 0.2)			
Change at Month 24: Uncontrolled hostility	4.5 (± 4.3)			
Baseline: Anxiety/depression	4.1 (± 0.7)			

Change at Month 24: Anxiety/depression	4.4 (± 3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Marder PANSS Subscales Score at Month 24 or Early Withdrawal (EW) (Period 2)

End point title	Change From Baseline in Marder PANSS Subscales Score at Month 24 or Early Withdrawal (EW) (Period 2)

End point description:

The PANSS is a 30-item scale to assess the neuropsychiatric symptoms of schizophrenia. The symptoms are rated on a 7-point Marder scale from 1 (absent) to 7 (extreme psychopathology). Positive symptoms subscale consists of 8 items with total score range of 8-56; negative symptoms subscale and disorganized thoughts subscale, each consists of 7 items with total score range of 7-49, UH or excitement subscale and anxiety or depression subscale, each consists of 4 items with total score range of 4-28. Higher score indicates greater severity. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 24 or EW

End point values	Risperidone Period 2			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Positive symptoms factor (n=31)	27.2 (± 4.4)			
Change at Month 24: Positive symptoms factor(n=30)	-9.8 (± 7.8)			
Baseline: Negative symptoms factor (n=31)	20.6 (± 7.1)			
Change at Month 24:Negative Symptoms factor (n=30)	-5.8 (± 5.5)			
Baseline: Disorganised Thoughts (n=31)	21.7 (± 4.2)			
Change at Month 24: Disorganised Thoughts (n=30)	-5.7 (± 5.9)			
Baseline: Uncontrolled Hostility (n=31)	8.2 (± 3.6)			
Change at Month 24: Uncontrolled Hostility (n=30)	-2.5 (± 5.2)			
Baseline: Anxiety/Depression (n=31)	8.7 (± 2.9)			
Change at Month 24: Anxiety/Depression (n=30)	-3.9 (± 3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Disease Remission Based on PANSS (Period 1)

End point title	Number of Subjects With Disease Remission Based on PANSS (Period 1)

End point description:

A subject was 'in remission' when he/she was symptomatically stable and showed progressive improvement in total recovery according to severity (mild or less simultaneously on 8 PANSS items:P1 delusions, P2 conceptual disorganization, P3 hallucinatory behavior, G9 unusual thought content, G5 mannerisms and posturing, N1 blunted affect, N4 social withdrawal, N6 lack of spontaneity or flow of conversation) and time (scores for 8 PANSS items above did not exceed the severity criterion mild at any time point of assessment for at least 6 months to meet the criteria of remission) criteria. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Month 36 or EW

End point values	Risperidone Period 1			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: subjects				
Baseline	28			
Month 36	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Disease Remission Based on PANSS (Period 2)

End point title	Number of Subjects With Disease Remission Based on PANSS (Period 2)

End point description:

A subject was 'in remission' when he/she was symptomatically stable and showed progressive improvement in total recovery according to severity (mild or less simultaneously on 8 PANSS items:P1 delusions, P2 conceptual disorganization, P3 hallucinatory behavior, G9 unusual thought content, G5 mannerisms and posturing, N1 blunted affect, N4 social withdrawal, N6 lack of spontaneity or flow of conversation) and time (scores for 8 PANSS items above did not exceed the severity criterion mild at any time point of assessment for at least 6 months to meet the criteria of remission) criteria. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment. Disease Remission Based on PANSS was not seen till the end of period 2 (Month 24).

End point type	Secondary

End point timeframe:

Early Withdrawal (Period 2)

End point values	Risperidone Period 2			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: subjects	14			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Global Impression of Severity (CGI-S) Score at Month 36 or Early Withdrawal (EW) (Period 1)

End point title	Change From Baseline in Clinical Global Impression of Severity (CGI-S) Score at Month 36 or Early Withdrawal (EW) (Period 1)

End point description:

The CGI-S scale is a 7-point global assessment that measures the Clinician's impression of the severity of illness exhibited by a subject. A rating of '1=Normal, not at all ill' and a rating of '7=Among the most extremely ill subjects'. Higher scores indicate worsening. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 36 or EW

End point values	Risperidone Period 1			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=33)	1.3 (± 0.6)			
Change at Month 36 (n=33)	2.7 (± 1.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Global Impression of Severity (CGI-S) Score at Month 24 or Early Withdrawal (EW) (Period 2)

End point title	Change From Baseline in Clinical Global Impression of Severity (CGI-S) Score at Month 24 or Early Withdrawal (EW) (Period 2)

End point description:

The CGI-S scale is a 7-point global assessment that measures the Clinician's impression of the severity of illness exhibited by a subject. A rating of '1=Normal, not at all ill' and a rating of '7=Among the most extremely ill subjects'. Higher scores indicate worsening. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 24 or EW

End point values	Risperidone Period 2			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=31)	4 (± 0.7)			
Change at Month 24 (n=30)	-1.9 (± 1.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Calgary Depression Scale Score for Schizophrenia (CDSS) at Month 36 or Early Withdrawal (EW) (Period 1)

End point title	Change From Baseline in Calgary Depression Scale Score for Schizophrenia (CDSS) at Month 36 or Early Withdrawal (EW) (Period 1)

End point description:

The CDSS assesses the level of depression in subjects with schizophrenia. It consists of 9 items: depression, hopelessness, self-depreciation, pathological guilt, guilty ideas of reference, morning depression, early awakening, suicidal, observed depression, each scored on a 4-point scale (0=absent, 1=mild, 2=moderate, 3=severe). The total score is a sum of the scores of each item and may range from 0 to 27. Higher score indicates more severe pathology. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 36 or EW

End point values	Risperidone Period 1			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=33)	0.4 (± 1.9)			
Change at Month 36 (n=33)	1.8 (± 3.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Calgary Depression Scale Score for Schizophrenia (CDSS) at Month 24 or Early Withdrawal (EW) (Period 2)

End point title	Change From Baseline in Calgary Depression Scale Score for Schizophrenia (CDSS) at Month 24 or Early Withdrawal (EW) (Period 2)

End point description:

The CDSS assesses the level of depression in subjects with schizophrenia. It consists of 9 items: depression, hopelessness, self depreciation, pathological guilt, guilty ideas of reference, morning depression, early awakening, suicidal, observed depression, each scored on a 4-point scale (0=absent, 1=mild, 2=moderate, 3=severe). The total score is a sum of the scores of each item and may range from 0 to 27. Higher score indicates more severe pathology. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 24 or EW

End point values	Risperidone Period 2			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=31)	2.4 (± 3.2)			
Change at Month 24 (n=30)	-2.2 (± 3.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Social and Occupational Functioning Assessment Scale (SOFAS) Score at Month 36 or Early Withdrawal (EW) (Period 1)

End point title	Change From Baseline in Social and Occupational Functioning Assessment Scale (SOFAS) Score at Month 36 or Early Withdrawal (EW) (Period 1)

End point description:

The SOFAS is a 100-point single item scale that assesses level of social and occupational functioning of a subject and is not directly influenced by the overall severity of the individual's psychological symptoms. The scale values range from 1=most impaired to100=healthiest individual. The scale also included a rating point of 0=missing information. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 36 or EW

End point values	Risperidone Period 1			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=33)	66.4 (± 4.7)			
Change at Month 36 or EW (n=33)	-25 (± 10.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Social and Occupational Functioning Assessment Scale (SOFAS) Score at Month 24 or Early Withdrawal (EW) (Period 2)

End point title	Change From Baseline in Social and Occupational Functioning Assessment Scale (SOFAS) Score at Month 24 or Early Withdrawal (EW) (Period 2)

End point description:

The SOFAS is a 100-point single item scale that assesses level of social and occupational functioning of a subject and is not directly influenced by the overall severity of the individual's psychological symptoms. The scale values range from 1=most impaired to 100=healthiest individual. The scale also included a rating point of 0=missing information. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 24 or EW

End point values	Risperidone Period 2			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=31)	41.5 (± 8)			
Change at Month 24 (n=30)	14.7 (± 14.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline (n=33)Change From Baseline in Patient Global Impression-Severity (PGI-S) Score at Month 36 or Early Withdrawal (EW) (Period 1)

End point title	Baseline (n=33)Change From Baseline in Patient Global Impression-Severity (PGI-S) Score at Month 36 or Early Withdrawal (EW) (Period 1)

End point description:

The PGI-S is an 11-point (0=very well to 10=very poor) scale that requires the subjects to rate the severity of their illness at the time of assessment, relative to the subject's past experience. The response options are: very much improved; much improved; improved (just enough to make a difference); no change; worse (just enough to make a difference); much worse; or very much worse. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 36 or EW

End point values	Risperidone Period 1			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=33)	1.2 (± 0.5)			
Change at Month 36 or EW (n=33)	1.3 (± 1.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression-Change (PGI-C) Score at Month 36 or Early Withdrawal (EW) (Period 1)

End point title	Patient Global Impression-Change (PGI-C) Score at Month 36 or Early Withdrawal (EW) (Period 1)

End point description:

The PGI-C is a 7-point scale that requires the subjects to assess how much their illness has improved or worsened relative to a baseline state at the beginning of the intervention. The response options are: very much improved; much improved; improved (just enough to make a difference); no change; worse (just enough to make a difference); much worse; or very much worse. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Month 36 or EW

End point values	Risperidone Period 1			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=33)	1.2 (± 0.5)			
Change at Month 36 or EW (n=32)	1.3 (± 1.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient Global Impression-Severity (PGI-S) Score at Month 24 or Early Withdrawal (EW) (Period 2)

End point title	Change From Baseline in Patient Global Impression-Severity (PGI-S) Score at Month 24 or Early Withdrawal (EW) (Period 2)

End point description:

The PGI-S is an 11-point (0=very well to 10=very poor) scale that requires the subjects to rate the severity of their illness at the time of assessment, relative to the subject's past experience. The response options are: very much improved; much improved; improved (just enough to make a difference); no change; worse (just enough to make a difference); much worse; or very much worse. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 24 or EW

End point values	Risperidone Period 2			
Subject group type	Reporting group			
Number of subjects analysed	30[7]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=30)	2.7 (± 1.3)			
Change at Month 24 (n=29)	-1 (± 1.8)			

Notes:

[7] - Here 'N' signifies number of subjects analysed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression-Change (PGI-C) Score at Month 24 or Early Withdrawal (EW) (Period 2)

End point title	Patient Global Impression-Change (PGI-C) Score at Month 24 or Early Withdrawal (EW) (Period 2)

End point description:

The PGI-C is a 7-point scale that requires the subjects to assess how much their illness has improved or worsened relative to a baseline state at the beginning of the intervention. The response options are: very much improved; much improved; improved (just enough to make a difference); no change; worse (just enough to make a difference); much worse; or very much worse. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Month 24 or EW

End point values	Risperidone Period 2			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=31)	2.7 (± 1.3)			
Month 24 (n=30)	2.6 (± 1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 12-Item Short-Form (SF-12) Score -Quality of Life Survey at Month 36 or Early Withdrawal (EW) (Period 1)

End point title	Change From Baseline in 12-Item Short-Form (SF-12) Score - Quality of Life Survey at Month 36 or Early Withdrawal (EW) (Period 1)

End point description:

The SF-12 is a validated 12 question quality-of-life questionnaire. The SF-12 extracts 12 items from the SF-36 questionnaire in 2 six-item subscales: physical component summary (PCS) and MCS (mental component summary). The SF-12 score ranges from 10=maximum impairment to 70=no impairment. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 36 or EW

End point values	Risperidone Period 1			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: units on a scale				
arithmetic mean (standard deviation)				
Physical component, Baseline (n=33)	52 (± 6.2)			
Physical Component: change at M 36 or EW (N=32)	-6.1 (± 10.7)			
Mental Component, Baseline (n=33)	48.3 (± 10.8)			
Mental Component: change at M 36 or EW (n=32)	-7.2 (± 12.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 12-Item Short-Form (SF-12) Score - Quality of Life Survey at Month 24 or Early Withdrawal (EW) (Period 2)

End point title	Change From Baseline in 12-Item Short-Form (SF-12) Score - Quality of Life Survey at Month 24 or Early Withdrawal (EW) (Period 2)

End point description:

The SF-12 is a validated 12 question quality-of-life questionnaire. The SF-12 extracts 12 items from the SF-36 questionnaire in 2 six-item subscales: physical component summary (PCS) and MCS (mental component summary). The SF-12 scores range from 10=maximum impairment to 70=no impairment. The efficacy analysis set included all subjects from the ITT analysis set who had at least one follow-up efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline and Month 24 or EW

End point values	Risperidone Period 2			
Subject group type	Reporting group			
Number of subjects analysed	30[8]			
Units: units on a scale				
arithmetic mean (standard deviation)				
Physical Component, Baseline (n=30)	45.1 (± 9.8)			
Physical Component, Change at M24 (n=29)	2.6 (± 12.3)			
Mental Component, Baseline (n=30)	40.8 (± 10.7)			
Mental Component, Change at M 24 (n=29)	5.8 (± 12.1)			

Notes:

[8] - Here 'N' signifies number of subjects analysed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to Month 36 (Period 1) or Month 24 (Period 24)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups	
Reporting group title	Risperidone PERIOD 2
Reporting group description:	
In period 2-Risperidone RLAI was initiated at a dose of 25 mg once every 2 weeks.	
Reporting group title	Risperidone PERIOD 1
Reporting group description:	
In period 1-RLAI was tapered and discontinued over a period of up to 6 weeks.	

Serious adverse events	Risperidone PERIOD 2	Risperidone PERIOD 1	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 31 (29.03%)	5 / 33 (15.15%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Road Traffic Accident			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicidal Ideation			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic Disorder			
subjects affected / exposed	6 / 31 (19.35%)	5 / 33 (15.15%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Diabetes Mellitus			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Risperidone PERIOD 2	Risperidone PERIOD 1	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 31 (70.97%)	33 / 33 (100.00%)	
Investigations			
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Blood Cholesterol Increased			
subjects affected / exposed	0 / 31 (0.00%)	4 / 33 (12.12%)	
occurrences (all)	0	4	
Blood Glucose Increased			
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Blood Prolactin Increased			
subjects affected / exposed	6 / 31 (19.35%)	2 / 33 (6.06%)	
occurrences (all)	6	2	
Weight Increased			
subjects affected / exposed	8 / 31 (25.81%)	0 / 33 (0.00%)	
occurrences (all)	8	0	
Blood Triglycerides Increased			
subjects affected / exposed	3 / 31 (9.68%)	1 / 33 (3.03%)	
occurrences (all)	3	1	
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Weight Decreased			
subjects affected / exposed	2 / 31 (6.45%)	6 / 33 (18.18%)	
occurrences (all)	2	6	

Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 31 (16.13%)	2 / 33 (6.06%)	
occurrences (all)	5	2	
Parkinsonism			
subjects affected / exposed	3 / 31 (9.68%)	0 / 33 (0.00%)	
occurrences (all)	3	0	
Sedation			
subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)	
occurrences (all)	3	0	
Tremor			
subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 31 (12.90%)	0 / 33 (0.00%)	
occurrences (all)	4	0	
Nausea			
subjects affected / exposed	4 / 31 (12.90%)	1 / 33 (3.03%)	
occurrences (all)	5	1	
Toothache			
subjects affected / exposed	3 / 31 (9.68%)	1 / 33 (3.03%)	
occurrences (all)	4	1	
Vomiting			
subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)	
occurrences (all)	3	0	
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Psychiatric disorders			

Depression			
subjects affected / exposed	3 / 31 (9.68%)	1 / 33 (3.03%)	
occurrences (all)	5	1	
Anxiety			
subjects affected / exposed	2 / 31 (6.45%)	1 / 33 (3.03%)	
occurrences (all)	2	1	
Insomnia			
subjects affected / exposed	6 / 31 (19.35%)	7 / 33 (21.21%)	
occurrences (all)	13	9	
Psychotic Disorder			
subjects affected / exposed	8 / 31 (25.81%)	29 / 33 (87.88%)	
occurrences (all)	13	29	
Restlessness			
subjects affected / exposed	7 / 31 (22.58%)	8 / 33 (24.24%)	
occurrences (all)	8	8	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal Stiffness			
subjects affected / exposed	3 / 31 (9.68%)	0 / 33 (0.00%)	
occurrences (all)	4	0	
Infections and infestations			
Influenza			
subjects affected / exposed	4 / 31 (12.90%)	0 / 33 (0.00%)	
occurrences (all)	5	0	
Nasopharyngitis			
subjects affected / exposed	3 / 31 (9.68%)	0 / 33 (0.00%)	
occurrences (all)	5	0	

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