Clinical trial results:
A 52-Week, Open-Label, Prospective, Multicenter, International Study of a Transition to the Paliperidone Palmitate 3-Month Formulation in Patients with Schizophrenia Previously Stabilized on the Paliperidone Palmitate 1-Month Formulation

Summary

EudraCT number	2015-004835-10
Trial protocol	GB NL DE ES DK GR HR IT
Global end of trial date	26 March 2018

Results information

Result version number	v1 (current)
This version publication date	06 April 2019
First version publication date	06 April 2019

Trial information

Trial identification

Sponsor protocol code	R092670SCH3015

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02713282
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International NV
Sponsor organisation address	Turnhoutseweg 30, B-2340, Beerse, Belgium, 2170
Public contact	Clinical Registry group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry group, Janssen-Cilag International NV, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 March 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to estimate the proportion of subjects who fulfilled the criteria for symptomatic remission (defined as a score of mild or less [ie, less than or equal to (=<) 3] on all selected PANSS items (P1, P2, P3, N1, N4, N6, G5, and G9) maintained for at least 6 months) following a transition to 12 months' treatment with flexible-dose paliperidone palmitate 3-month formulation (PP3M) in subjects with schizophrenia previously adequately treated with PP1M for at least 4 months.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practices and applicable regulatory requirements. The safety assessments included adverse events (AEs), Extrapyramidal Symptom Rating Scale (ESRS), Urine pregnancy test, body weight, and height; body mass index (BMI), vital sign measurements including blood pressure and heart rate measurements and physical examinations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 May 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Croatia: 8
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	France: 21
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Greece: 22
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Korea, Republic of: 33
Country: Number of subjects enrolled	Malaysia: 21
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Russian Federation: 50
Country: Number of subjects enrolled	Saudi Arabia: 8
Country: Number of subjects enrolled	Spain: 44
Country: Number of subjects enrolled	Taiwan: 17
Country: Number of subjects enrolled	Turkey: 24
Country: Number of subjects enrolled	United Kingdom: 3

Worldwide total number of subjects	305
EEA total number of subjects	148

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)	305
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 312 subjects screened for the study, 305 were enrolled and treated. A total of 291 (95.4%) subjects completed the study.

Period 1

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

Arms

Arm title	Total (PP3M Treatment)

Arm description:

Subjects received intramuscular (IM) injection of Paliperidone Palmitate 3-Month Formulation (PP3M) on Day 1 at a starting dose of 175 milligram equivalent (mg eq) up to 525 mg eq. based on last Paliperidone Palmitate 1-Month Formulation (PP1M) dose (at a dose of 3.5-fold multiple of the subject's last PP1M dose). Subsequent PP3M injections were given at Month 3, Month 6, and Month 9 and dose adjustment of PP3M could have been made every 3 months in increments within the range of 175 to 525 mg eq. The last dose of PP3M was administered on Day 270.

Arm type	Experimental
Investigational medicinal product name	PP3M
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received intramuscular (IM) injection of Paliperidone Palmitate 3-Month Formulation (PP3M) on Day 1 at a starting dose of 175-milligram equivalent (mg eq) up to 525 mg eq. based on last Paliperidone Palmitate 1-Month Formulation (PP1M) dose (at a dose of a 3.5-fold multiple of the subject's last PP1M dose). Subsequent PP3M injections were given at Month 3, Month 6, and Month 9 and dose can be adjusted flexibly in increments within the range of 175 to 525 mg eq.

Number of subjects in period 1	Total (PP3M Treatment)
Started	305
Safety	303
Completed	291
Not completed	14
Consent withdrawn by subject	8
Adverse event, non-fatal	2
Adverse event serious non-fatal	2
Lack of efficacy	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Total (PP3M Treatment)

Reporting group description:

Subjects received intramuscular (IM) injection of Paliperidone Palmitate 3-Month Formulation (PP3M) on Day 1 at a starting dose of 175 milligram equivalent (mg eq) up to 525 mg eq. based on last Paliperidone Palmitate 1-Month Formulation (PP1M) dose (at a dose of 3.5-fold multiple of the subject's last PP1M dose). Subsequent PP3M injections were given at Month 3, Month 6, and Month 9 and dose adjustment of PP3M could have been made every 3 months in increments within the range of 175 to 525 mg eq. The last dose of PP3M was administered on Day 270.

Reporting group values	Total (PP3M Treatment)	Total	
Number of subjects	305	305	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	305	305	
From 65 to 84 years	0	0	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	36.5		
standard deviation	± 7.97	-	
Title for Gender Units: subjects			
Female	105	105	
Male	200	200	

End points

End points reporting groups

Reporting group title	Total (PP3M Treatment)

Reporting group description:

Subjects received intramuscular (IM) injection of Paliperidone Palmitate 3-Month Formulation (PP3M) on Day 1 at a starting dose of 175 milligram equivalent (mg eq) up to 525 mg eq. based on last Paliperidone Palmitate 1-Month Formulation (PP1M) dose (at a dose of 3.5-fold multiple of the subject's last PP1M dose). Subsequent PP3M injections were given at Month 3, Month 6, and Month 9 and dose adjustment of PP3M could have been made every 3 months in increments within the range of 175 to 525 mg eq. The last dose of PP3M was administered on Day 270.

Primary: Percentage of Subjects with Symptomatic Remission (SR) Based on Positive and Negative Syndrome Scale (PANSS) at LOCF Endpoint

End point title	Percentage of Subjects with Symptomatic Remission (SR) Based on Positive and Negative Syndrome Scale (PANSS) at LOCF Endpoint[1]

End point description:

PANSS: 30-item scale to assess neuropsychiatric symptoms of schizophrenia (psychiatric disorder with symptoms of emotional instability, detachment from reality, often delusions and hallucinations,withdrawal into the self). PANSS provides total score sum scores of 30 items, scores for 3 subscales, positive-7, negative-7, general psychopathology-16 items, each item scored on scale of 1-absent,2-minimal,3-mild,4-moderate,5-moderately severe, 6-severe,7-extreme: score ranges from 30 to 210; higher score indicates greater severity. SR: defined as having a score of mild or less (ie, <=3) on all selected PANSS items (P1, P2, P3, N1, N4, N6, G5, and G9) maintained for at least 6 months +/- 14 days. mITT efficacy analysis set consists of all subjects from the mITT analysis set (subjects who provide their written consent and receive at least 1 dose of study drug (PP3M) during the treatment phase) who had at least 1 post-baseline efficacy assessment.

End point type	Primary

End point timeframe:

LOCF Endpoint (Month 12 or early discontinuation)

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	303			
Units: Percentage of subjects				
number (confidence interval 95%)	56.77 (50.98 to 62.42)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Symptomatic Remission Based on PANSS at Month 6, 9 and Month 12

End point title	Percentage of Subjects with Symptomatic Remission Based on PANSS at Month 6, 9 and Month 12

End point description:

PANSS: 30-item scale to assess neuropsychiatric symptoms of schizophrenia (psychiatric disorder with symptoms of emotional instability, detachment from reality, often delusions and hallucinations, withdrawal into the self). PANSS provides total score sum scores of 30 items, scores for 3 subscales, positive-7, negative-7, general psychopathology-16 items, each item scored on scale of 1-absent,2-minimal,3-mild,4-moderate,5-moderately severe, 6-severe,7-extreme: score ranges from 30 to 210; higher score indicates greater severity. Symptomatic Remission defined as having a score of mild or less (ie, <=3) on all selected PANSS items (P1, P2, P3, N1, N4, N6, G5, and G9) maintained for at least 6 months +/-14 days. mITT efficacy analysis set included. 'n' signifies a number of subjects analyzed at the specified time point.

End point type	Secondary

End point timeframe:

Month 6, Month 9, and Month 12

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	303			
Units: Percentage of Subjects				
number (confidence interval 95%)				
Month-6 (n=297)	49.83 (44.00 to 55.66)			
Month-9 (n=293)	55.66 (50.77 to 62.41)			
Month-12 (n=289)	59.17 (53.26 to 64.89)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to Symptomatic Remission

End point title	Median Time to Symptomatic Remission

End point description:

Symptomatic remission is defined as having a score of mild or less (ie, <=3) on all selected PANSS items (P1, P2, P3, N1, N4, N6, G5, and G9) maintained for at least 6 months +/-14 days. The time to symptomatic remission was based on Kaplan-Meier product limit estimates using the date of the first PP3M injection as a starting point. mITT efficacy analysis set consists of all subjects from the mITT analysis set who had at least 1 post-baseline efficacy assessment and with data on Symptomatic Remission.

End point type	Secondary

End point timeframe:

Up to Month 12

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Days				
median (confidence interval 95%)	247.00 (189.00 to 275.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who met the Remission Severity Criterion

End point title	Percentage of Subjects who met the Remission Severity Criterion

End point description:

Percentage of subjects who met remission severity criterion (i.e., a score of mild or less (=<3) on all selected PANSS items [P1, P2, P3, N1, N4, N6, G5, and G9]) at each specified time point (Baseline, Month 3, 6, 9 and Month 12) was evaluated. mITT efficacy analysis set consists of all subjects from the mITT analysis set (subjects who provide their written consent and receive at least 1 dose of study drug (PP3M) during the treatment phase) who had at least 1 post-baseline efficacy assessment. The population included all the subjects who reached symptomatic remission at LOCF endpoint.

End point type	Secondary

End point timeframe:

Baseline, Month 3, Month 6, Month 9 and Month 12

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	172			
Units: Percentage of subjects				
number (not applicable)	46.86			

Statistical analyses

No statistical analyses for this end point

Secondary: Non-Inferiority of Change in PANSS Total Score From Baseline to LOCF Endpoint (Maintained Efficacy)

End point title	Non-Inferiority of Change in PANSS Total Score From Baseline to LOCF Endpoint (Maintained Efficacy)

End point description:

Maintained efficacy was defined as a non-inferior change in PANSS total score from baseline to endpoint, with the non-inferiority margin set to 5 points, based on Schuirmann’s test. mITT efficacy analysis was defined as all subjects from the mITT analysis set who had at least 1 post-baseline efficacy assessment with both baseline and at least one post-baseline assessments.

End point type	Secondary

End point timeframe:

Baseline, LOCF Endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Score on a scale				
arithmetic mean (confidence interval 90%)	-3.0762 (-3.9402 to -2.2121)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with PANSS Response

End point title	Percentage of Subjects with PANSS Response

End point description:

PANSS response, defined as an improvement in PANSS total score of greater than or equal to (>=) 20% from baseline to LOCF endpoint. 30-item PANSS scale (each item rated 1 (absent) to 7 (extreme), used to assess neuropsychiatric symptoms of schizophrenia that provided a total score (sum of the scores of all 30 items) and scores for 3 subscales, the positive subscale (7 items), the negative subscale (7 items), and the general psychopathology subscale (16 items). The PANSS total score ranges from 30 to 210. PANSS subscale scores range from 7 to 49 for the positive and negative subscales and from 16 to 112 for the general subscale. Higher PANSS scores indicate higher symptom severity. mITT efficacy analysis set consists of all subjects from the mITT analysis set (subjects who provide their written consent and receive at least 1 dose of study drug (PP3M) during the treatment phase) who had at least 1 post-baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline up to LOCF endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Percentage of Subjects				
number (not applicable)	16.23			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PANSS Total Score at LOCF Endpoint

End point title	Change From Baseline in PANSS Total Score at LOCF Endpoint

End point description:

PANSS: 30-item scale to assess neuropsychiatric symptoms of schizophrenia (psychiatric disorder with symptoms of emotional instability,detachment from reality,often delusions and hallucinations,withdrawal into the self). PANSS provides total score sum scores of 30 items, scores for 3 subscales, positive-7, negative-7 and general psychopathology-16 items, each item scored on scale of 1-absent,2- minimal,3-mild,4-moderate,5-moderately severe,6-severe,7-extreme; ranges from 30-210; higher score indicates greater severity. mITT efficacy analysis: all subjects from the mITT analysis set who had at least 1 post-baseline efficacy assessment with both baseline and at least one post-baseline assessments.

End point type	Secondary

End point timeframe:

Baseline, LOCF Endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	303			
Units: Score on a scale				
arithmetic mean (standard deviation)	-3.07 (± 9.103)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PANSS Subscales at LOCF Endpoint

End point title	Change From Baseline in PANSS Subscales at LOCF Endpoint

End point description:

PANSS: 30-item scale to assess neuropsychiatric symptoms of schizophrenia (psychiatric disorder with symptoms of emotional instability, detachment from reality, often delusions and hallucinations, withdrawal into the self). PANSS provides total score sum scores of 30 items, scores for 3 subscales, positive-7, negative-7, general psychopathology-16 items, each item scored on scale of 1-absent,2-minimal,3-mild,4-moderate,5-moderately severe, 6-severe,7-extreme: score ranges from 30 to 210; higher score indicates greater severity. The mITT analysis set consists of all subjects who provided their written consent and received at least 1 dose of study drug (PP3M) during the treatment phase with both baseline and at least one post-baseline assessments.

End point type	Secondary

End point timeframe:

Baseline, LOCF endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Score on a scale				
arithmetic mean (standard deviation)				
PANSS Positive Subscale	-0.76 (± 2.809)			

PANSS Negative Subscale	-1.1 (± 3.571)			
PANSS General Subscale	-1.21 (± 5.191)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From baseline in PANSS Marder Factor Scores at LOCF Endpoint

End point title	Change From baseline in PANSS Marder Factor Scores at LOCF Endpoint

End point description:

PANSS Mardar 5 factors based on Marder et al. was calculated 1. Positive symptoms factor; 2. Negative symptoms factor; 3. Disorganized Thought factor; 4. Uncontrolled hostility/excitement factor; and 5. Anxiety/depression factor. PANSS Marder factor scores range from 7 to 49 for the positive and negative symptoms factor scores, from 6 to 42 for the disorganized thought factor score, and from 4 to 28 for the uncontrolled hostility/excitement and anxiety/depression scores. Higher PANSS Marder factor scores higher the symptom severity. Change of 1 point in the PANSS Marder factor scores is considered clinically relevant. mITT efficacy analysis set consists of all subjects from the mITT analysis set during the treatment phase who had at least 1 post-baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline, LOCF endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Score on a scale				
arithmetic mean (standard deviation)				
PANSS Marder Positive Symptoms	-0.83 (± 3.269)			
PANSS Marder Negative Symptoms	-1.28 (± 3.665)			
PANSS Marder Disorganized Thought	-0.43 (± 2.605)			
PANSS Marder Uncontrolled Hostility	-0.1 (± 1.652)			
PANSS Marder Anxiety/Depression	-0.44 (± 2.148)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Global Impression of Severity (CGI-S) Score at LOCF endpoint

End point title	Change from Baseline in Clinical Global Impression of Severity (CGI-S) Score at LOCF endpoint

End point description:

The CGI-S is a 7-point ordinal scale on the severity of the disease which rates from 1= 'Normal, not at all ill' to 7= 'Among the most extremely ill subject'. CGI-S is rated at baseline, Month-6, and Month-12. mITT efficacy analysis set consists of all subjects from the mITT analysis set (all subjects who provided their written consent and received at least 1 dose of study drug during the treatment phase) who had at least 1 post-baseline efficacy assessment. Here "N" (number of subjects analyzed) signifies the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, LOCF Endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	291			
Units: Score on a scale				
arithmetic mean (standard deviation)	-0.16 (± 0.965)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Global Impression (CGI-C) Score at LOCF Endpoint

End point title	Change From Baseline in Clinical Global Impression (CGI-C) Score at LOCF Endpoint

End point description:

The CGI-C is a 7-point ordinal scale on the change of the disease which rates from 1=' Very much improved' to 7=' Very much worse'. CGI-C is rated at month-12. mITT efficacy analysis set consists of all subjects from the mITT analysis set (all subjects who provided their written consent and received at least 1 dose of study drug during the treatment phase) who had at least 1 post-baseline efficacy assessment. Here "N" (number of subjects analyzed) signifies the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, LOCF Endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	289			
Units: Score on a scale				
arithmetic mean (standard deviation)	3.04 (± 0.978)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Personal and Social Performance (PSP) Scale at LOCF Endpoint

End point title	Change From Baseline in Personal and Social Performance (PSP) Scale at LOCF Endpoint

End point description:

The PSP assesses degree of subject's dysfunction within 4 domains of behavior, socially useful activities, personal and social relationships, self-care, and disturbing and aggressive behavior. The score ranges from 1 to 100, divided into 10 equal intervals to rate degree of difficulty (1=absent to 6=very severe) in each of 4 domains. Based on the 4 domains there will be one total score. Participants with a score of 71 to 100 have a mild degree of difficulty; from 31 to 70, varying degrees of disability; less than or equal to 30, functioning so poorly as to require intensive supervision. Efficacy analysis set: subjects from the mITT analysis set (all subjects who provide their written consent and receive at least 1 dose of study drug (PP3M) during the treatment phase) who had at least 1 post-baseline efficacy assessment. Here, N (number of subjects analyzed) signifies the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, LOCF endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	294			
Units: Score on scale				
arithmetic mean (standard deviation)				
PSP - Total Score	1.04 (± 11.272)			
Social useful activities	-0.04 (± 0.891)			
Personal and social relationship	-0.04 (± 0.85)			
Self-care	0 (± 0.886)			
Disturbing and aggressive behavior	-0.03 (± 0.481)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in World Health Organization Disability Assessment Schedule (WHODAS) 2.0 at LOCF Endpoint

End point title	Change From Baseline in World Health Organization Disability Assessment Schedule (WHODAS) 2.0 at LOCF Endpoint

End point description:

WHODAS 2.0 captures level of functioning in total score and 6 domains of life: 1:Cognition–understanding and communicating; 2:Mobility–moving and getting around; 3:Self-care–attending to one's hygiene, dressing, eating and staying alone; 4:Getting along–interacting with other people; 5:Life activities–domestic responsibilities, leisure, work and school; and 6:Participation–joining in community activities, participating in society. Each item of 36 items is rated on 5-point Likert scale: 0=No Difficulty;1=Mild Difficulty;2=Moderate Difficulty;3=Severe Difficulty;4=Extreme Difficulty or Cannot Do. From the results, scores for the 6 domains and an overall

100 (higher scores indicate worse functioning). mITT analysis set: all subjects who provided their written consent and received at least 1 dose of study drug (PP3M) during the treatment phase. "N" (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, LOCF endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	292			
Units: Score on scale				
arithmetic mean (standard deviation)				
Total Score	-2.4 (± 13.0)			
Domain 1: Cognition	-3.2 (± 17.2)			
Domain 2: Mobility	-0.5 (± 14.0)			
Domain 3: Self-care	-1.4 (± 13.7)			
Domain 4: Getting along	-3.9 (± 23.8)			
Domain 5: Life activities	-3.6 (± 24.1)			
Domain 6: Participation	-2.3 (± 15.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Subjective Well-being Under Neuroleptics Scale (SWN-S) at LOCF Endpoint

End point title	Change From Baseline in Subjective Well-being Under Neuroleptics Scale (SWN-S) at LOCF Endpoint

End point description:

SWN is an instrument to measure subtle subjective changes, such as restrictions in emotionality, clarity of thinking and spontaneity. A shortened version is used and consists of 20 items:10 positively,10 negatively phrased. Based on these 20 items total SWN score is calculated and 5 subscales are constructed, each consisting of 2 positive and 2 negative items: Mental functioning; Self-control; Emotional regulation; Physical functioning; and Social integration. Total score of SWN-S ranges from 20-120. 5 subscale scores range from 4-24. All items were coded in such a way that higher values express better well-being (Positive items Coding: 2, 3, 5, 7, 8, 13, 15, 18, 19, 20; Negative items Coding: 1, 4, 6, 9, 10, 11, 12, 14, 16, 17). mITT efficacy analysis set consists of all subjects from the mITT analysis set during the treatment phase who had at least 1 post-baseline efficacy assessment. Here, N (number of subjects analyzed) signifies a number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, LOCF endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	297			
Units: Score on scale				
arithmetic mean (standard deviation)				
Total Score	0.31 (± 12.514)			
Mental functioning Score	0.35 (± 3.496)			
Self-control Score	-0.15 (± 3.202)			
Emotional regulation Score	0.21 (± 3.367)			
Physical functioning Score	-0.27 (± 3.668)			
Social integration Score	0.18 (± 3.196)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Schizophrenia Quality of Life Scale Revision 4 (SQLS-R4) at LOCF Endpoint

End point title	Change From Baseline in Schizophrenia Quality of Life Scale Revision 4 (SQLS-R4) at LOCF Endpoint

End point description:

SQLS-R4 comprises 33 items incorporated in 2 domains: psychosocial feelings (20 items) and cognition and vitality (13 items). Individual domain and total scores are standardized using a scoring algorithm to a 0 to 100 scale, with higher scores indicating comparatively lower quality of life. 0 = no problem at all: 100 = maximum level of problem. The general formula for scoring each domain and the total score is: Score = (Sum of scores of each item in domain/4 (i.e. max score per question) * numbers of items in the domain)*100. mITT efficacy analysis set consists of all subjects from the mITT analysis set who had at least 1 post-baseline efficacy assessment and at least one post-baseline assessments. Here, N (number of subjects analyzed) signifies a number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, LOCF endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	297			
Units: Score on scale				
arithmetic mean (standard deviation)				
SQLS-R4: Total Score	-2.4 (± 14.527)			
SQLS-R4: Psychosocial	-2.38 (± 16.263)			
SQLS-R4: Vitality	-2.42 (± 14.362)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Heinrichs–Carpenter Quality of Life Scale (QLS) at LOCF Endpoint

End point title	Change from Baseline in Heinrichs–Carpenter Quality of Life Scale (QLS) at LOCF Endpoint

End point description:

QLS is a 21-item scale. Each rated on 7-point scale with descriptive anchors for every other point. Specific descriptors vary among items, but high end of scales(scores of 5 and 6)reflects normal or unimpaired functioning, and low end of scales(scores of 0 and 1)reflects severe impairment of function in question. Total score and 4 category scores are calculated. Categories consists Intrapsychic Foundations(IF): items 13,14,15,16,17,20,21; Interpersonal Relations(IR): item 1, 2, 3, 4, 5, 6, 7, 8; Instrumental Role(IRo): items 9,10,11,12; and Common Objects and Activities(COA): item 18, 19. QLS total score ranges from 0-126, IF from 0-42, IR from 0-48, IRo from 0-24, and COA from 0 to 12. Total score and 4 category scores are calculated as average of item scores. mITT analysis set included. Here, N (number of subjects analyzed) signifies a number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, LOCF endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	294			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Total Score	1.19 (± 18.168)			
QLS: IF Score	0.01 (± 6.652)			
QLS: IR Score	0.63 (± 8.398)			
QLS: IRo Score	0.44 (± 5.182)			
QLS: COA Score	0.1 (± 2.54)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient's Satisfaction with Medication (MSQ) at LOCF Endpoint

End point title	Change From Baseline in Patient's Satisfaction with Medication (MSQ) at LOCF Endpoint

End point description:

MSQ is a single item questionnaire with responses on a 7-point Likert-scale as follows: 1=extremely dissatisfied, 2=very dissatisfied, 3=somewhat dissatisfied, 4=neither satisfied nor dissatisfied, 5=somewhat satisfied, 6=very satisfied, 7=extremely satisfied. A 1-point change on the MSQ may be considered clinically meaningful. The mITT analysis set consists of all subjects who provided their written consent and received at least 1 dose of study drug (PP3M) during the treatment phase with both baseline and at least one post-baseline assessments.

End point type	Secondary

End point timeframe:

Baseline, LOCF endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	297			
Units: Score on a scale				
arithmetic mean (standard deviation)	-0.03 (± 1.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physician Treatment Satisfaction at LOCF Endpoint

End point title	Change From Baseline in Physician Treatment Satisfaction at LOCF Endpoint

End point description:

Physician treatment satisfaction is a 7-point categorical scale (1=Extremely satisfied, 2=Very satisfied, 3=Somewhat satisfied, 4=Neither Satisfied nor Dissatisfied, 5=Somewhat dissatisfied, 6=Very dissatisfied, 7=Extremely dissatisfied). The scale will be used to assess physician's satisfaction on 3 domains: efficacy, safety, and mode of administration as well as overall satisfaction. The mITT analysis set consist of all subjects who provided their written consent and received at least 1 dose of study drug (PP3M) during the treatment phase with both baseline and at least one post-baseline assessments.

End point type	Secondary

End point timeframe:

Baseline, LOCF endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	293			
Units: Score on scale				
arithmetic mean (standard deviation)				
Overall	-0.14 (± 1.15)			
Efficacy	-0.08 (± 1.23)			
Safety	-0.21 (± 1.283)			

Mode of Admin	-0.26 (± 1.278)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Involvement Evaluation Questionnaire (IEQ) at LOCF Endpoint

End point title	Change From Baseline in Involvement Evaluation Questionnaire (IEQ) at LOCF Endpoint

End point description:

IEQ consists of 7 modules: (a) Sociodemographics of patient and family (item: 1-15); (b) Caregiving consequences of psychiatric disorders (item: 16-46); (c) Extra financial expenses (item: 47-54); (d) General Health Questionnaire 12 (item: 55-66); (e) Professional help for patient's relative (item: 67-69); (f) Consequences for patient's children (item: 70-80) and (g) Open question for remarks and additions (item: 81). Module 2 is the IEQ core module. All items from module 2 are scored on a 5-point Likert scale (0 = never, 1 = sometimes, 2 = regularly, 3 = often, 4 = always). Module 2, the core module, can be summarized in four subscales with score ranges: Tension (0-36), supervision (0-24), worrying (0-24), urging (0-32) and sum score (0-108). mITT efficacy analysis set included. Here, N (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, LOCF endpoint (Month 12 or early discontinuation)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	158			
Units: Score on scale				
arithmetic mean (standard deviation)				
Total Score	-4.02 (± 12.198)			
IEQ-Tension	-0.3 (± 3.544)			
IEQ-Supervision	-1.12 (± 3.629)			
IEQ-Worrying	-1.65 (± 4.469)			
IEQ-Urging	-1.99 (± 5.461)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with at Least one Hospitalization During the 12 Months Prior to PP3M Start and During Follow-up

End point title	Number of Subjects with at Least one Hospitalization During the 12 Months Prior to PP3M Start and During Follow-up

End point description:

Number of subjects with at least one hospitalization during the 12 months prior to PP3M start and during follow-up was reported. mITT efficacy analysis was defined as all subjects from the mITT analysis set who had at least 1 post-baseline efficacy assessment. Here, 'n' signifies the number of subjects analyzed at a specified time point.

End point type	Secondary

End point timeframe:

During 12 months prior to PP3M start, during follow up (Approximately 2 years)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	303			
Units: Subjects				
number (not applicable)				
During 12 months prior to PP3M start	41			
During follow up	14			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Hospitalization Prior to 12 Months of PP3M Start and During Follow-up

End point title	Duration of Hospitalization Prior to 12 Months of PP3M Start and During Follow-up

End point description:

Duration of hospitalization prior to the start of pp3m and during the follow-up phase was reported. mITT efficacy analysis was defined as all subjects from the mITT analysis set who had at least 1 post-baseline efficacy assessment. Here, 'n' signifies the number of subjects analyzed at a specified time point.

End point type	Secondary

End point timeframe:

During 12 months prior to PP3M start, during follow up (Approximately 2 years)

End point values	Total (PP3M Treatment)			
Subject group type	Reporting group			
Number of subjects analysed	303			
Units: Days				
arithmetic mean (standard deviation)				
During 12 months prior to PP3M start (n=41)	33.2 (± 22.44)			
During Follow up (n=14)	15.2 (± 10.82)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Approximately 2 years

Adverse event reporting additional description:

The safety analysis set consists of all subjects from the mITT analysis set who had at least 1 post-baseline safety assessment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Total (PP3M Treatment)

Reporting group description:

Subjects received intramuscular (IM) injection of Paliperidone Palmitate 3-Month Formulation (PP3M) on Day 1 at a starting dose of 175 milligram equivalent (mg eq) up to 525 mg eq. based on last Paliperidone Palmitate 1-Month Formulation (PP1M) dose (at a dose of 3.5-fold multiple of the subject's last PP1M dose). Subsequent PP3M injections will be given at Month 3, Month 6, and Month 9 and dose can be adjusted flexibly in increments within the range of 175 to 525 mg eq.

Serious adverse events	Total (PP3M Treatment)		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 303 (5.94%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of Colon			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Foot Fracture			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road Traffic Accident			

subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Orchidectomy			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Speech Disorder			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			

subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural Effusion			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Aggression			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Agitation			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Alcohol Withdrawal Syndrome			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anxiety			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blunted Affect			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Delusion			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

Hallucination, Auditory			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric Decompensation			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychotic Disorder			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Schizophrenia			
subjects affected / exposed	3 / 303 (0.99%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Suicidal Ideation			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Total (PP3M Treatment)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	153 / 303 (50.50%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Benign Neoplasm			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Fibroma			

subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Papilloma			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Administration Site Pain			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	4		
Fatigue			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	3		
Induration			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Inflammation			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Influenza Like Illness			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Injection Site Pain			
subjects affected / exposed	18 / 303 (5.94%)		
occurrences (all)	26		
Injection Site Swelling			

subjects affected / exposed	4 / 303 (1.32%)		
occurrences (all)	5		
Malaise			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	2		
Mass			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Peripheral Swelling			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Adnexa Uteri Pain			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Amenorrhoea			
subjects affected / exposed	6 / 303 (1.98%)		
occurrences (all)	6		
Erectile Dysfunction			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Galactorrhoea			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Menstruation Irregular			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Metrorrhagia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Retrograde Ejaculation			

subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Sexual Dysfunction			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 303 (1.32%)		
occurrences (all)	4		
Dysphonia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Oropharyngeal Pain			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Psychiatric disorders			
Abnormal Dreams			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Acute Stress Disorder			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Affect Lability			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Alcohol Abuse			
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	3		
Anxiety			
subjects affected / exposed	6 / 303 (1.98%)		
occurrences (all)	6		
Confusional State			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	3		
Delusion			

subjects affected / exposed	3 / 303 (0.99%)			
occurrences (all)	3			
Depressive Symptom				
subjects affected / exposed	3 / 303 (0.99%)			
occurrences (all)	3			
Emotional Distress				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Dyssomnia				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Hallucination, Auditory				
subjects affected / exposed	6 / 303 (1.98%)			
occurrences (all)	6			
Hallucination				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Ideas of Reference				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Insomnia				
subjects affected / exposed	11 / 303 (3.63%)			
occurrences (all)	13			
Intentional Self-Injury				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Loss of Libido				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Persecutory Delusion				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	2			
Persistent Depressive Disorder				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Psychomotor Retardation				

subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Psychotic Disorder			
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	4		
Psychotic Symptom			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Restlessness			
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	4		
Schizophrenia			
subjects affected / exposed	8 / 303 (2.64%)		
occurrences (all)	9		
Sleep Disorder			
subjects affected / exposed	5 / 303 (1.65%)		
occurrences (all)	5		
Suicidal Ideation			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Terminal Insomnia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Blood Cholesterol Increased			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Blood Prolactin Increased			

subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Hepatic Enzyme Increased			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Vitamin D Decreased			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Weight Decreased			
subjects affected / exposed	10 / 303 (3.30%)		
occurrences (all)	10		
Weight Increased			
subjects affected / exposed	26 / 303 (8.58%)		
occurrences (all)	29		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Drug Administration Error			
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	3		
Joint Dislocation			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Ligament Sprain			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Rib Fracture			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Road Traffic Accident			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Tooth Injury			

subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Nervous system disorders			
Akathisia			
subjects affected / exposed	11 / 303 (3.63%)		
occurrences (all)	12		
Disturbance in Attention			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	4 / 303 (1.32%)		
occurrences (all)	4		
Dizziness Exertional			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Dyskinesia			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Dystonia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Extrapyramidal Disorder			
subjects affected / exposed	4 / 303 (1.32%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	7 / 303 (2.31%)		
occurrences (all)	8		
Hyperaesthesia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Hypersomnia			

subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Hypoaesthesia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Hypokinesia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Motor Dysfunction			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Parkinsonism			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Sciatica			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	3		
Sedation			
subjects affected / exposed	6 / 303 (1.98%)		
occurrences (all)	9		
Tardive Dyskinesia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	5 / 303 (1.65%)		
occurrences (all)	5		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Increased Tendency to Bruise			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		

Iron Deficiency Anaemia subjects affected / exposed occurrences (all)	1 / 303 (0.33%) 1		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 303 (0.33%) 1		
Eye disorders Myopia subjects affected / exposed occurrences (all) Oculogyric Crisis subjects affected / exposed occurrences (all) Vision Blurred subjects affected / exposed occurrences (all)	1 / 303 (0.33%) 1 1 / 303 (0.33%) 1 1 / 303 (0.33%) 1		
Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Dysphagia subjects affected / exposed occurrences (all) Gastritis Erosive subjects affected / exposed occurrences (all) Haematochezia	1 / 303 (0.33%) 1 2 / 303 (0.66%) 3 4 / 303 (1.32%) 4 1 / 303 (0.33%) 1 1 / 303 (0.33%) 1 1 / 303 (0.33%) 1		

subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Lip Ulceration			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	2		
Salivary Hypersecretion			
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	3		
Tooth Impacted			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	4 / 303 (1.32%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Androgenetic Alopecia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Dermatitis			
subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	3		
Eczema			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	2		
Pityriasis			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		

Pruritus subjects affected / exposed occurrences (all) Psoriasis subjects affected / exposed occurrences (all) Scar Pain subjects affected / exposed occurrences (all) Seborrhoeic Dermatitis subjects affected / exposed occurrences (all)	1 / 303 (0.33%) 1 1 / 303 (0.33%) 1 1 / 303 (0.33%) 1 1 / 303 (0.33%) 1		
Renal and urinary disorders Hypertonic Bladder subjects affected / exposed occurrences (all) Polyuria subjects affected / exposed occurrences (all) Renal Colic subjects affected / exposed occurrences (all) Urinary Incontinence subjects affected / exposed occurrences (all)	1 / 303 (0.33%) 1 1 / 303 (0.33%) 1 1 / 303 (0.33%) 1 1 / 303 (0.33%) 1		
Endocrine disorders Hyperprolactinaemia subjects affected / exposed occurrences (all)	7 / 303 (2.31%) 7		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back Pain subjects affected / exposed occurrences (all)	1 / 303 (0.33%) 1 1 / 303 (0.33%) 2		

Bursitis			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	2		
Muscle Rigidity			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Muscle Spasms			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Musculoskeletal Pain			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	3 / 303 (0.99%)		
occurrences (all)	3		
Pain in Extremity			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Infections and infestations			
Acute Sinusitis			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Angular Cheilitis			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Bronchiolitis			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	2		
Conjunctivitis			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Cystitis			

subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Enterobiasis				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Folliculitis				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Furuncle				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Gastroenteritis				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Gastroenteritis Viral				
subjects affected / exposed	2 / 303 (0.66%)			
occurrences (all)	2			
Influenza				
subjects affected / exposed	6 / 303 (1.98%)			
occurrences (all)	6			
Injection Site Abscess				
subjects affected / exposed	2 / 303 (0.66%)			
occurrences (all)	2			
Nasopharyngitis				
subjects affected / exposed	3 / 303 (0.99%)			
occurrences (all)	3			
Onychomycosis				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	2			
Otitis Media Acute				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Periodontitis				
subjects affected / exposed	1 / 303 (0.33%)			
occurrences (all)	1			
Pharyngitis				

subjects affected / exposed	2 / 303 (0.66%)		
occurrences (all)	3		
Respiratory Tract Infection			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Upper Respiratory Tract Infection			
subjects affected / exposed	4 / 303 (1.32%)		
occurrences (all)	4		
Vaginal Infection			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	11 / 303 (3.63%)		
occurrences (all)	17		
Metabolism and nutrition disorders			
Diabetes Mellitus			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Hypercholesterolaemia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Hyperlipidaemia			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		
Increased Appetite			
subjects affected / exposed	1 / 303 (0.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 March 2016	Included the addition of a telephone call for safety follow-up 3 months after the last study visit for assessment of AEs, clarification for the exclusion of subjects with severe substance use disorder and subjects enrolled in an investigational study and outlined procedures for switching of subjects to commercially available antipsychotics after completing the study. Additional changes were made to indicate that screening and baseline procedures/assessments could be performed on the same day, to clarify requirements for pre-study and concomitant psychotropic/antipsychotic medications, to provide further guidance on dosing and precautionary measures in special populations, and some minor corrections and editorial changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported