Clinical trial results:
A Randomized, Multicenter, Double-Blind, Relapse Prevention Study of Paliperidone Palmitate 3-Month Formulation for the Treatment of Subjects with Schizophrenia

Summary

EudraCT number	2011-004676-11
Trial protocol	RO
Global end of trial date	09 April 2014

Results information

Result version number	v1 (current)
This version publication date	15 July 2016
First version publication date	15 July 2016

Trial information

Trial identification

Sponsor protocol code	R092670-PSY-3012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01529515
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	Archimedsweg 29-2333CM, Leiden, Netherlands, B235-0
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, 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	09 April 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 April 2014
Global end of trial reached?	Yes
Global end of trial date	09 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of paliperidone palmitate 3-month formulation (PP3M) compared with placebo in delaying the time to first occurrence of relapse of the symptoms of schizophrenia.

Protection of trial subjects:

The safety assessments included treatment emergent adverse events (TEAEs) pre- and post-baseline, laboratory results (including HOMA modeling and glucose abnormalities), vital sign measurement, weight, waist circumference, BMI, ECG data, EPS ratings and assessment scales (AIMS, BARS, SAS), use of anticholinergic medication, injection site evaluations, and the Columbia Suicide Severity Rating Scale (C-SSRS) was administered to assess suicidality. Adverse events and vital signs were monitored throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 April 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Colombia: 41
Country: Number of subjects enrolled	Korea, Republic of: 10
Country: Number of subjects enrolled	Mexico: 28
Country: Number of subjects enrolled	Malaysia: 29
Country: Number of subjects enrolled	Romania: 42
Country: Number of subjects enrolled	Turkey: 17
Country: Number of subjects enrolled	Ukraine: 181
Country: Number of subjects enrolled	United States: 158
Worldwide total number of subjects	506
EEA total number of subjects	42

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	504
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 509 participants were enrolled in to the study and 506 participants were entered the Open label Transition and received at least one dose of study drug (PP1M). 2 participants were enrolled but not received study drug and 1 participant was screen failure.

Period 1

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

Arms

Arm title	Open-Label Transition Phase: Paliperidone Palmitate 1-Month

Arm description:

Paliperidone palmitate intramuscular (IM) injection was administered at a dose of 150 milligram equivalents (mg eq) on Day 1, 100 mg eq on Day 8, flexible dose (50, 75, 100, or 150 mg eq) on Day 36 and 64, and on Day 92 same dose as on Day 64.

Arm type	Experimental
Investigational medicinal product name	Paliperidone Palmitate - extended release suspension for injection - 50 mg eq.
Investigational medicinal product code	R092670
Other name	Paliperidone Palmitate
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants were administered Paliperidone palmitate intramuscular (IM) injection at a dose of 100 mg eq.

Investigational medicinal product name	Paliperidone Palmitate - extended release suspension for injection - 75 mg eq.
Investigational medicinal product code	R092670
Other name	Paliperidone Palmitate
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants were administered Paliperidone Palmitate intramuscular (IM) injection at a dose of 75 mg eq.

Investigational medicinal product name	Paliperidone Palmitate - extended release suspension for injection - 100 mg eq.
Investigational medicinal product code	R092670
Other name	Paliperidone Palmitate
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants were administered Paliperidone Palmitate intramuscular (IM) injection at a dose of 100 mg eq.

Investigational medicinal product name	Paliperidone Palmitate - extended release suspension for injection - 150 mg eq.
Investigational medicinal product code	R092670
Other name	Paliperidone Palmitate

Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants were administered Paliperidone Palmitate intramuscular (IM) injection at a dose of 150 mg eq.

Number of subjects in period 1	Open-Label Transition Phase: Paliperidone Palmitate 1-Month
Started	506
Completed	379
Not completed	127
Consent withdrawn by subject	51
Adverse event, non-fatal	16
Death	1
Failed Maintenance Phase Criteria	8
Unspecified	9
Lost to follow-up	19
Lack of efficacy	19
Protocol deviation	4

Period 2

Period 2 title	Open Label Maintenance Phase
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Open-Label Maintenance Phase: Paliperidone Palmitate 3-Month

Arm description:

Paliperidone palmitate intramuscular (IM) injection was administered at a dose of 3.5-fold multiple of the PP1M dose received on Day 92 during the Transition Phase.

Arm type	Experimental
Investigational medicinal product name	Paliperidone Palmitate - extended release suspension for injection
Investigational medicinal product code	R092670
Other name	Paliperidone Palmitate
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Paliperidone palmitate IM was administered at a dose of 3.5-fold multiple of the PP1M dose (175 mg eq.

to 525 mg eq.) received on Day 92 during the Transition Phase.

Number of subjects in period 2	Open-Label Maintenance Phase: Paliperidone Palmitate 3-Month
Started	379
Completed	305
Not completed	74
Consent withdrawn by subject	15
Failed Randomization Criteria	13
Adverse event, non-fatal	10
Unspecified	10
Lost to follow-up	5
Lack of efficacy	9
Protocol deviation	12

Period 3	
Period 3 title	Double Blind Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms	
Are arms mutually exclusive?	Yes
Arm title	Double-Blind Phase: Placebo

Arm description:

Matching placebo [20 percent (%) Intralipid solution] was administered intramuscular (IM) injection every 12 weeks up to participants had a relapse event or met discontinuation criteria.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Matching placebo [20 percent (%) Intralipid solution] was administered intramuscular (IM) injection.

Arm title	Double-Blind Phase: Paliperidone Palmitate 3-Month (PP3M)

Arm description:

Paliperidone palmitate was administered at a dose of 175, 263, 350, or 525 milligram equivalents (mg eq) intramuscular (IM) injection every 12 weeks up to participants had a relapse event or met discontinuation criteria. Participants received the same dose of study agent that was administered on Day 120 of the Maintenance Phase.

Arm type	Experimental
Investigational medicinal product name	Paliperidone Palmitate - extended release suspension for injection
Investigational medicinal product code	R092670
Other name	Paliperidone Palmitate
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants were administered Paliperidone Palmitate IM at a dose of 175 mg eq., 263 mg eq., 350 mg eq. or 525 mg eq. every 12 weeks.

Number of subjects in period 3	Double-Blind Phase: Placebo	Double-Blind Phase: Paliperidone Palmitate 3-Month (PP3M)
Started	145	160
Completed	122	148
Not completed	23	12
Consent withdrawn by subject	10	7
Adverse event, non-fatal	1	-
Pregnancy	1	-
Unspecified	9	2
Lost to follow-up	1	3
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Open-Label Transition Phase: Paliperidone Palmitate 1-Month
Reporting group description:	
Paliperidone palmitate intramuscular (IM) injection was administered at a dose of 150 milligram equivalents (mg eq) on Day 1, 100 mg eq on Day 8, flexible dose (50, 75, 100, or 150 mg eq) on Day 36 and 64, and on Day 92 same dose as on Day 64.	

Reporting group values	Open-Label Transition Phase: Paliperidone Palmitate 1-Month	Total	
Number of subjects	506	506	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	504	504	
From 65 to 84 years	2	2	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	38.4		
standard deviation	± 11.15	-	
Title for Gender Units: subjects			
Female	127	127	
Male	379	379	

End points

End points reporting groups

Reporting group title	Open-Label Transition Phase: Paliperidone Palmitate 1-Month

Reporting group description:

Paliperidone palmitate intramuscular (IM) injection was administered at a dose of 150 milligram equivalents (mg eq) on Day 1, 100 mg eq on Day 8, flexible dose (50, 75, 100, or 150 mg eq) on Day 36 and 64, and on Day 92 same dose as on Day 64.

Reporting group title	Open-Label Maintenance Phase: Paliperidone Palmitate 3-Month

Reporting group description:

Paliperidone palmitate intramuscular (IM) injection was administered at a dose of 3.5-fold multiple of the PP1M dose received on Day 92 during the Transition Phase.

Reporting group title	Double-Blind Phase: Placebo

Reporting group description:

Matching placebo [20 percent (%) Intralipid solution] was administered intramuscular (IM) injection every 12 weeks up to participants had a relapse event or met discontinuation criteria.

Reporting group title	Double-Blind Phase: Paliperidone Palmitate 3-Month (PP3M)

Reporting group description:

Paliperidone palmitate was administered at a dose of 175, 263, 350, or 525 milligram equivalents (mg eq) intramuscular (IM) injection every 12 weeks up to participants had a relapse event or met discontinuation criteria. Participants received the same dose of study agent that was administered on Day 120 of the Maintenance Phase.

Subject analysis set title	Intent-to-treat (ITT) double blind (DB)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The intent-to-treat (ITT) double blind (DB) population included all participants who were randomly assigned to treatment during the Double-blind Phase and received at least one dose of Double-blind study agent.

Primary: Time to Relapse During the Double-Blind Phase

End point title	Time to Relapse During the Double-Blind Phase

End point description:

Time to relapse defined as the time between participant randomization into the double blind Phase and the first documentation of a relapse event. Median time to relapse was estimated by the Kaplan-Meier method. The value '99999' indicates data for this time points is not available.

End point type	Primary

End point timeframe:

Approximately Week 60

End point values	Double-Blind Phase: Placebo	Double-Blind Phase: Paliperidone Palmitate 3-Month (PP3M)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	145	160		
Units: Percentage of days				
median (confidence interval 95%)	395 (274 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis-I
Comparison groups	Double-Blind Phase: Placebo v Double-Blind Phase: Paliperidone Palmitate 3-Month (PP3M)
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	3.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.08
upper limit	6.99

Secondary: Change in Positive and Negative Syndrome Scale (PANSS) (Total Score) From Baseline to Endpoint in the Double-Blind Phase

End point title	Change in Positive and Negative Syndrome Scale (PANSS) (Total Score) From Baseline to Endpoint in the Double-Blind Phase

End point description:

The PANSS provides 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). Each item is rated 1 (absent) to 7 (extreme). The total score ranging from 30 to 210. Higher scores indicate more severe neuropsychiatric symptoms of schizophrenia.

End point type	Secondary

End point timeframe:

Baseline (Day 1 prior to randomization) and Endpoint (Approximately Week 60)

End point values	Double-Blind Phase: Placebo	Double-Blind Phase: Paliperidone Palmitate 3-Month (PP3M)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	159		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Baseline	54.3 (± 9.2)	54.8 (± 9.96)		

Change at Endpoint (Approximately Week 60)	6.7 (± 14.4)	-0.5 (± 8.36)		

Statistical analyses

Statistical analysis title	Statistical Analysis I
Comparison groups	Double-Blind Phase: Placebo v Double-Blind Phase: Paliperidone Palmitate 3-Month (PP3M)
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference of LS Means
Point estimate	-7.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.87
upper limit	-4.6

Secondary: Change in Clinical Global Impression Severity (CGI-S) Scale From Baseline to Endpoint in the Double-Blind Phase

End point title	Change in Clinical Global Impression Severity (CGI-S) Scale From Baseline to Endpoint in the Double-Blind Phase

End point description:

The CGI-S rating scale used to rate the severity of a participant's overall clinical condition on a 7-point scale ranging from 1 (not ill) to 7 (extremely severe).

End point type	Secondary

End point timeframe:

Baseline (Day 1 prior to randomization) and Endpoint (Approximately Week 60)

End point values	Double-Blind Phase: Placebo	Double-Blind Phase: Paliperidone Palmitate 3-Month (PP3M)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	159		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Baseline	2.8 (± 0.65)	2.7 (± 0.68)		
Change at Endpoint (Approximately Week 60)	0.4 (± 0.87)	0.1 (± 0.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis-I
Comparison groups	Double-Blind Phase: Placebo v Double-Blind Phase: Paliperidone Palmitate 3-Month (PP3M)
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference of LS Means
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.18

Secondary: Change in Personal and Social Performance (PSP) Scale From Baseline to Endpoint in the Double-Blind Phase

End point title	Change in Personal and Social Performance (PSP) Scale From Baseline to Endpoint in the Double-Blind Phase

End point description:

The PSP scale measures personal and social functioning in the domains of: a) Socially useful activities, b) Personal and social relationships, c) Self-care, and d) Disturbing and aggressive behavior. The results of the assessment were converted to a numerical score which ranges from 1 to 100. A score lying between 71 and 100 indicates a mild degree of dysfunction; scores between 31 and 70 indicate varying degrees of difficulty, and a participant with a score of <=30 had functioning so poor that he or she required intensive supervision.

End point type	Secondary

End point timeframe:

Baseline (Day 1 prior to randomization) and Endpoint (Approximately Week 60)

End point values	Double-Blind Phase: Placebo	Double-Blind Phase: Paliperidone Palmitate 3-Month (PP3M)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	157		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Baseline	68.5 (± 8.93)	68.9 (± 9.34)		

Change at Endpoint (Approximately Week 60)	-4.2 (± 9.7)	-0.5 (± 6.63)		

Statistical analyses

Statistical analysis title	Statistical Analysis I
Comparison groups	Double-Blind Phase: Placebo v Double-Blind Phase: Paliperidone Palmitate 3-Month (PP3M)
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Difference of LS Means
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.89
upper limit	5.65

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to Week 92	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0
Reporting groups	
Reporting group title	PP3M
Reporting group description: Paliperidone Palmitate 3-month formulation	
Reporting group title	Placebo
Reporting group description: Placebo	

Serious adverse events	PP3M	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 160 (2.50%)	15 / 145 (10.34%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Transaminases Increased			
subjects affected / exposed	0 / 160 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 160 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	1 / 160 (0.63%)	11 / 145 (7.59%)	
occurrences causally related to treatment / all	0 / 1	2 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia, Paranoid Type			

subjects affected / exposed	1 / 160 (0.63%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal Ideation			
subjects affected / exposed	0 / 160 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide Attempt			
subjects affected / exposed	2 / 160 (1.25%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 160 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	PP3M	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	71 / 160 (44.38%)	65 / 145 (44.83%)	
Investigations			
Blood Glucose Increased			
subjects affected / exposed	3 / 160 (1.88%)	3 / 145 (2.07%)	
occurrences (all)	3	3	
Weight Decreased			
subjects affected / exposed	2 / 160 (1.25%)	11 / 145 (7.59%)	
occurrences (all)	2	12	
Weight Increased			
subjects affected / exposed	14 / 160 (8.75%)	5 / 145 (3.45%)	
occurrences (all)	14	5	
Nervous system disorders			
Akathisia			

subjects affected / exposed	7 / 160 (4.38%)	1 / 145 (0.69%)	
occurrences (all)	7	1	
Headache			
subjects affected / exposed	14 / 160 (8.75%)	6 / 145 (4.14%)	
occurrences (all)	17	6	
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	1 / 160 (0.63%)	3 / 145 (2.07%)	
occurrences (all)	1	4	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 160 (3.13%)	3 / 145 (2.07%)	
occurrences (all)	5	3	
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 160 (1.25%)	3 / 145 (2.07%)	
occurrences (all)	2	3	
Anxiety			
subjects affected / exposed	13 / 160 (8.13%)	15 / 145 (10.34%)	
occurrences (all)	14	19	
Insomnia			
subjects affected / exposed	11 / 160 (6.88%)	17 / 145 (11.72%)	
occurrences (all)	12	17	
Schizophrenia			
subjects affected / exposed	1 / 160 (0.63%)	8 / 145 (5.52%)	
occurrences (all)	1	8	
Suicidal Ideation			
subjects affected / exposed	0 / 160 (0.00%)	3 / 145 (2.07%)	
occurrences (all)	0	3	
Infections and infestations			
Influenza			
subjects affected / exposed	3 / 160 (1.88%)	3 / 145 (2.07%)	
occurrences (all)	5	3	
Nasopharyngitis			
subjects affected / exposed	9 / 160 (5.63%)	2 / 145 (1.38%)	
occurrences (all)	9	2	

Upper Respiratory Tract Infection			
subjects affected / exposed	6 / 160 (3.75%)	3 / 145 (2.07%)	
occurrences (all)	7	3	
Urinary Tract Infection			
subjects affected / exposed	5 / 160 (3.13%)	2 / 145 (1.38%)	
occurrences (all)	5	2	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 160 (0.63%)	3 / 145 (2.07%)	
occurrences (all)	1	3	
Hyperglycaemia			
subjects affected / exposed	0 / 160 (0.00%)	4 / 145 (2.76%)	
occurrences (all)	0	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2012	The overall reason for the amendment was to include the following changes:1) Procedures to initiate study agent administration in participants 2) Inclusion and exclusion criteria were changed 3) Patient Stated-choice Preference Survey was added.4) Instructions for collection, handling, and shipping of samples for PK analysis and for screening of prohibited antipsychotics were revised, and addition of urine drug screen test strip for investigators was included.5) Blood type Rh factor was removed from the Time and Events Schedule due to logistical difficulties .6) The Double-blind Phase eligibility criteria and number of blood samples collected per participants were corrected.7) Study Agent Administrator task clarified.
02 July 2012	The overall reason for the amendment was to include the following changes from :1) The United States (US) Food and Drug Administration (FDA) instructed to increase the number of relapse events at interim analysis and the use of error spending function based on the O'Brien Fleming method was started.2) As per IEC/IRB and/or investigators visits were added to monitor for potential impending relapses during the Double-blind Phase. 3) Changes in the exclusion criteria were made to remove that was too restrictive wording.
13 May 2013	The overall reason for the amendment was to include the following changes 1) A new biomarker component was incorporated to measure serum biomarkers that predict : impending symptom exacerbation,symptom stability correlations with systemic drug exposure of paliperidone during the Maintenance and Double-blind Phases.
25 July 2013	The overall reason for the amendment was to include following changes: (1) Countries that were to participate in the biomarker component of the study were specified; (2) Clarification on where urine drug screen was to be performed was provided, (3) Clarification on procedures for serum biomarker sample handling was added. Minor formatting and edits were made for consistency and clarity. At the time of this amendment, 506 subjects were enrolled in the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported