Clinical trial results:
A 6-Month, Open-Label, Prospective, Multicenter, International, Exploratory Study of a Transition to Flexibly-Dosed Paliperidone Palmitate in Patients with Schizophrenia Previously Unsuccessfully Treated with Oral or Long-Acting Injectable Antipsychotics

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2009-018022-30
Trial protocol	PT HU DE NL BE ES GB SE DK IT LV AT EE LT
Global end of trial date	29 November 2013

Results information

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

Trial information

Trial identification

Sponsor protocol code	R092670SCH3010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01281527
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International NV
Sponsor organisation address	Turnhoutseweg 30, 2340 Beerse, Belgium,
Public contact	Janssen-Cilag International NV, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Janssen-Cilag International NV, 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	29 November 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to explore the tolerability, safety and treatment response (maintained/improved efficacy); based on total Positive and Negative Syndrome Scale (PANSS) score, following a transition to flexibly dosed once-monthly paliperidone palmitate (PP) in subjects with schizophrenia previously unsuccessfully treated with oral or long-acting injectable (LAI) antipsychotics. Subjects with either acute or non-acute symptoms of schizophrenia were eligible to enter the study.

Protection of trial subjects:

Safety and tolerability were monitored by evaluating adverse events, vital signs, physical examination, body weight/body mass index (BMI), and assessment of extrapyramidal symptoms (using the Extrapyramidal Symptom Rating Scale [ESRS]), and urine pregnancy test.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2010
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	Austria: 11
Country: Number of subjects enrolled	Belgium: 67
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Croatia: 4
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	Estonia: 9
Country: Number of subjects enrolled	France: 82
Country: Number of subjects enrolled	Germany: 114
Country: Number of subjects enrolled	United Kingdom: 34
Country: Number of subjects enrolled	Greece: 27
Country: Number of subjects enrolled	Hungary: 18
Country: Number of subjects enrolled	Israel: 17
Country: Number of subjects enrolled	Italy: 123
Country: Number of subjects enrolled	Latvia: 56
Country: Number of subjects enrolled	Lithuania: 8

Country: Number of subjects enrolled	Portugal: 32
Country: Number of subjects enrolled	Spain: 170
Country: Number of subjects enrolled	Sweden: 16
Country: Number of subjects enrolled	Switzerland: 10
Country: Number of subjects enrolled	Turkey: 78
Country: Number of subjects enrolled	Ukraine: 149
Worldwide total number of subjects	1035
EEA total number of subjects	781

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)	1009
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study consisted of a screening period, a 6-month study period, and an optional open-label extension phase. 3 groups of subjects were pre-specified with schizophrenia who transitioned to PP: Group A (600 non-acute) and C (200 acute)- subjects switched due to oral antipsychotics; Group B(200 non-acute)- subjects switched due to LAI antipsychotic.

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

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

Group A included approximately 600 non--acute but symptomatic subjects with schizophrenia who were transitioned to PP because of prior unsuccessful treatment with an oral anti psychotic in the 4 weeks prior to enrollment.

Arm type	Experimental
Investigational medicinal product name	Paliperidone palmitate - Extended Release (ER)
Investigational medicinal product code	R092670
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received intramuscular injection of PP on Day 1 at a dose of 150 milligram equivalent (mg eq.) and their second injection on Day 8 (100 mg eq.). Subsequent injections were given once monthly within the dose range of 50 to 150 mg eq. at the discretion of the investigator.

Arm title	Group B

Arm description:

Group B included approximately 200 non--acute but symptomatic subjects with schizophrenia who were transitioned to PP because of prior unsuccessful treatment with a frequently used LAI anti psychotics (i.e., haloperidol decanoate, flupentixol decanoate, fluphenazine decanoate, zuclopenthixol decanoate, or risperidone LAI) in the 4 weeks prior to enrollment.

Arm type	Experimental
Investigational medicinal product name	Paliperidone palmitate - Extended Release (ER)
Investigational medicinal product code	R092670
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received intramuscular injection of PP on Day 1 with in a range of 50 - 150 mg eq. Subsequent injections were given once monthly within the dose range of 50 to 150 mg eq. at the discretion of the investigator.

Arm title	Group C

Arm description:

Group C included approximately 200 subjects with acute symptoms of schizophrenia who were transition ed to PP because of unsuccessful

treatment with an oral antipsychotic in the 4 weeks prior to enrollment.

Arm type	Experimental
Investigational medicinal product name	Paliperidone palmitate - Extended Release (ER)
Investigational medicinal product code	R092670
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received intramuscular injection of PP on Day 1 at a dose of 150 mg eq. and their second injection on Day 8 (100 mg eq.). Subsequent injections were given once monthly within the dose range of 50 to 150 mg eq. at the discretion of the investigator.

Number of subjects in period 1	Group A	Group B	Group C
Started	593	230	212
Completed	442	172	149
Not completed	151	58	63
Physician decision	8	3	-
Consent withdrawn by subject	60	19	20
Death	1	-	2
Other	2	3	3
Adverse event	36	17	19
Noncompliance with study drug	4	2	1
Lost to follow-up	19	5	10
Protocol deviation	6	2	2
Lack of efficacy	15	7	6

Baseline characteristics

Reporting groups	
Reporting group title	Group A
Reporting group description:	
Group A included approximately 600 non--acute but symptomatic subjects with schizophrenia who were transitioned to PP because of prior unsuccessful treatment with an oral anti psychotic in the 4 weeks prior to enrollment.	
Reporting group title	Group B
Reporting group description:	
Group B included approximately 200 non--acute but symptomatic subjects with schizophrenia who were transitioned to PP because of prior unsuccessful treatment with a frequently used LAI anti psychotics (i.e., haloperidol decanoate, flupentixol decanoate, fluphenazine decanoate, zuclopenthixol decanoate, or risperidone LAI) in the 4 weeks prior to enrollment.	
Reporting group title	Group C
Reporting group description:	
Group C included approximately 200 subjects with acute symptoms of schizophrenia who were transition ed to PP because of unsuccessful treatment with an oral antipsychotic in the 4 weeks prior to enrollment.	

Reporting group values	Group A	Group B	Group C
Number of subjects	593	230	212
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	1	0	0
Adults (18-64 years)	581	220	208
From 65 to 84 years	11	10	4
85 years and over	0	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	38.4	42.5	36.4
standard deviation	± 11.83	± 10.83	± 12.06
Title for Gender			
Units: subjects			
Female	219	83	87
Male	374	147	125

Reporting group values	Total		
Number of subjects	1035		
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	1		
Adults (18-64 years)	1009		
From 65 to 84 years	25		
85 years and over	0		
Title for AgeContinuous			
Units: years			
arithmetic mean			
standard deviation	-		

Title for Gender Units: subjects			
Female	389		
Male	646		

End points

End points reporting groups

Reporting group title	Group A
Reporting group description:	
Group A included approximately 600 non--acute but symptomatic subjects with schizophrenia who were transitioned to PP because of prior unsuccessful treatment with an oral anti psychotic in the 4 weeks prior to enrollment.	
Reporting group title	Group B
Reporting group description:	
Group B included approximately 200 non--acute but symptomatic subjects with schizophrenia who were transitioned to PP because of prior unsuccessful treatment with a frequently used LAI anti psychotics (i.e., haloperidol decanoate, flupentixol decanoate, fluphenazine decanoate, zuclopenthixol decanoate, or risperidone LAI) in the 4 weeks prior to enrollment.	
Reporting group title	Group C
Reporting group description:	
Group C included approximately 200 subjects with acute symptoms of schizophrenia who were transition ed to PP because of unsuccessful treatment with an oral antipsychotic in the 4 weeks prior to enrollment.	
Subject analysis set title	Group A1: Subjects Switched for Efficacy Reason
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Efficacy analysis set included all Intent-to-treat (ITT) subjects who had at least one post baseline observation on any efficacy parameter.	
Subject analysis set title	Group A2: Subjects Switched for Other Reason
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Efficacy analysis set included all ITT subjects who had at least one post baseline observation on any efficacy parameter.	
Subject analysis set title	Group B1: Subjects Switched from Haloperidol Decanoate
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Efficacy analysis set included all ITT subjects who had at least one post baseline observation on any efficacy parameter.	
Subject analysis set title	Group B2: Subjects Switched from Flupentixol Decanoate
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Efficacy analysis set included all ITT subjects who had at least one post baseline observation on any efficacy parameter.	
Subject analysis set title	Group B3: Subjects Switched from Fluphenazine Decanoate
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Efficacy analysis set included all ITT subjects who had at least one post baseline observation on any efficacy parameter.	
Subject analysis set title	Group B4: Subjects Switched from Zuclopentixol-Decanoate
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Efficacy analysis set included all ITT subjects who had at least one post baseline observation on any efficacy parameter.	
Subject analysis set title	Group B5: Subjects Switched from Risperidone Micropsheres
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Efficacy analysis set included all ITT subjects who had at least one post baseline observation on any efficacy parameter.	
Subject analysis set title	Group C

Subject analysis set type	Sub-group analysis

Subject analysis set description:

Group C included approximately 200 subjects with acute symptoms of schizophrenia who were transition ed to PP because of unsuccessful treatment with an oral antipsychotic in the 4 weeks prior to enrollment.

Primary: Group A1 (Non acute Patients Switched From oral Anti psychotics due to Lack of Efficacy): Percentage of Participants with Improved Efficacy in PANSS Total Score from Baseline to Month 6 LOCF

End point title	Group A1 (Non acute Patients Switched From oral Anti psychotics due to Lack of Efficacy): Percentage of Participants with Improved Efficacy in PANSS Total Score from Baseline to Month 6 LOCF[1]

End point description:

Improved efficacy, defined as the proportion of patients who showed an improvement in PANSS total score of at ≥20% from baseline to endpoint (LOCF). PANSS is a 30-item scale, with each item rated on a scale of 1 (absent) to 7 (extreme). The PANSS provides a total score (range, 30-210) and scores for the following 3 subscales: positive subscale (range, 7-49): sum of Items P1 to P7 in the positive subscale; negative subscale (range, 7-49): sum of Items N1 to N7 in the negative subscale; general psychopathology subscale (range, 16-112): sum of Items G1 to G16 in the general psychopathology subscale. Efficacy analysis included all subjects who received at least 1 dose of paliperidone palmitate (PP) and had at least 1 post baseline observation on any efficacy parameter.

End point type	Primary

End point timeframe:

Month 6 LOCF

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	Group A1: Subjects Switched for Efficacy Reason			
Subject group type	Subject analysis set			
Number of subjects analysed	143			
Units: percentage of participants				
median (confidence interval 95%)	61.5 (53.4 to 69.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Group B: (Non-acute Patients Switched From Long Acting Injectable Antipsychotics): Participants with Explore Treatment Response

End point title	Group B: (Non-acute Patients Switched From Long Acting Injectable Antipsychotics): Participants with Explore Treatment Response[2]

End point description:

Participants with explore treatment response switched from Long Acting Injectable (LAI) anti-psychotics (haloperidol decanoate, flupentixol decanoate, fluphenazine decanoate,zuclopenthixol decanoate, risperidone LAI) defined as the proportion of subjects achieving a ≥20% improvement in PANSS total score from baseline to endpoint (LOCF). The PANSS is a 30-item scale, with each item rated on a scale of 1 (absent) to 7 (extreme). The PANSS provides a total score (range, 30-210) and scores for the following 3 subscales: positive subscale (range, 7-49): sum of Items P1 to P7 in the positive subscale; negative subscale (range, 7-49): sum of Items N1 to N7 in the negative subscale; general

psychopathology subscale (range, 16-112): sum of Items G1 to G16 in the general psychopathology subscale. Efficacy analysis included all subjects who received at least 1 dose of study medication (PP) and had at least 1 post baseline observation on any efficacy parameter.

End point type	Primary

End point timeframe:

Baseline and Month 6 LOCF

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Group B1: Subjects Switched from Haloperidol Decanoate	Group B2: Subjects Switched from Flupentixol Decanoate	Group B3: Subjects Switched from Fluphenazine Decanoate	Group B4: Subjects Switched from Zuclopentixol-Decanoate
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	53	34	44	41
Units: Percentage of participants				
median (confidence interval 95%)	54.7 (41.4 to 67.3)	61.8 (45 to 76.1)	59.1 (44.4 to 72.3)	53.7 (38.8 to 67.9)

End point values	Group B5: Subjects Switched from Risperidone Micropsheres			
Subject group type	Subject analysis set			
Number of subjects analysed	55			
Units: Percentage of participants				
median (confidence interval 95%)	61.1 (47.8 to 73)			

Statistical analyses

No statistical analyses for this end point

Primary: Group C (Acute Patients Switched From Ooral Anti psychotics): Participants with Improved Efficacy From Baseline to Month 6 LOCF

End point title	Group C (Acute Patients Switched From Ooral Anti psychotics): Participants with Improved Efficacy From Baseline to Month 6 LOCF[3][4]

End point description:

participants with improved efficacy defined as the proportion of patients achieving a ≥30% improvement in PANSS total score from baseline to endpoint (LOCF). The PANSS is a 30-item scale, with each item rated on a scale of 1 (absent) to 7 (extreme). The PANSS provides a total score (range, 30-210) and scores for the following 3 subscales: positive subscale (range, 7-49): sum of Items P1 to P7 in the positive subscale; negative subscale (range, 7-49): sum of Items N1 to N7 in the negative subscale; general psychopathology subscale (range, 16-112): sum of Items G1 to G16 in the general psychopathology subscale. Efficacy analysis included all subjects who received at least 1 dose of paliperidone palmitate (PP) and had at least 1 post baseline observation on any efficacy parameter.

End point type	Primary

End point timeframe:

Baseline to Month 6 LOCF

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

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Group C			
Subject group type	Reporting group			
Number of subjects analysed	207			
Units: Percentage of participants				
median (confidence interval 95%)	66.7 (60 to 72.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Group A2 (Non-acute Participants Switched From Oral Anti-psychotics due to Other Reasons): Percentage of Participants With Maintained Efficacy From baseline to Month 6 LOCF

End point title	Group A2 (Non-acute Participants Switched From Oral Anti-psychotics due to Other Reasons): Percentage of Participants With Maintained Efficacy From baseline to Month 6 LOCF[5]

End point description:

Percentage of participants with maintained efficacy, defined as a non-inferior change in PANSS total score from baseline to endpoint based on the Schuirmann's test. PANSS is a 30-item scale, with each item rated on a scale of 1 (absent) to 7 (extreme). The PANSS provides a total score (range, 30-210) and scores for the following 3 subscales: positive subscale (range, 7-49): sum of Items P1 to P7 in the positive subscale; negative subscale (range, 7-49): sum of Items N1 to N7 in the negative subscale; general psychopathology subscale (range, 16-112): sum of Items G1 to G16 in the general psychopathology subscale. Efficacy analysis included all subjects who received at least 1 dose of paliperidone palmitate (PP) and had at least 1 post baseline observation on any efficacy parameter.

End point type	Primary

End point timeframe:

Baseline and Month 6 LOCF

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

End point values	Group A2: Subjects Switched for Other Reason			
Subject group type	Subject analysis set			
Number of subjects analysed	446			
Units: Percentage of participants				
median (confidence interval 95%)				
Baseline	69 (67.3 to 70)			

Month 6 (LOCF)	-11 (-13.1 to -10.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Global Impression-Severity Scale [CGI-S] at Month 6

End point title	Change from Baseline in Clinical Global Impression-Severity Scale [CGI- S] at Month 6

End point description:

The Clinical Global Impression-Severity Scale (CGI-S) rating scale is used to rate the severity of a subject's psychotic condition on a 7-point
scale ranging from 1 (not ill) to 7 (extremely severe). Efficacy analysis included all subjects who received at least 1 dose of PP and had at least 1 post baseline observation on any efficacy parameter. Here 'n' signifies number of subjects analysed for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Month 6 LOCF

End point values	Group A1: Subjects Switched for Efficacy Reason	Group A2: Subjects Switched for Other Reason	Group B1: Subjects Switched from Haloperidol Decanoate	Group B2: Subjects Switched from Flupentixol Decanoate
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	143	446	53	34
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=143,442,53,34,44,41,55,205)	4.2 (± 0.89)	3.8 (± 0.91)	4.2 (± 0.91)	3.9 (± 0.77)
Month 6 LOCF(n=143,442,53,34,44,41,55,205)	-0.6 (± 0.86)	-0.6 (± 1.09)	-0.4 (± 1.1)	-0.4 (± 0.86)

End point values	Group B3: Subjects Switched from Fluphenazine Decanoate	Group B4: Subjects Switched from Zuclopentixol-Decanoate	Group B5: Subjects Switched from Risperidone Micropsheres	Group C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	55	207
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=143,442,53,34,44,41,55,205)	4 (± 1.03)	4.1 (± 1)	3.7 (± 1.21)	5 (± 0.75)
Month 6 LOCF(n=143,442,53,34,44,41,55,205)	-0.4 (± 0.94)	-0.5 (± 1.19)	-0.4 (± 1.19)	-1.5 (± 1.27)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Personal And Social Functioning (Personal and Social Performance Scale [PSP]) at Month 6

End point title	Change from Baseline in Personal And Social Functioning (Personal and Social Performance Scale [PSP]) at Month 6

End point description:

The PSP scale was used to assess the degree of functioning a subject exhibited within 4 domains: a) socially useful activities, b) personal and social relationships, c) self-care, and d) disturbing and aggressive behavior. Each of the 4 domains was rated on a 6-point scale (0=absent, 1=mild, 2=manifest, 3=marked, 4=severe, and 5=very severe) and then converted to one total score (ranging from 1 to 100). A total PSP score of 71 to 100 indicated a mild degree of difficulty; a score of 31 to 70 indicated varying degrees of disability; and a score 30 indicated functioning so poor that the subject requires intensive support or supervision. Efficacy analysis included all subjects who received at least 1 dose of study medication (PP) and had at least 1 post baseline observation on any efficacy parameter. Here 'n' signifies number of subjects analysed for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Month 6 LOCF

End point values	Group A1: Subjects Switched for Efficacy Reason	Group A2: Subjects Switched for Other Reason	Group B1: Subjects Switched from Haloperidol Decanoate	Group B2: Subjects Switched from Flupentixol Decanoate
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	143	446	53	34
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=139,429,53,34,44,41,55,86,197)	55.3 (± 12.31)	59 (± 13.62)	48.7 (± 12.53)	59.6 (± 11.2)
Month 6 LOCF(n=139,429,53,34,44,41,55,197)	5.5 (± 12.31)	8.8 (± 14.37)	5.2 (± 13)	6.1 (± 14.94)

End point values	Group B3: Subjects Switched from Fluphenazine Decanoate	Group B4: Subjects Switched from Zuclopentixol-Decanoate	Group B5: Subjects Switched from Risperidone Micropsheres	Group C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	55	207
Units: units on a scale				
arithmetic mean (standard deviation)				

Baseline (n=139,429,53,34,44,41,55,86,197)	53.5 (± 12.16)	52.9 (± 15.63)	60.1 (± 17.92)	43.9 (± 14.99)
Month 6 LOCF(n=139,429,53,34,44,41,55,197)	6 (± 11.58)	6.4 (± 15.21)	5.2 (± 15.31)	19 (± 18.67)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Health Status (Self-Reported Health Status Questionnaire [SF-36]) at Month 6

End point title	Change from Baseline in Health Status (Self-Reported Health Status Questionnaire [SF-36]) at Month 6

End point description:

The SF-36 is a validated self-rated health status instrument used to assess subjects across several domains. The SF-36 consists of 8 multi-item scales: limitations in physical functioning due to health problems; limitations in usual role activities due to physical health problems; bodily pain; general health perception; vitality (energy and fatigue); limitations in social functioning due to physical or mental health problems; limitations in usual role activities due to personal or emotional problems; and general mental health (psychological distress and well-being). These scales are scored from 0 to 100, with higher scores indicating better health. The SF-36 was also scored as- Physical Component - Scale Score (PCS) and Mental Component - Scale Score (MCS). Higher scores indicated better health. Efficacy analysis included all subjects who received at least 1 dose of PP and had at least 1 post baseline observation on any efficacy parameter.

End point type	Secondary

End point timeframe:

Baseline and Month 6 LOCF

End point values	Group A1: Subjects Switched for Efficacy Reason	Group A2: Subjects Switched for Other Reason	Group B1: Subjects Switched from Haloperidol Decanoate	Group B2: Subjects Switched from Flupentixol Decanoate
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	143	446	53	34
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline-PCS (n=130,399,46,33,42,38,49,182)	48 (± 9.47)	48.7 (± 8.76)	49.4 (± 7.48)	49.3 (± 9.71)
Month 6 LOCF-PCS (n=130,399,46,33,42,38,49,182)	2.2 (± 7.7)	1.2 (± 8.22)	1.4 (± 6.5)	2.2 (± 7.43)
Baseline-MCS (n=130,399,46,33,42,38,49,182)	33.5 (± 12.43)	35.9 (± 12.65)	38.1 (± 12.5)	37.8 (± 15.39)
Month 6 LOCF-MCS (n=130,399,46,33,42,38,49,182)	6.6 (± 10.67)	5.4 (± 12.8)	4.4 (± 13.22)	6.8 (± 15.19)

End point values	Group B3: Subjects Switched from Fluphenazine Decanoate	Group B4: Subjects Switched from Zuclopentixol-Decanoate	Group B5: Subjects Switched from Risperidone Micropsheres	Group C

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	55	207
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline-PCS (n=130,399,46,33,42,38,49,182)	46.9 (± 9.59)	48.7 (± 9.7)	49.2 (± 9.72)	47.3 (± 9.5)
Month 6 LOCF-PCS (n=130,399,46,33,42,38,49,182)	2.6 (± 10.27)	0 (± 7.69)	0.1 (± 8.21)	1.9 (± 8.96)
Baseline-MCS (n=130,399,46,33,42,38,49,182)	36.6 (± 13.41)	36.2 (± 12.7)	35.8 (± 16)	28.7 (± 12.93)
Month 6 LOCF-MCS (n=130,399,46,33,42,38,49,182)	2.9 (± 13.96)	8.7 (± 12.17)	5.4 (± 13.52)	11 (± 15.19)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Measure of Health Outcome (EQ-5D) Visual Analog Scale (VAS) at Month 6

End point title	Change from Baseline in Measure of Health Outcome (EQ-5D) Visual Analog Scale (VAS) at Month 6

End point description:

The EQ-5D is designed for self-completion by subjects and consists of 2 scales - the EQ-5D descriptive system and the EQ visual analog scale
(EQ VAS). The EQ-5D descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 3 levels: 1=no problems, 2=some problems, or 3=severe problems. The EQ VAS records the subjects self-rated health on a vertical, visual analog scale, with 0 representing the worst imaginable health state and 100 representing the best imaginable health state. The EQ VAS is used as a quantitative measure of health outcome as scored by the individual subject. Efficacy analysis included all subjects who received at least 1 dose of PP and had at least 1 post baseline observation on any efficacy parameter. Here 'n' signifies number of subjects analysed for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Month 6 LOCF

End point values	Group A1: Subjects Switched for Efficacy Reason	Group A2: Subjects Switched for Other Reason	Group B1: Subjects Switched from Haloperidol Decanoate	Group B2: Subjects Switched from Flupentixol Decanoate
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	143	446	53	34
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=132,398,46,33,43,38,49,179)	57.98 (± 21.179)	61.18 (± 19.987)	60.37 (± 20.93)	61.32 (± 21.574)
Month 6 LOCF(n=132,398,46,33,43,38,49,179)	8.94 (± 18.89)	8.09 (± 22.543)	8.1 (± 24.876)	15.32 (± 19.729)

End point values	Group B3: Subjects Switched from Fluphenazine Decanoate	Group B4: Subjects Switched from Zuclopentixol-Decanoate	Group B5: Subjects Switched from Risperidone Micropsheres	Group C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	55	207
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=132,398,46,33,43,38,49,179)	61.53 (± 22.105)	64.21 (± 18.805)	56.26 (± 28.171)	55.3 (± 22.608)
Month 6 LOCF(n=132,398,46,33,43,38,49,179)	4.95 (± 21.94)	7.3 (± 22.765)	9.31 (± 27.865)	12.15 (± 28.022)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Subject well-being (Subjective Well-Being under Neuroleptics Scale [SWN-S]) at Month 6

End point title	Change from Baseline in Subject well-being (Subjective Well-Being under Neuroleptics Scale [SWN-S]) at Month 6

End point description:

The SWN-S is an instrument to measure the subjective changes, such as restrictions in emotionality, the clarity of thinking, and spontaneity, that are often referred as 'pharmacogenic depression' or the 'neuroleptic induced deficit syndrome'. It consist of 20 items (10 positive items and 10 negative items). Each item of the SWN -S is rated on 6-point Likert scale (1=not at all, 2=hardly at all, 3=a little, 4=somewhat, 5=much, 6=very much). There are 5 sub scores (mental functioning, social integration, emotional regulation, physical functioning and self-control) and a SWN-S total score. After reversing the score of the 10 negative items, the item scores are added to generate the subscale scores and the total score. Efficacy analysis included all subjects who received at least 1 dose of PP and had at least 1 post baseline observation on any efficacy parameter. Here 'n' signifies number of subjects analysed for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Month 6

End point values	Group A1: Subjects Switched for Efficacy Reason	Group A2: Subjects Switched for Other Reason	Group B1: Subjects Switched from Haloperidol Decanoate	Group B2: Subjects Switched from Flupentixol Decanoate
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	143	446	53	34
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=129,392,46,33,43,37,47,180)	77.2 (± 17.97)	81 (± 16.9)	83.7 (± 12.48)	83.5 (± 18.64)
Month 6 LOCF(n=129,392,46,33,43,37,47,180)	6.6 (± 14.06)	5 (± 16.14)	3.2 (± 13.59)	8.3 (± 17.46)

End point values	Group B3: Subjects Switched from Fluphenazine Decanoate	Group B4: Subjects Switched from Zuclopentixol-Decanoate	Group B5: Subjects Switched from Risperidone Micropsheres	Group C
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	44	41	55	207
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=129,392,46,33,43,37,47,180)	81 (± 17.2)	83 (± 15.29)	80.8 (± 22.19)	73.8 (± 15.5)
Month 6 LOCF(n=129,392,46,33,43,37,47,180)	2.9 (± 15.5)	4.3 (± 14.84)	3.6 (± 15.65)	9.7 (± 20.57)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to Month 6	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.0
Reporting groups	
Reporting group title	Group A
Reporting group description: Non-acute subjects switched from oral antipsychotics	
Reporting group title	Group C
Reporting group description: Acute subjects switched from oral antipsychotics	
Reporting group title	Group B
Reporting group description: Non-acute subjects switched from long acting antipsychotics	

Serious adverse events	Group A	Group C	Group B
Total subjects affected by serious adverse events			
subjects affected / exposed	90 / 593 (15.18%)	25 / 212 (11.79%)	34 / 230 (14.78%)
number of deaths (all causes)	2	2	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung Squamous Cell Carcinoma Stage Ii			
subjects affected / exposed	0 / 593 (0.00%)	1 / 212 (0.47%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial Stenosis Limb			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis Obliterans			

subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep Vein Thrombosis			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive Crisis			
subjects affected / exposed	0 / 593 (0.00%)	1 / 212 (0.47%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Cochlea Implant			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	0 / 593 (0.00%)	1 / 212 (0.47%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Miscarriage of Partner			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Failure			

subjects affected / exposed	0 / 593 (0.00%)	1 / 212 (0.47%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Oedema			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal Behaviour			
subjects affected / exposed	2 / 593 (0.34%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Psychosis			
subjects affected / exposed	0 / 593 (0.00%)	1 / 212 (0.47%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aggression			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol Abuse			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			

subjects affected / exposed	5 / 593 (0.84%)	0 / 212 (0.00%)	2 / 230 (0.87%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	8 / 593 (1.35%)	2 / 212 (0.94%)	2 / 230 (0.87%)
occurrences causally related to treatment / all	4 / 9	2 / 2	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Apathy			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed Suicide			
subjects affected / exposed	2 / 593 (0.34%)	1 / 212 (0.47%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
Catatonia			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delusion			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delusional Disorder, Unspecified Type			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 593 (0.17%)	1 / 212 (0.47%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug Abuse			

subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination, Visual			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypochondriasis			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Insomnia			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomania			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intentional Self-Injury			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obsessive-Compulsive Disorder			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Personality Disorder			

subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric Decompensation			
subjects affected / exposed	2 / 593 (0.34%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic Disorder			
subjects affected / exposed	21 / 593 (3.54%)	12 / 212 (5.66%)	12 / 230 (5.22%)
occurrences causally related to treatment / all	9 / 25	5 / 13	10 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	12 / 593 (2.02%)	4 / 212 (1.89%)	6 / 230 (2.61%)
occurrences causally related to treatment / all	5 / 12	2 / 4	3 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia, Paranoid Type			
subjects affected / exposed	4 / 593 (0.67%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	1 / 4	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social Avoidant Behaviour			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal Ideation			
subjects affected / exposed	3 / 593 (0.51%)	1 / 212 (0.47%)	3 / 230 (1.30%)
occurrences causally related to treatment / all	0 / 4	0 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide Attempt			

subjects affected / exposed	3 / 593 (0.51%)	2 / 212 (0.94%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tension			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thinking Abnormal			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral Neck Fracture			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Animal Bite			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur Fracture			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina Pectoris			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Myocardial Infarction			

subjects affected / exposed	0 / 593 (0.00%)	1 / 212 (0.47%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Atrial Fibrillation			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus Tachycardia			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Akathisia			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyskinesia			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extrapyramidal Disorder			
subjects affected / exposed	2 / 593 (0.34%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertonia			
subjects affected / exposed	0 / 593 (0.00%)	1 / 212 (0.47%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychomotor Hyperactivity			

subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain Lower			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Pain			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal Prolapse			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis Haemorrhagic			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver Disorder			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Back Pain			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 593 (0.17%)	0 / 212 (0.00%)	0 / 230 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 593 (0.00%)	0 / 212 (0.00%)	1 / 230 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Group A	Group C	Group B
Total subjects affected by non-serious adverse events			
subjects affected / exposed	162 / 593 (27.32%)	65 / 212 (30.66%)	48 / 230 (20.87%)
Nervous system disorders			
Headache			

subjects affected / exposed	33 / 593 (5.56%)	13 / 212 (6.13%)	14 / 230 (6.09%)
occurrences (all)	36	22	22
General disorders and administration site conditions			
Injection Site Pain			
subjects affected / exposed	73 / 593 (12.31%)	29 / 212 (13.68%)	14 / 230 (6.09%)
occurrences (all)	122	49	19
Psychiatric disorders			
Insomnia			
subjects affected / exposed	51 / 593 (8.60%)	23 / 212 (10.85%)	15 / 230 (6.52%)
occurrences (all)	58	30	15
Anxiety			
subjects affected / exposed	34 / 593 (5.73%)	11 / 212 (5.19%)	10 / 230 (4.35%)
occurrences (all)	48	19	11
Psychotic Disorder			
subjects affected / exposed	16 / 593 (2.70%)	11 / 212 (5.19%)	7 / 230 (3.04%)
occurrences (all)	18	12	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2010	Amendment INT-1 was implemented prior to first-subject/first-visit and included the following changes: Additional clarification of the inclusion criteria regarding the definition of acute and non-acute subjects and corrections of the recruitment instructions and dosing and switching instructions.
10 June 2010	Amendment INT-2 was implemented prior to first-subject/first-visit and consisted of updates and corrections regarding the assessment scales included in the attachments.
29 October 2010	Amendment INT-3 was implemented before any subject had started the optional extension phase and consisted of the following changes: 1) The duration of the optional extension phase was changed from a maximum of 12 months per subject to a maximum of 12 months after the last subject had completed the 6-month study period, or until PP became available in the respective country; 2) Additional text was added to clarify that IEQ would only be administered in a limited number of countries, depending on availability of the scale in local languages; 3) In some countries, it is standard practice that PANSS is assessed by other qualified personnel besides the investigator (e.g. nurses specialized in psychiatry with specific PANSS training). In order to allow this type of qualified personnel to rate the PANSS, the text was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Study limitations were the open-label and single-arm design.

Notes: