

**Clinical trial results:****A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of Paliperidone Palmitate Evaluating Time to Relapse in Subjects With Schizoaffective Disorder**

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

**Summary**

EudraCT number	2009-017271-17
Trial protocol	BG
Global end of trial date	22 October 2013

**Results information**

Result version number	v2 (current)
This version publication date	29 May 2016
First version publication date	25 June 2015
Version creation reason	• Correction of full data set Review of data

**Trial information****Trial identification**

Sponsor protocol code	R092670-SCA-3004
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01193153
WHO universal trial number (UTN)	-

Notes:

**Sponsors**

Sponsor organisation name	Janssen Scientific Affairs, LLC
Sponsor organisation address	1125 Trenton-Harbourton Road, Titusville, United States,
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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	22 October 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 October 2013
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the efficacy of paliperidone palmitate compared with placebo in the delay of relapse of the symptoms of schizoaffective disorder and to assess the safety and tolerability of paliperidone palmitate in subjects with schizoaffective disorder.

Protection of trial subjects:

Safety evaluations for this study included the monitoring of adverse events, clinical laboratory tests, electrocardiograms (ECGs), vital sign measurements (temperature, pulse, and blood pressure), weight, and the monitoring of extrapyramidal symptoms using the Extrapyramidal Symptom Rating Scale-Abbreviated (ESRS-A). Suicidality was assessed by the Columbia Suicide Severity Rating Scale (C-SSRS). The protocol included strict requirements to ensure adequate protection of subjects participating in the study. Subjects were carefully screened using medical and psychiatric examinations and those with unstable medical conditions or suicidal behavior were excluded. In the double-blind Relapse Prevention Period, subjects who were clinically stable, exposed to double-blind medication, including placebo. The exposure of these subjects with schizoaffective disorder to placebo over an extended period under the well-controlled conditions of a clinical study was unlikely to result in any permanent damage or disability.

Background therapy:

The protocol allowed subject to continue their stable doses of antidepressants and mood stabilizers. Approximately half of subjects in the study were on adjunctive antidepressants or mood stabilizers.

Evidence for comparator: -

Actual start date of recruitment	20 September 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	Bulgaria: 39
Country: Number of subjects enrolled	India: 68
Country: Number of subjects enrolled	Malaysia: 17
Country: Number of subjects enrolled	Philippines: 17
Country: Number of subjects enrolled	Romania: 85
Country: Number of subjects enrolled	Ukraine: 116
Country: Number of subjects enrolled	United States: 316
Country: Number of subjects enrolled	South Africa: 9
Worldwide total number of subjects	667
EEA total number of subjects	124

Notes:

<b>Subjects enrolled per age group</b>	
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)	665
From 65 to 84 years	2
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects without previous exposure to paliperidone extended-release (ER) (Invega), or risperidone, received paliperidone ER 6 milligram per day (mg/day) for 4 to 6 days (during Screening) to test oral tolerability. Subjects, who had ability to tolerate the drug, as judged by treating physician, were eligible for enrollment in the study.

### Period 1

Period 1 title	Open Label
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	Paliperidone Palmitate
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Arm description:

Open Label (OL) Lead-In (13 weeks): 234 milligram (mg) injection on Day 1, 156 mg on Day 8, flexible dose between 78-234 mg on Days 36, 64, and 92. OL Stabilization (12 weeks): Same dose as Day 92 for Day 120 and 148. Double Blind (15 months): Same dose as Day 92 every 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Paliperidone Palmitate
Investigational medicinal product code	F013
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

OL (Open Label) Lead-in (13 weeks): 234 milligram (mg) injection on Day 1, 156 mg on Day 8, flexible dose between 78-234 mg on Days 36, 64, and 92. Participants who met criteria: Positive and Negative Syndrome Scale (PANSS) total score less than or equal to ( $\leq$ ) 70, and Young Mania Rating Scale [YMRS] and Hamilton Rating Scale for Depression [HAM-D-21]  $\leq 12$  at the end of open label lead-in period entered OL stabilization period (12 weeks).

Number of subjects in period 1	Paliperidone Palmitate
Started	667
Completed	334
Not completed	333
Sub failed crit ent stab prd	47
Consent withdrawn by subject	98
> 6 weeks between 2 study drug	4
Death	3
Other	22
Pregnancy	1
Adverse event	50

Lost to follow-up	42
Sub failed crt db rel prv prd	35
Lack of efficacy	31

## Period 2

Period 2 title	Double Blind Relapse Prevention Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Paliperidone Palmitate

### Arm description:

In Double Blind Relapse Prevention Period, on Day 176, subjects were randomized in a 1:1 ratio to receive either a fixed dose (fixed on day 92) injection every 4 weeks of paliperidone palmitate or matching placebo.

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

### Dosage and administration details:

Same dose as Day 92 once every 4 weeks until one of the following occurred: met the prospectively defined relapse criteria; discontinued treatment for a reason other than relapse; withdrew consent; lost to follow-up; completed 15 months of double-blind treatment.

<b>Arm title</b>	Placebo
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### Arm description:

Subjects did not receive placebo during OL lead in period and OL stabilization period. Subjects received matching placebo injections of 20 percent Intralipid (200 milligram per milliliter [mg/mL]) emulsion, once every 4 weeks during double-blind relapse prevention period.

Arm type	Placebo
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:

Subjects received matching placebo injections of 20 percent Intralipid (200 milligram per milliliter [mg/mL]) emulsion, once every 4 weeks during double-blind relapse prevention period.

<b>Number of subjects in period 2</b>	Paliperidone Palmitate	Placebo
Started	164	170
Completed	100	65
Not completed	64	105
Consent withdrawn by subject	19	30
Experienced relapse	25	57
> 6 weeks between 2 study drug	1	3
Death	2	-
Other	2	3
Pregnancy	1	-
Adverse event	12	3
Lost to follow-up	2	9

## Baseline characteristics

### Reporting groups

Reporting group title	Paliperidone Palmitate
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Reporting group description:

Open Label (OL) Lead-In (13 weeks): 234 milligram (mg) injection on Day 1, 156 mg on Day 8, flexible dose between 78-234 mg on Days 36, 64, and 92. OL Stabilization (12 weeks): Same dose as Day 92 for Day 120 and 148. Double Blind (15 months): Same dose as Day 92 every 4 weeks.

Reporting group values	Paliperidone Palmitate	Total	
Number of subjects	667	667	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	665	665	
From 65 to 84 years	2	2	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	39.5		
standard deviation	± 10.7	-	
Title for Gender Units: subjects			
Female	310	310	
Male	357	357	

## End points

### End points reporting groups

Reporting group title	Paliperidone Palmitate
Reporting group description: Open Label (OL) Lead-In (13 weeks): 234 milligram (mg) injection on Day 1, 156 mg on Day 8, flexible dose between 78-234 mg on Days 36, 64, and 92. OL Stabilization (12 weeks): Same dose as Day 92 for Day 120 and 148. Double Blind (15 months): Same dose as Day 92 every 4 weeks.	
Reporting group title	Paliperidone Palmitate
Reporting group description: In Double Blind Relapse Prevention Period, on Day 176, subjects were randomized in a 1:1 ratio to receive either a fixed dose (fixed on day 92) injection every 4 weeks of paliperidone palmitate or matching placebo.	
Reporting group title	Placebo
Reporting group description: Subjects did not receive placebo during OL lead in period and OL stabilization period. Subjects received matching placebo injections of 20 percent Intralipid (200 milligram per milliliter [mg/mL]) emulsion, once every 4 weeks during double-blind relapse prevention period.	

### Primary: Double-blind: Percentage of Participants Who Experienced Relapse

End point title	Double-blind: Percentage of Participants Who Experienced Relapse
End point description: Relapse was defined as occurrence of: psychiatric hospitalization/any intervention employed to prevent imminent hospitalization due to worsening symptoms or need for additional antipsychotic, antidepressants; deliberate self-injury, suicidal ideation that is clinically significant) determined by investigator, or violent behavior resulting in clinically significant injury to another person or property damage; worsening of any 1 or more of 8 selected Positive And Negative Syndrome Scale(PANSS) items to score of more than equal to ( $\geq 6$ ) after randomization (if the score for the corresponding item was $\leq 4$ at randomization); worsening of other measures at 2 consecutive visits. Relapse by subgroup of subjects on monotherapy, adjunctive therapy to antidepressants, subjects with psychotic and mood symptoms was examined. Double blind intent-to-treat (DB-ITT) analysis set included all subjects who received at least 1 dose of DB study medication. n= subjects evaluable at specific time-point.	
End point type	Primary
End point timeframe: Day 1 up to Month 15 of double blind relapse prevention period	

End point values	Paliperidone Palmitate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	170		
Units: percentage of participants				
number (not applicable)				
All Participants (n=164, 170)	15.2	33.5		
Monotherapy subset (n=78, 73)	11.5	32.9		
Adjunct therapy subset (n=86, 97)	18.6	34		
Psychotic Symptoms (n=164, 170)	12.8	31.2		
Mood Symptoms;Any Mood Symptoms (n=164, 170)	11	28.2		
Mood Symptoms;Manic (n=164, 170)	3	9.4		



Mood Symptoms; Depressive (n=164, 170)	4.9	13.5		
Mood Symptoms; Mixed (n=164, 170)	3	5.3		

## Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis 1
Statistical analysis description: All participants: p-value was calculated using log-rank test on time to first relapse.	
Comparison groups	Paliperidone Palmitate v Placebo
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.55
upper limit	3.99

<b>Statistical analysis title</b>	Statistical Analysis 2
Statistical analysis description: Monotherapy subset: Hazard ratio and corresponding p-value, and 95% Confidence Interval (CI) were calculated from Cox proportional hazard regression model.	
Comparison groups	Paliperidone Palmitate v Placebo
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	3.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.57
upper limit	7.28

<b>Statistical analysis title</b>	Statistical Analysis 3
Statistical analysis description: Adjunct therapy subset: Hazard ratio and corresponding p-value, and 95% CI were calculated from Cox proportional hazard regression model.	

Comparison groups	Paliperidone Palmitate v Placebo
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	2.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	3.68

<b>Statistical analysis title</b>	Statistical Analysis 4
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Statistical analysis description:

Psychotic Symptoms: Hazard ratio and corresponding p-value, and 95% CI were calculated from Cox proportional hazard regression model.

Comparison groups	Paliperidone Palmitate v Placebo
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	2.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	4.67

<b>Statistical analysis title</b>	Statistical Analysis 5
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Statistical analysis description:

Mood Symptoms (Any Mood Symptoms): Hazard ratio and corresponding p-value, and 95% CI were calculated from Cox proportional hazard regression model.

Comparison groups	Paliperidone Palmitate v Placebo
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	2.93

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	5.04

<b>Statistical analysis title</b>	Statistical Analysis 6
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Statistical analysis description:

Mood Symptoms (Manic): Hazard ratio and corresponding p-value, and 95% CI were calculated from Cox proportional hazard regression model.

Comparison groups	Paliperidone Palmitate v Placebo
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	3.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.32
upper limit	9.89

<b>Statistical analysis title</b>	Statistical Analysis 7
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Statistical analysis description:

Mood Symptoms (Depressive): Hazard ratio and corresponding p-value, and 95% CI were calculated from Cox proportional hazard regression model.

Comparison groups	Paliperidone Palmitate v Placebo
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	3.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.39
upper limit	6.98

<b>Statistical analysis title</b>	Statistical Analysis 8
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## Statistical analysis description:

Mood Symptoms (Mixed): Hazard ratio and corresponding p-value, and 95% CI were calculated from Cox proportional hazard regression model.

Comparison groups	Paliperidone Palmitate v Placebo
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.238
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	5.78

### Secondary: Double-blind: Change From Baseline in Personal and Social Performance (PSP) Total Score at Week 64 (Mixed Model Repeated Measures [MMRM] Analysis of Covariance [ANCOVA])

End point title	Double-blind: Change From Baseline in Personal and Social Performance (PSP) Total Score at Week 64 (Mixed Model Repeated Measures [MMRM] Analysis of Covariance [ANCOVA])
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## End point description:

The PSP scale was designed to assess the degree of dysfunction a subject exhibits during a month prior to any visit within 4 domains of behavior: a) socially useful activities, b) personal and social relationships, c) self-care, and d) disturbing and aggressive behavior, each rated on 6-point scale (1=absent to 6=very severe). Total transformed score from 1 to 100 is generated from raw score based on clinical interpretation of scores generated in 4 areas of functioning. A score lying between 71 and 100 indicated a good functioning; one between 31 and 70 indicated varying degrees of difficulty, and a score of less than equal to ( $\leq$ ) 30 indicated functioning so poor that participant required intensive supervision. DB ITT analysis set which included all randomly assigned participants who received at least one injection of double-blind medication. Here 'n' signifies subjects who were evaluable at each specified time point for each arm.

End point type	Secondary
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## End point timeframe:

Baseline and Week 64 of double blind relapse prevention period

End point values	Paliperidone Palmitate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	170		
Units: Units on a scale				
least squares mean (standard error)				
Baseline (n=164, 170)	72.8 ( $\pm$ 0.81)	74.5 ( $\pm$ 0.81)		
Change at Week 64 (n=98, 65)	2 ( $\pm$ 0.92)	-1.3 ( $\pm$ 1.03)		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
The null hypothesis is that there is no difference in the mean of the PSP total score between the two treatment groups.	
Comparison groups	Paliperidone Palmitate v Placebo
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.014
Method	MMRM ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	5.95
Variability estimate	Standard error of the mean
Dispersion value	1.33

## Secondary: Open-label: Change From Baseline in Personal and Social Performance (PSP) Total Score at Endpoint

End point title	Open-label: Change From Baseline in Personal and Social Performance (PSP) Total Score at Endpoint
End point description:	
<p>The PSP scale was designed to assess the degree of dysfunction a subject exhibits during a month prior to any visit within 4 domains of behavior: a) socially useful activities, b) personal and social relationships, c) self-care, and d) disturbing and aggressive behavior, each rated on 6-point scale (1=absent to 6=very severe). Total transformed score from 1 to 100 is generated from raw score based on clinical interpretation of scores generated in 4 areas of functioning. A score lying between 71 and 100 = good functioning; 31 and 70 = varying degrees of difficulty, and a score of less than equal to (<math>\leq</math>) 30 indicated functioning so poor that participant required intensive supervision. OL ITT analysis set which included all subjects who received at least one injection of open-label study medication. Last Observation Carried Forward (LOCF) method was used to impute missing values. Here 'n' signifies participants who were evaluable at each specified time point.</p>	
End point type	Secondary
End point timeframe:	
Baseline and Endpoint (Week 13/LOCF) in Open-label (OL) Lead-in period, Endpoint (Week 25/LOCF) in open-label stabilization period	

End point values	Paliperidone Palmitate			
Subject group type	Reporting group			
Number of subjects analysed	667			
Units: Units on a Scale				
arithmetic mean (standard deviation)				
OL Lead-in Period:Baseline (n=667)	51.4 ( $\pm$ 11.02)			
OL Lead-in Period:Change at Endpoint (n=622)	12.6 ( $\pm$ 13.71)			

OL Stabilization Period:Change at Endpoint (n=622)	13.8 (± 14.92)			
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## Statistical analyses

No statistical analyses for this end point

## Secondary: Double-blind: Change From Baseline in Personal and Social Performance (PSP) Total Score at Endpoint

End point title	Double-blind: Change From Baseline in Personal and Social Performance (PSP) Total Score at Endpoint
End point description: The PSP scale was designed to assess the degree of dysfunction a subject exhibits during a month prior to any visit within 4 domains of behavior: a) socially useful activities, b) personal and social relationships, c) self-care, and d) disturbing and aggressive behavior, each rated on 6-point scale (1=absent to 6=very severe). Total transformed score from 1 to 100 is generated from raw score based on clinical interpretation of scores generated in 4 areas of functioning. A score lying between 71 and 100 indicated a good functioning; one between 31 and 70 indicated varying degrees of difficulty, and a score of ≤30 indicated functioning so poor that participant required intensive supervision. DB ITT analysis set which included all randomly assigned participants who received at least one injection of double-blind study medication. LOCF method was used to impute missing values. Here 'n' signifies subjects who were evaluable at each specified time point for each arm.	
End point type	Secondary
End point timeframe: Baseline and Endpoint (Week 64/LOCF) in double-blind period	

End point values	Paliperidone Palmitate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	170		
Units: Units on a Scale				
least squares mean (standard error)				
Double-blind: Baseline (n=164, 170)	74.5 (± 0.81)	72.8 (± 0.81)		
Double-blind: Change at Endpoint (n=161,168)	0.5 (± 1.15)	-4.1 (± 1.13)		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Paliperidone Palmitate v Placebo
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	4.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.94
upper limit	7.15

### Secondary: Double-blind: Number of Participants With Personal and Social Performance (PSP) Categorical Scores

End point title	Double-blind: Number of Participants With Personal and Social Performance (PSP) Categorical Scores
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#### End point description:

The PSP scale was designed to assess the degree of dysfunction a participant exhibits during a month prior to any visit within 4 domains of behavior: a) socially useful activities, b) personal and social relationships, c) self-care, and d) disturbing and aggressive behavior, each rated on 6-point scale (1=absent to 6=very severe). Total transformed score from 1 to 100 is generated from raw score based on clinical interpretation of scores generated in 4 areas of functioning. Number of participants in each specific category; good functioning (PSP total score >70), variable functioning (PSP total score between 31 and 70), and poor functioning (PSP total score ≤30) were assessed. DB ITT analysis set which included all randomly assigned participants who received at least one injection of double-blind study medication. LOCF method was used to impute missing values. Here 'n' signifies subjects who were evaluable at each specified time point for each arm, respectively.

End point type	Secondary
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#### End point timeframe:

Baseline and Endpoint (Week 64/LOCF) in DB period

End point values	Paliperidone Palmitate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	170		
Units: participants				
Baseline: Poor (n=164, 170)	0	0		
Baseline: Variable (n=164, 170)	69	84		
Baseline: Good (n=164, 170)	95	86		
Endpoint: Poor (n=161, 168)	1	4		
Endpoint: Variable (n=161, 168)	65	95		
Endpoint: Good (n=161, 168)	95	69		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Open-label: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Total Score at Endpoint

End point title	Open-label: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Total Score at Endpoint
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#### End point description:

The PANSS is a 30-item scale designed to assess various symptoms of schizophrenia including delusions, grandiosity, blunted affect, poor attention, and poor impulse control. The 30 symptoms are

rated on a 7-point scale that ranges from 1 (absent) to 7 (extreme psychopathology). The PANSS total score consists of the sum of all 30 PANSS items and ranges from 30 to 210. Higher scores indicate worsening. Open Label (OL) Intent-to-treat (ITT) analysis set which included all subjects who received at least one injection of open-label study medication. LOCF method was used to impute missing values. Here 'n' signifies subjects who were evaluable at each specified time point.

End point type	Secondary
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End point timeframe:

Baseline and Endpoint (Week 13/LOCF) in OL Lead-in period, Endpoint (Week 25/LOCF) in open-label stabilization period

End point values	Paliperidone Palmitate			
Subject group type	Reporting group			
Number of subjects analysed	667			
Units: Units on a scale				
arithmetic mean (standard deviation)				
OL Lead-in Period:Baseline (n=667)	85.8 (± 12.76)			
OL Lead-in Period:Change at Endpoint (n=653)	-21.8 (± 16.39)			
OL Stabilization Period:Change at Endpoint (n=653)	-23.8 (± 18.3)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Double-blind: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Total Score at Endpoint

End point title	Double-blind: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Total Score at Endpoint
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End point description:

The PANSS is a 30-item scale designed to assess various symptoms of schizophrenia including delusions, grandiosity, blunted affect, poor attention, and poor impulse control. The 30 symptoms are rated on a 7-point scale that ranges from 1 (absent) to 7 (extreme psychopathology). The PANSS total score consists of the sum of all 30 PANSS items and ranges from 30 to 210. Higher scores indicate worsening. DB ITT analysis set which included all randomly assigned participants who received at least one injection of double-blind study medication. LOCF method was used to impute missing values. Here 'n' signifies subjects who were evaluable at each specified time point for each arm, respectively.

End point type	Secondary
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End point timeframe:

Baseline and Endpoint (Week 64/LOCF) in double-blind period



End point values	Paliperidone Palmitate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	170		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Double-blind: Baseline (n=164, 170)	51.1 (± 9.5)	51.8 (± 9.47)		
Double-blind: Change at Endpoint (n=161, 168)	0.5 (± 14.01)	7.4 (± 18.53)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Open-label: Change From Baseline in Hamilton Rating Scale for Depression (HAM-D-21) Total Score at Endpoint

End point title	Open-label: Change From Baseline in Hamilton Rating Scale for Depression (HAM-D-21) Total Score at Endpoint
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End point description:

The HAM-D-21 is a 21-item, clinician-rated scale to evaluate depressed mood as well as the vegetative and cognitive symptoms of depression. The items are rated on a 5-point (0 to 4) scale. The 5-point scale items use a rating of 0 (absent), 1 (doubtful to mild), 2 (mild to moderate), 3 (moderate to severe), and 4 (very severe). A rating of 4 is usually reserved for extreme symptoms. The responses for all 21 items are summed to yield the HAM-D-21 total score that ranges from 0-63. OL ITT analysis set which included all subjects who received at least one injection of open-label study medication. LOCF method was used to impute missing values. Here 'n' signifies subjects who were evaluable at each specified time point.

End point type	Secondary
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End point timeframe:

Baseline and Endpoint (Week 13/LOCF) in OL Lead-in period, Endpoint (Week 25/LOCF) in open-label stabilization period

End point values	Paliperidone Palmitate			
Subject group type	Reporting group			
Number of subjects analysed	667			
Units: Units on a scale				
arithmetic mean (standard deviation)				
OL Lead-in Period:Baseline (n=667)	20.4 (± 7.81)			
OL Lead-in Period:Change at Endpoint (n=653)	-9.7 (± 8.53)			
OL Stabilization Period:Change at Endpoint (n=653)	-9.9 (± 9.08)			

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Double-blind: Change From Baseline in Hamilton Rating Scale for Depression (HAM-D-21) Total Score at Endpoint**

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End point title	Double-blind: Change From Baseline in Hamilton Rating Scale for Depression (HAM-D-21) Total Score at Endpoint
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**End point description:**

The HAM-D-21 is a 21-item, clinician-rated scale to evaluate depressed mood as well as the vegetative and cognitive symptoms of depression. The items are rated on a 5-point (0 to 4) scale. The 5-point scale items use a rating of 0 (absent), 1 (doubtful to mild), 2 (mild to moderate), 3 (moderate to severe), and 4 (very severe). A rating of 4 is usually reserved for extreme symptoms. The responses for all 21 items are summed to yield the HAM-D-21 total score that ranges from 0-63. DB ITT analysis set which included all randomly assigned subjects who received at least one injection of double-blind study medication. LOCF method was used to impute missing values. Here 'n' signifies subjects who were evaluable at each specified time point for each arm, respectively.

End point type	Secondary
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**End point timeframe:**

Baseline and Endpoint (Week 64/LOCF) in double-blind period

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End point values	Paliperidone Palmitate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	170		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Double-blind: Baseline (n=164, 170)	5.7 (± 3.24)	5.6 (± 3.32)		
Double-blind: Change at Endpoint (n=161, 168)	0.8 (± 5.4)	3.4 (± 7.42)		

**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Open-label: Change From Baseline in Young Mania Rating Scale (YMRS) Total Score at Endpoint**

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End point title	Open-label: Change From Baseline in Young Mania Rating Scale (YMRS) Total Score at Endpoint
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**End point description:**

The YMRS was designed to measure the severity of manic symptoms, to gauge the effect of treatment, and to detect a return of manic symptoms. YMRS is a checklist of 11 items that are ranked on a scale of 0 to 4 or 0 to 8. Seven of the items (elevated mood, increased motor activity, sexual interest, sleep, language-thought disorder, appearance, and insight) are ranked 0 to 4 and have descriptors associated with each severity level (0, 1, 2, 3, 4). Four of the items (irritability, speech, content, and disruptive-aggressive behavior) are scored 0 to 8 (that is, 0, 2, 4, 6, 8). The item score is based on participant's report and clinician's behavioral observations during the interview, with emphasis on the latter. Higher scores indicate worsening. Responses are summed to yield YMRS total score ranging from 0 to 60. OL ITT analysis set which included all subjects who received at least 1 injection of OL study medication. Here 'n' signifies participants who were evaluable at each point.

End point type	Secondary
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**End point timeframe:**

Baseline and Endpoint (Week 13/LOCF) in OL Lead-in period, Endpoint (Week 25/LOCF) in open-label stabilization period

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End point values	Paliperidone Palmitate			
Subject group type	Reporting group			
Number of subjects analysed	667			
Units: Units on a scale				
arithmetic mean (standard deviation)				
OL Lead-in Period:Baseline (n=667)	18.6 (± 9.48)			
OL Lead-in Period:Change at Endpoint (n=653)	-9.9 (± 9.45)			
OL Stabilization Period:Change at Endpoint (n=653)	-10.5 (± 10.14)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Double-blind: Change From Baseline in Young Mania Rating Scale (YMRS) Total Score at Endpoint

End point title	Double-blind: Change From Baseline in Young Mania Rating Scale (YMRS) Total Score at Endpoint
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End point description:

The YMRS was designed to measure the severity of manic symptoms, the effect of treatment on mania severity, and to detect a return of manic symptoms (for example relapse or recurrence). YMRS is a checklist of 11 items that are ranked on a scale of 0 to 4/0 to 8. Seven items (elevated mood, increased motor activity, sexual interest, sleep, language-thought disorder, appearance, and insight) are ranked 0 to 4 (that is, 0, 1, 2, 3, 4). Four of the items (irritability, speech, content, and disruptive-aggressive behavior) are scored 0 to 8 (that is, 0, 2, 4, 6, 8). The item score is based on subject's report of his or her condition and clinician's behavioral observations during the interview. Higher scores indicate worsening. Responses are summed to yield YMRS total score ranging from 0 to 60. DB ITT analysis set which included all randomly assigned participants who received at least 1 injection of OL study medication. Here 'n' signifies subjects who were evaluable at each time point.

End point type	Secondary
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End point timeframe:

Baseline and Endpoint (Week 64/LOCF) in double-blind period

End point values	Paliperidone Palmitate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	170		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Double-blind: Baseline (n=164, 170)	4.4 (± 3.46)	4.4 (± 3.4)		
Double-blind: Change at Endpoint (n=161,168)	-0.1 (± 5.47)	3.2 (± 7.21)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Open-label: Change From Baseline in Clinical Global Impression - Severity Schizoaffective Scale (CGI-S-SCA) Overall Score at Endpoint

End point title	Open-label: Change From Baseline in Clinical Global Impression - Severity Schizoaffective Scale (CGI-S-SCA) Overall Score at Endpoint
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End point description:

The CGI-S-SCA is a syndrome-specific 7-point scale (from 1 indicating not ill to 7 indicating very severely ill) that includes an overall severity score as well as scores for the positive, negative, manic, and depressive domains of the illness. The CGI-S-SCA was used to assess the level of overall impairment, as well as that related to each domain, at the time of the visit and for the week prior to the visit". OL ITT analysis set which included all subjects who received at least one injection of open-label study medication. LOCF method was used to impute missing values. Here 'n' signifies subjects who were evaluable at each specified time point.

End point type	Secondary
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End point timeframe:

Baseline and Endpoint (Week 13/LOCF) in OL Lead-in period, Endpoint (Week 25/LOCF) in open-label stabilization period

<b>End point values</b>	Paliperidone Palmitate			
Subject group type	Reporting group			
Number of subjects analysed	667			
Units: Units on a scale				
arithmetic mean (standard deviation)				
OL Lead-in Period:Baseline (n=667)	4.4 (± 0.58)			
OL Lead-in Period:Change at Endpoint (n=652)	-1.3 (± 0.99)			
OL Stabilization Period:Change at Endpoint (n=652)	-1.3 (± 1.07)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Double-blind: Change From Baseline in Clinical Global Impression - Severity Schizoaffective Scale (CGI-S-SCA) Overall Score at Endpoint

End point title	Double-blind: Change From Baseline in Clinical Global Impression - Severity Schizoaffective Scale (CGI-S-SCA) Overall Score at Endpoint
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End point description:

The CGI-S-SCA is a syndrome-specific 7-point scale (from 1 indicating not ill to 7 indicating very severely ill) that includes an overall severity score as well as scores for the positive, negative, manic, and depressive domains of the illness. The CGI-S-SCA was used to assess the level of overall impairment, as well as that related to each domain, at the time of the visit and for the week prior to the visit". DB ITT analysis set which included all randomly assigned subjects who received at least one injection of double-blind study medication. LOCF method was used to impute missing values. Here 'n' signifies subjects who were evaluable at each specified time point for each arm, respectively.

End point type	Secondary
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End point timeframe:

Baseline and Endpoint (Week 64/LOCF) in double-blind period

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<b>End point values</b>	Paliperidone Palmitate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	170		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Double-blind: Baseline (n=164, 170)	2.4 (± 0.68)	2.5 (± 0.69)		
Double-blind: Change at Endpoint (n=161,168)	0 (± 1.02)	0.4 (± 1.15)		

### **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to Day 176

Adverse event reporting additional description:

Adverse events were recorded for all participants according to each period. Number of participants analyzed were all participants in Open Label period who received paliperidone palmitate, participants in double Blind - paliperidone palmitate and participants in double Blind period who received Placebo.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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### Reporting groups

Reporting group title	Open Label - Paliperidone Palmitate
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Reporting group description: -

Reporting group title	Double Blind - Placebo
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Reporting group description: -

Reporting group title	Double Blind - Paliperidone Palmitate
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Reporting group description: -

Serious adverse events	Open Label - Paliperidone Palmitate	Double Blind - Placebo	Double Blind - Paliperidone Palmitate
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 667 (8.10%)	16 / 170 (9.41%)	9 / 164 (5.49%)
number of deaths (all causes)	4	1	2
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Brain Contusion			
subjects affected / exposed	0 / 667 (0.00%)	1 / 170 (0.59%)	0 / 164 (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
Multiple Injuries			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Overdose			

subjects affected / exposed	0 / 667 (0.00%)	0 / 170 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Road Traffic Accident			
subjects affected / exposed	0 / 667 (0.00%)	1 / 170 (0.59%)	0 / 164 (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			
Deep Vein Thrombosis			
subjects affected / exposed	2 / 667 (0.30%)	0 / 170 (0.00%)	0 / 164 (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
Cardiac disorders			
Atrioventricular Block Complete			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac Failure Congestive			
subjects affected / exposed	0 / 667 (0.00%)	0 / 170 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic Shock			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Congestive Cardiomyopathy			
subjects affected / exposed	0 / 667 (0.00%)	0 / 170 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary Artery Disease			
subjects affected / exposed	0 / 667 (0.00%)	0 / 170 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myocardial Infarction			

subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Surgical and medical procedures			
Therapy Regimen Changed			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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			
Coma			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Viith Nerve Paralysis			
subjects affected / exposed	0 / 667 (0.00%)	1 / 170 (0.59%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	0 / 667 (0.00%)	0 / 170 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Ear and labyrinth disorders			
Meniere's Disease			
subjects affected / exposed	0 / 667 (0.00%)	1 / 170 (0.59%)	0 / 164 (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
Gastrointestinal disorders			
Colitis			



subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Gastroesophageal Reflux Disease			
subjects affected / exposed	0 / 667 (0.00%)	0 / 170 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Psychiatric disorders			
Completed Suicide			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Confusional State			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Delusion			
subjects affected / exposed	0 / 667 (0.00%)	1 / 170 (0.59%)	0 / 164 (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
Depression			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	2 / 164 (1.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression Suicidal			

subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Depressive Symptom			
subjects affected / exposed	2 / 667 (0.30%)	0 / 170 (0.00%)	0 / 164 (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
Hallucination, Auditory			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Homicidal Ideation			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Mania			
subjects affected / exposed	3 / 667 (0.45%)	1 / 170 (0.59%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paranoia			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Psychotic Disorder			
subjects affected / exposed	4 / 667 (0.60%)	2 / 170 (1.18%)	2 / 164 (1.22%)
occurrences causally related to treatment / all	2 / 4	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Restlessness			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Schizoaffective Disorder			

subjects affected / exposed	16 / 667 (2.40%)	7 / 170 (4.12%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	2 / 17	0 / 7	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal Ideation			
subjects affected / exposed	15 / 667 (2.25%)	2 / 170 (1.18%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	1 / 16	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide Attempt			
subjects affected / exposed	2 / 667 (0.30%)	0 / 170 (0.00%)	0 / 164 (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
Renal and urinary disorders			
Bladder Prolapse			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 667 (0.00%)	0 / 170 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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
Lobar Pneumonia			
subjects affected / exposed	1 / 667 (0.15%)	0 / 170 (0.00%)	0 / 164 (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

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

<b>Non-serious adverse events</b>	Open Label - Paliperidone Palmitate	Double Blind - Placebo	Double Blind - Paliperidone Palmitate
Total subjects affected by non-serious adverse events			
subjects affected / exposed	332 / 667 (49.78%)	62 / 170 (36.47%)	79 / 164 (48.17%)
Investigations			
Glycosylated Haemoglobin Increased			
subjects affected / exposed	1 / 667 (0.15%)	4 / 170 (2.35%)	2 / 164 (1.22%)
occurrences (all)	1	4	2
Blood Prolactin Increased			
subjects affected / exposed	4 / 667 (0.60%)	2 / 170 (1.18%)	4 / 164 (2.44%)
occurrences (all)	4	2	4
Weight Decreased			
subjects affected / exposed	2 / 667 (0.30%)	2 / 170 (1.18%)	5 / 164 (3.05%)
occurrences (all)	2	2	5
Weight Increased			
subjects affected / exposed	57 / 667 (8.55%)	8 / 170 (4.71%)	14 / 164 (8.54%)
occurrences (all)	58	9	14
Nervous system disorders			
Akathisia			
subjects affected / exposed	74 / 667 (11.09%)	3 / 170 (1.76%)	5 / 164 (3.05%)
occurrences (all)	85	3	5
Dyskinesia			
subjects affected / exposed	14 / 667 (2.10%)	3 / 170 (1.76%)	1 / 164 (0.61%)
occurrences (all)	14	4	1
Headache			
subjects affected / exposed	36 / 667 (5.40%)	6 / 170 (3.53%)	9 / 164 (5.49%)
occurrences (all)	48	6	16
Parkinsonism			
subjects affected / exposed	43 / 667 (6.45%)	3 / 170 (1.76%)	3 / 164 (1.83%)
occurrences (all)	47	4	3
Somnolence			
subjects affected / exposed	21 / 667 (3.15%)	2 / 170 (1.18%)	2 / 164 (1.22%)
occurrences (all)	26	2	2
Tremor			
subjects affected / exposed	23 / 667 (3.45%)	4 / 170 (2.35%)	2 / 164 (1.22%)
occurrences (all)	24	5	2
General disorders and administration site conditions			

Injection Site Pain subjects affected / exposed occurrences (all)	71 / 667 (10.64%) 109	2 / 170 (1.18%) 3	1 / 164 (0.61%) 1
Fatigue subjects affected / exposed occurrences (all)	20 / 667 (3.00%) 20	0 / 170 (0.00%) 0	3 / 164 (1.83%) 5
Pyrexia subjects affected / exposed occurrences (all)	8 / 667 (1.20%) 8	2 / 170 (1.18%) 2	6 / 164 (3.66%) 6
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	14 / 667 (2.10%) 16	0 / 170 (0.00%) 0	2 / 164 (1.22%) 3
Diarrhoea subjects affected / exposed occurrences (all)	20 / 667 (3.00%) 23	2 / 170 (1.18%) 2	4 / 164 (2.44%) 8
Dry Mouth subjects affected / exposed occurrences (all)	15 / 667 (2.25%) 15	1 / 170 (0.59%) 1	0 / 164 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	17 / 667 (2.55%) 18	3 / 170 (1.76%) 3	2 / 164 (1.22%) 2
Toothache subjects affected / exposed occurrences (all)	8 / 667 (1.20%) 8	2 / 170 (1.18%) 2	5 / 164 (3.05%) 6
Reproductive system and breast disorders			
Amenorrhoea subjects affected / exposed occurrences (all)	18 / 667 (2.70%) 18	2 / 170 (1.18%) 2	3 / 164 (1.83%) 5
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	10 / 667 (1.50%) 11	2 / 170 (1.18%) 4	5 / 164 (3.05%) 5
Psychiatric disorders			
Anxiety			

subjects affected / exposed occurrences (all)	9 / 667 (1.35%) 9	4 / 170 (2.35%) 4	3 / 164 (1.83%) 3
Schizoaffective Disorder subjects affected / exposed occurrences (all)	6 / 667 (0.90%) 8	3 / 170 (1.76%) 3	4 / 164 (2.44%) 4
Insomnia subjects affected / exposed occurrences (all)	67 / 667 (10.04%) 81	12 / 170 (7.06%) 13	8 / 164 (4.88%) 27
Suicidal Ideation subjects affected / exposed occurrences (all)	16 / 667 (2.40%) 19	2 / 170 (1.18%) 2	5 / 164 (3.05%) 5
Endocrine disorders Hyperprolactinaemia subjects affected / exposed occurrences (all)	9 / 667 (1.35%) 9	2 / 170 (1.18%) 2	7 / 164 (4.27%) 7
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	14 / 667 (2.10%) 16	3 / 170 (1.76%) 4	2 / 164 (1.22%) 2
Infections and infestations Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	14 / 667 (2.10%) 14	4 / 170 (2.35%) 4	7 / 164 (4.27%) 12
Nasopharyngitis subjects affected / exposed occurrences (all)	9 / 667 (1.35%) 10	6 / 170 (3.53%) 8	9 / 164 (5.49%) 11
Urinary Tract Infection subjects affected / exposed occurrences (all)	8 / 667 (1.20%) 8	4 / 170 (2.35%) 4	5 / 164 (3.05%) 5
Metabolism and nutrition disorders Increased Appetite subjects affected / exposed occurrences (all)	18 / 667 (2.70%) 18	0 / 170 (0.00%) 0	0 / 164 (0.00%) 0

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 January 2011	<p>The original protocol (dated: 24 Nov 2009 ) was updated 4 times. Out of which the third amendment dated (04 Jan 2011) was considered substantial. The amendment stated that:</p> <p>Additional analysis of the long-term antidepressants effects of paliperidone palmitate should be performed at the request of the European Regulatory Authority using the Hamilton Rating Scale for Depression (HAM-D-17), which was the first 17 items in the currently collected HAM-D- 21. In addition, switch-to-depression, worsening of preexisting depression, and de novo depression were to be evaluated at the request of the European Regulatory Authority.</p> <p>Change in the upper limit of age for inclusion in the study has been removed to allow for evaluation of efficacy and safety in subjects older than 65 years of age made at the request of the European Regulatory Authority.</p> <p>Clarification of adjunctive therapy including stable dose definition and addition of definition for essentially free of mood stabilizers or antidepressants use was allowed for subjects with limited use of mood stabilizers or antidepressants within 30 days prior to screening to be enrolled in the monotherapy group.</p> <p>At the request of the European Regulatory Authority, additional analysis were carried out for time to early discontinuation of study medication during the double-blind period for any reason including relapse (not including termination of the study by the sponsor) and for any reason not including relapse.</p>

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.

In studies for regulatory submission, subject population was chosen to minimize confounding factors. The study had a fixed duration of 15-month DB treatment. The findings may differ for other durations. There was no comparator group in OL evaluation.

Notes: