



## Clinical trial results:

### An Open-label Prospective Trial to Explore the Tolerability, Safety and Efficacy of Flexibly Dosed Paliperidone ER in Subjects With Schizophrenia

#### Summary

EudraCT number	2006-004265-34
Trial protocol	LT DE FR IT BE
Global end of trial date	04 March 2020

#### Results information

Result version number	v1 (current)
This version publication date	14 March 2021
First version publication date	14 March 2021

#### Trial information

##### Trial identification

Sponsor protocol code	R076477SCH3017
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00460512
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	Janssen-Cilag International N.V.
Sponsor organisation address	Turnhoutseweg 30, Beerse, Belgium, B-2340
Public contact	Clinical Registry Group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International N.V., 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	04 March 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 March 2020
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this study was to explore the efficacy, based on total positive and negative syndrome scale (PANSS) score, of flexibly dosed paliperidone extended-release (ER) in subjects with schizophrenia previously unsuccessfully treated with other oral antipsychotics.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practices and applicable regulatory requirements. The safety assessments included adverse events (AEs), pregnancy test, extrapyramidal symptom rating scale (ESRS), body weight, vital signs and physical examination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 April 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	9 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 77
Country: Number of subjects enrolled	Bulgaria: 40
Country: Number of subjects enrolled	Switzerland: 41
Country: Number of subjects enrolled	Germany: 326
Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	Spain: 84
Country: Number of subjects enrolled	Finland: 13
Country: Number of subjects enrolled	France: 140
Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	Greece: 130
Country: Number of subjects enrolled	Croatia: 50
Country: Number of subjects enrolled	Hungary: 55
Country: Number of subjects enrolled	Israel: 32
Country: Number of subjects enrolled	Italy: 133
Country: Number of subjects enrolled	Lithuania: 52
Country: Number of subjects enrolled	Latvia: 52
Country: Number of subjects enrolled	Netherlands: 50

Country: Number of subjects enrolled	Poland: 45
Country: Number of subjects enrolled	Portugal: 82
Country: Number of subjects enrolled	Russian Federation: 235
Country: Number of subjects enrolled	Serbia: 48
Country: Number of subjects enrolled	Sweden: 48
Country: Number of subjects enrolled	Turkey: 47
Worldwide total number of subjects	1812
EEA total number of subjects	1388

Notes:

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### **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)	1737
From 65 to 84 years	73
85 years and over	1

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 1848 subjects were screened, out of which 23 subjects were failed screening and 13 subjects did not receive study medication. Only, 1812 subjects were eligible for treatment who took at least one dose of study medication.

### Period 1

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

### Arms

<b>Arm title</b>	Paliperidone Extended Release (ER)
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Arm description:

Paliperidone ER tablet in dose range of 3 to 12 milligrams (mg) per day was given orally per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics due to lack of efficacy, lack of tolerability, lack of compliance or other reasons up to 6 months.

Arm type	Experimental
Investigational medicinal product name	Paliperidone ER
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Paliperidone ER tablet in dose range of 3 to 12 milligrams (mg) per day was given orally in core phase.

<b>Number of subjects in period 1</b>	Paliperidone Extended Release (ER)
Started	1812
Completed	1283
Not completed	529
Consent withdrawn by subject	160
Adverse event and lack of efficacy	73
Other	43
Study medication non-compliance	35
Death	3
Adverse event	91
Lost to follow-up	33
Lack of efficacy	91

**Period 2**

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

**Arms**

<b>Arm title</b>	Paliperidone Extended Release (ER)
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## Arm description:

Paliperidone ER oral tablet in dose range of 3 to 12 mg per day were continued in Extension phase as per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics due to lack of efficacy, lack of tolerability, lack of compliance or other reasons. Subjects who completed 6 months Core Treatment Phase and choose to continue receiving Paliperidone in Extension Phase (main and modified extension phase) received Paliperidone ER until it is commercially available.

Arm type	Experimental
Investigational medicinal product name	Paliperidone ER
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

## Dosage and administration details:

Paliperidone ER tablet in dose range of 3 to 12 mg per day was given orally in extension phase.

<b>Number of subjects in period 2</b>	Paliperidone Extended Release (ER)
Started	605
Completed	324
Not completed	281
Consent withdrawn by subject	104
AE or SAE	19
Other	54
Study medication non-compliance	21
Modified Extension Phase	2
Lost to follow-up	11
AE/SAE and lack of efficacy	24
Lack of efficacy	33
Missing reason	13

## Baseline characteristics

### Reporting groups

Reporting group title	Paliperidone Extended Release (ER)
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Reporting group description:

Paliperidone ER tablet in dose range of 3 to 12 milligrams (mg) per day was given orally per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics due to lack of efficacy, lack of tolerability, lack of compliance or other reasons up to 6 months.

Reporting group values	Paliperidone Extended Release (ER)	Total	
Number of subjects	1812	1812	
Title for AgeCategorical Units: subjects			
Adolescents (12-17 years)	1	1	
Adults (18-64 years)	1737	1737	
From 65 to 84 years	73	73	
85 years and over	1	1	
Title for AgeContinuous Units: years			
arithmetic mean	40.1		
standard deviation	± 12.6	-	
Title for Gender Units: subjects			
Female	726	726	
Male	1086	1086	

## End points

### End points reporting groups

Reporting group title	Paliperidone Extended Release (ER)
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Reporting group description:

Paliperidone ER tablet in dose range of 3 to 12 milligrams (mg) per day was given orally per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics due to lack of efficacy, lack of tolerability, lack of compliance or other reasons up to 6 months.

Reporting group title	Paliperidone Extended Release (ER)
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Reporting group description:

Paliperidone ER oral tablet in dose range of 3 to 12 mg per day were continued in Extension phase as per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics due to lack of efficacy, lack of tolerability, lack of compliance or other reasons. Subjects who completed 6 months Core Treatment Phase and choose to continue receiving Paliperidone in Extension Phase (main and modified extension phase) received Paliperidone ER until it is commercially available.

Subject analysis set title	Lack of Efficacy
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Paliperidone extended release (ER) tablet in dose range of 3 to 12 milligrams (mg) per day was given orally for 6 months as per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics for the main reason of lack of efficacy (defined as subjects with a baseline total Positive and Negative Syndrome Scale [PANSS] score more than or equal to [ $\geq$ ] 70 or  $\geq 2$  items scoring  $\geq 4$  in the Positive or Negative Symptom Subscale or  $\geq 3$  items scoring  $\geq 4$  in the General Psychopathology Subscale).

Subject analysis set title	Lack of Tolerability
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Paliperidone ER tablet in dose range of 3 to 12 mg per day was given orally for 6 months as per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics for the main reason of lack of tolerability (defined as the presence of clinically relevant side effects with the previous antipsychotic medication).

Subject analysis set title	Lack of Compliance
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Paliperidone ER tablet in dose range of 3 to 12 mg per day was given orally for 6 months as per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics for the main reason of lack of compliance.

Subject analysis set title	Other
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Paliperidone ER tablet in dose range of 3 to 12 mg per day was given orally for 6 months as per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics due to other reasons.

Subject analysis set title	Lack of Efficacy
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Paliperidone ER oral tablet in dose range of 3 to 12 mg per day were continued in Extension phase as per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics due to lack of efficacy (defined as subjects with a baseline total PANSS score  $\geq 70$  or  $\geq 2$  items scoring  $\geq 4$  in the Positive or Negative Symptom Subscale or  $\geq 3$  items scoring  $\geq 4$  in the General Psychopathology Subscale). Subjects who completed 6 months Core Treatment Phase and choose to continue receiving Paliperidone in Extension Phase (main and modified extension phase) received Paliperidone ER until it is commercially available.

Subject analysis set title	Lack of Tolerability
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Paliperidone ER oral tablet in dose range of 3 to 12 mg per day were continued in Extension phase as

per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics due to lack of tolerability (defined as the presence of clinically relevant side effects with the previous antipsychotic medication). Subjects who completed 6 months Core Treatment Phase and choose to continue receiving Paliperidone in Extension Phase (main and modified extension phase) received Paliperidone ER until it is commercially available.

Subject analysis set title	Lack of Compliance
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Paliperidone ER oral tablet in dose range of 3 to 12 mg per day were continued in Extension phase as per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics due to lack of compliance. Subjects who completed 6 months Core Treatment Phase and choose to continue receiving Paliperidone in Extension Phase (main and modified extension phase) received Paliperidone ER until it is commercially available.

Subject analysis set title	Other
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Paliperidone ER oral tablet in dose range of 3 to 12 mg per day were continued in Extension phase as per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics due to other reasons. Subjects who completed 6 months Core Treatment Phase and choose to continue receiving Paliperidone in Extension Phase (main and modified extension phase) received Paliperidone ER until it is commercially available.

**Primary: Core Phase: Percentage of Subjects With at Least 20 Percent Improvement in Total Positive and Negative Syndrome Scale (PANSS) Score in Those Subjects who Transitioned due to Lack of Efficacy**

End point title	Core Phase: Percentage of Subjects With at Least 20 Percent Improvement in Total Positive and Negative Syndrome Scale (PANSS) Score in Those Subjects who Transitioned due to Lack of Efficacy <sup>[1]</sup>
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End point description:

The PANSS is a 30-item scale to assess the neuropsychiatric symptoms of schizophrenia (psychiatric disorder with symptoms of emotional instability, detachment from reality, often with delusions and hallucinations, and withdrawal into the self). The PANSS provides a total score and scores for 3 subscales, the positive subscale (7 items), the negative subscale (7 items), and the general psychopathology subscale (16 items), each item scored on a scale of 1 (absent) to 7 (extreme). The total score ranges from 30 to 210 and higher score indicates greater severity. Intent to Treat (ITT) population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement.

End point type	Primary
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End point timeframe:

Up to Week 26

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical hypothesis testing was planned for this study due to the descriptive nature of this study.

<b>End point values</b>	Lack of Efficacy			
Subject group type	Subject analysis set			
Number of subjects analysed	998			
Units: percentage of subjects				
number (confidence interval 95%)	61.3 (58.2 to 64.4)			

**Statistical analyses**

No statistical analyses for this end point

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**Primary: Core Phase: Change From Baseline in Total Positive and Negative Syndrome Scale (PANSS) Score in Subjects who Transitioned due to Lack of Compliance, Lack of Tolerability and Other Reasons**

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End point title	Core Phase: Change From Baseline in Total Positive and Negative Syndrome Scale (PANSS) Score in Subjects who Transitioned due to Lack of Compliance, Lack of Tolerability and Other Reasons <sup>[2]</sup>
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End point description:

The PANSS is a 30-item scale to assess the neuropsychiatric symptoms of schizophrenia. The PANSS provides a total score and scores for 3 subscales, the positive subscale (7 items), the negative subscale (7 items), and the general psychopathology subscale (16 items), each item scored on a scale of 1 (absent) to 7 (extreme). The total score ranges from 30 to 210 and higher score indicates greater severity. ITT population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type	Primary
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End point timeframe:

Baseline up to Week 26

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: No formal statistical hypothesis testing was planned for this study due to the descriptive nature of this study.

End point values	Lack of Tolerability	Lack of Compliance	Other	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	475	155	128	
Units: units on a scale				
arithmetic mean (standard deviation)	-8.4 (± 19.2)	-18.4 (± 21.2)	-9.5 (± 17.3)	

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Core Phase: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Subscale Scores**

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End point title	Core Phase: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Subscale Scores
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End point description:

The PANSS is a 30-item scale to assess the neuropsychiatric symptoms of schizophrenia. The PANSS provides a total score and scores for 3 subscales, the positive subscale (7 items), the negative subscale (7 items), and the general psychopathology (GP) subscale (16 items), each item scored on a scale of 1 (absent) to 7 (extreme). Positive subscale score ranges from 7 (absent) to 49 (extreme psychopathology), negative subscale score ranges from 7 (absent) to 49 (extreme psychopathology) and general psychopathology subscale score ranges from 16 (absent) to 112 (extreme psychopathology). ITT population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline up to Week 26

<b>End point values</b>	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	998	475	155	128
Units: units on a scale				
arithmetic mean (standard deviation)				
Positive: Change up to Week 26	-3.8 (± 5.7)	-1.2 (± 5.7)	-4.5 (± 5.9)	-2.9 (± 5.5)
Negative: Change up to Week 26	-4.2 (± 5.9)	-3.2 (± 5.3)	-4.8 (± 6.4)	-2.5 (± 4.7)
GP: Change up to Week 26	-7.3 (± 10.5)	-4.0 (± 10.5)	-9.1 (± 11.2)	-4.2 (± 8.8)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Percentage of Subjects With at Least 20 Percent Improvement in Total Positive and Negative Syndrome Scale (PANSS) Score

End point title	Core Phase: Percentage of Subjects With at Least 20 Percent Improvement in Total Positive and Negative Syndrome Scale (PANSS) Score
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End point description:

The PANSS is a 30-item scale to assess the neuropsychiatric symptoms of schizophrenia (psychiatric disorder with symptoms of emotional instability, detachment from reality, often with delusions and hallucinations, and withdrawal into the self). The PANSS provides a total score and scores for 3 subscales, the positive subscale (7 items), the negative subscale (7 items), and the general psychopathology subscale (16 items), each item scored on a scale of 1 (absent) to 7 (extreme). The total score ranges from 30 to 210 and higher score indicates greater severity. ITT population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Up to Week 26

<b>End point values</b>	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	998	475	155	128
Units: percentage of subjects				
number (confidence interval 95%)	61.3 (58.2 to 64.4)	55.6 (51.0 to 60.1)	72.3 (64.5 to 79.1)	55.5 (46.4 to 64.3)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Marder Subscale Scores

End point title | Core Phase: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Marder Subscale Scores

End point description:

The PANSS is a 30-item scale to assess the neuropsychiatric symptoms of schizophrenia. The symptoms are rated on a 7-point scale from 1 (absent) to 7 (extreme psychopathology). Marder PANSS subscales include positive symptoms subscale consisting of 8 items with total score range of 8-56; negative symptoms subscale and disorganized thoughts subscale, each consisting of 7 items with total score range of 7-49; and uncontrolled hostility/excitement subscale and anxiety/depression subscale, each consisting of 4 items with total score range of 4-28. Higher score indicates greater severity. ITT population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type | Secondary

End point timeframe:

Baseline up to Week 26

End point values	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	998	475	155	128
Units: units on a scale				
arithmetic mean (standard deviation)				
Positive symptoms	-4.6 (± 6.3)	-1.8 (± 6.4)	-5.1 (± 6.8)	-3.2 (± 6.0)
Negative symptoms	-4.3 (± 5.9)	-3.3 (± 5.4)	-4.8 (± 6.3)	-2.4 (± 4.4)
Disorganized thoughts	-3.0 (± 4.9)	-1.8 (± 4.6)	-4.1 (± 5.1)	-1.8 (± 4.0)
Uncontrolled hostility/excitement	-1.0 (± 3.4)	-0.1 (± 3.0)	-1.7 (± 3.2)	-0.8 (± 2.9)
Anxiety/depression	-2.3 (± 3.6)	-1.3 (± 3.5)	-2.7 (± 3.7)	-1.3 (± 3.4)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Change From Baseline in Clinical Global Impression-Severity (CGI-S) Score

End point title | Core Phase: Change From Baseline in Clinical Global Impression-Severity (CGI-S) Score

End point description:

The CGI-S rating scale assesses the severity of a participant's psychotic condition on a 7-point scale ranging from 1 (not ill) to 7 (extremely severe). ITT population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement.

End point type | Secondary

End point timeframe:

Baseline up to Week 26

<b>End point values</b>	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	998	477	155	128
Units: units on a scale				
arithmetic mean (standard deviation)	-0.6 (± 1.0)	-0.3 (± 1.1)	-0.7 (± 0.9)	-0.4 (± 1.1)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Change From Baseline in Total Personal and Social Performance (PSP) Score

End point title	Core Phase: Change From Baseline in Total Personal and Social Performance (PSP) Score
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End point description:

The PSP scale assesses the degree of dysfunction within 4 domains of behavior: socially useful activities, personal and social relationships, self-care and disturbing and aggressive behavior. The score ranges from 1 to 100, divided into 10 equal intervals to rate the degree of difficulty (absent to very severe). Based on the 4 domains, the total PSP score ranges from 1 to 100 and is divided into 10 equal intervals to rate the degree of difficulty. Total PSP scores from 71 to 100 reflect a mild degree of difficulty, scores from 31 to 70 varying degrees of disability, and from 1 to 30 a functioning so poorly the subject requires intensive supervision. ITT population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline up to Week 26

<b>End point values</b>	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	966	453	147	122
Units: units on a scale				
arithmetic mean (standard deviation)	7.0 (± 12.9)	5.0 (± 14.7)	9.2 (± 13.7)	3.4 (± 12.2)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Change From Baseline in Short-Form 36 Health Survey (SF-36) Score

End point title	Core Phase: Change From Baseline in Short-Form 36 Health Survey (SF-36) Score
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End point description:

The SF-36 is a self-rated 36-item questionnaire measuring 8 dimensions (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health) that are subsequently aggregated into 2 summary scales, the physical component summary (PCS) and mental component summary (MCS). Responses to questions within each dimension were transformed to scale scores that ranged from 0 to 100, with higher scores reflecting a better health-related functional status. Secondly, the PCS and MCS were standardized to have a mean of 50 and a standard deviation of 10 so that scale scores below 50 reflect a health status below average. An increase in the norm-based scores therefore indicates an improvement. ITT population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type Secondary

End point timeframe:

Baseline up to Week 26

End point values	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	868	412	139	113
Units: units on a scale				
arithmetic mean (standard deviation)				
PCS: Change up to Week 26	1.4 (± 7.3)	1.2 (± 7.0)	1.2 (± 7.2)	1.0 (± 6.9)
MCS: Change up to Week 26	5.7 (± 11.8)	4.1 (± 13.6)	7.6 (± 13.3)	5.5 (± 11.3)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Core Phase: Number of Subjects With Satisfaction With the Study Treatment

End point title Core Phase: Number of Subjects With Satisfaction With the Study Treatment

End point description:

Subjects assessed their satisfaction with paliperidone ER on a 5-point scale: 1 (very good), 2 (good), 3 (moderate), 4 (poor) and 5 (very poor). ITT population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type Secondary

End point timeframe:

Up to Week 26

End point values	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	938	443	143	119
Units: subjects				
Very Good	147	116	35	26
Good	448	191	76	66

Moderate	199	62	15	16
Poor	112	55	13	8
Very Poor	32	19	4	3

## Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Change From Baseline in Sleep and Daytime Drowsiness Evaluation Score

End point title	Core Phase: Change From Baseline in Sleep and Daytime Drowsiness Evaluation Score
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End point description:

The Sleep and Daytime Drowsiness Evaluation Scale is a self-administered scale that rates quality of sleep and daytime drowsiness. Participants indicate on an 11 point scale how well they have slept in the previous 7 days, score ranging from 0 (very badly) to 10 (very well) and how often they have felt drowsy within the previous 7 days, score ranging from 0 (not at all) to 10 (all the time). ITT population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Here, n (number analyzed) included all subjects evaluable for specified category.

End point type	Secondary
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End point timeframe:

Baseline up to Week 26

End point values	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	979	461	154	125
Units: units on a scale				
arithmetic mean (standard deviation)				
Quality of sleep (n= 978, 461, 153, 125)	0.9 (± 2.8)	0.1 (± 2.9)	1.2 (± 2.9)	0.5 (± 2.8)
Daytime drowsiness (n= 979, 461, 154, 125)	-1.3 (± 3.1)	-1.3 (± 3.2)	-1.3 (± 3.0)	-1.0 (± 3.1)

## Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Change From Baseline in Total Extrapiramidal Symptoms Rating Scale (ESRS) Score

End point title	Core Phase: Change From Baseline in Total Extrapiramidal Symptoms Rating Scale (ESRS) Score
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End point description:

The ESRS scale assesses parkinsonism (slow movements), dystonia (abnormal muscle movement causing focal/generalized, sustained muscle contractions, postures, and involuntary movements) and dyskinetic (involuntary muscle contractions) movement subscale. Parkinsonism consists of 8 items rated

on a 7-point scale (0=absent/normal and 6=worst score), Dystonia consists of 2 items rated on a 7-point scale (0=absent and 6=extremely severe) and Dyskinetic movements consists of 7 items rated on a 7-point scale (0=none and 6=worst score). Total score: 0-102. Lower scores indicate better condition. ITT population for safety included all subjects who received paliperidone ER at least once and provided any post baseline safety information. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary
End point timeframe:	
Baseline up to Week 26	

End point values	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1001	475	155	128
Units: units on a scale				
arithmetic mean (standard deviation)	-1.2 (± 4.2)	-2.3 (± 5.3)	-0.5 (± 3.4)	-0.5 (± 2.3)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Change From Baseline in Body Weight

End point title	Core Phase: Change From Baseline in Body Weight
End point description:	
Change from baseline in body weight up to Week 26 was reported. ITT population for safety included all subjects who received paliperidone ER at least once and provided any post baseline safety information. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.	
End point type	Secondary
End point timeframe:	
Baseline up to Week 26	

End point values	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	958	444	146	118
Units: kilogram				
arithmetic mean (standard deviation)	0.39 (± 4.82)	-0.46 (± 4.75)	1.47 (± 5.13)	0.97 (± 3.67)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Change From Baseline in Pulse Rate

End point title	Core Phase: Change From Baseline in Pulse Rate
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End point description:

Change from baseline in pulse rate up to Week 26 was reported. ITT population for safety included all subjects who received paliperidone ER at least once and provided any post baseline safety information. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type Secondary

End point timeframe:

Baseline up to Week 26

End point values	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	990	472	154	125
Units: beats per minute (bpm)				
arithmetic mean (standard deviation)	0.5 (± 11.3)	-0.1 (± 12.7)	-1.9 (± 12.5)	-1.6 (± 10.6)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Change From Baseline in Systolic Blood Pressure

End point title Core Phase: Change From Baseline in Systolic Blood Pressure

End point description:

Change from baseline in systolic blood pressure up to Week 26 was reported. ITT population for safety included all subjects who received paliperidone ER at least once and provided any post baseline safety information. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type Secondary

End point timeframe:

Baseline up to Week 26

End point values	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	991	472	154	125
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)	-0.1 (± 12.4)	-1.2 (± 12.9)	-1.0 (± 15.5)	-1.0 (± 13.3)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Change From Baseline in diastolic blood pressure

End point title Core Phase: Change From Baseline in diastolic blood pressure

End point description:

Change from baseline in diastolic blood pressure up to Week 26 was reported. ITT population for safety included all subjects who received paliperidone ER at least once and provided any post baseline safety information. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type Secondary

End point timeframe:

Baseline up to Week 26

End point values	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	991	472	154	125
Units: mmHg				
arithmetic mean (standard deviation)	-0.3 (± 9.2)	-1.4 (± 9.1)	-1.3 (± 9.9)	-1.0 (± 8.9)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Number of Subjects With an Abnormal Physical Examination

End point title Core Phase: Number of Subjects With an Abnormal Physical Examination

End point description:

Number of subjects with an abnormal physical examination at week 26 were reported. ITT population for safety included all subjects who received paliperidone ER at least once and provided any post baseline safety information. Here, 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type Secondary

End point timeframe:

Week 26

End point values	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	941	441	143	120
Units: subject	177	101	17	30

### Statistical analyses

No statistical analyses for this end point

### Secondary: Core Phase: Number of Subjects with Treatment Emergent Adverse Event

End point title	Core Phase: Number of Subjects with Treatment Emergent Adverse Event
End point description: An adverse event (AE) is any untoward medical occurrence in a participant participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. TEAEs are defined as AEs with onset or worsening on or after date of first dose of study treatment. ITT population for safety included all subjects who received paliperidone ER at least once and provided any post baseline safety information.	
End point type	Secondary
End point timeframe: Up to Week 26	

End point values	Lack of Efficacy	Lack of Tolerability	Lack of Compliance	Other
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1025	490	165	131
Units: subject	552	319	69	67

### Statistical analyses

No statistical analyses for this end point

### Secondary: Extension Phase: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Total Score

End point title	Extension Phase: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Total Score
End point description: The PANSS is a 30-item scale to assess the neuropsychiatric symptoms of schizophrenia (psychiatric disorder with symptoms of emotional instability, detachment from reality, often with delusions and hallucinations, and withdrawal into the self). The PANSS provides a total score and scores for 3 subscales, the positive subscale (7 items), the negative subscale (7 items), and the general psychopathology subscale (16 items), each item scored on a scale of 1 (absent) to 7 (extreme). The total score ranges from 30 to 210 and higher score indicates greater severity. ITT population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement. Here, 'n' (number analyzed) included all subjects evaluable for specified category.	
End point type	Secondary
End point timeframe: Baseline, Week 26, Year 1, 2, 3 and Endpoint (ranging from 0.5 to 9.2 years)	

End point values	Paliperidone Extended Release (ER)			
Subject group type	Reporting group			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 26 (n=605)	-19.0 (± 16.3)			
Year 1 (n=454)	-20.3 (± 18.4)			

Year 2 (n=133)	-22.8 (± 20.6)			
Year 3 (n=56)	-24.9 (± 22.4)			
Endpoint (n=593)	-18.6 (± 21.1)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Extension Phase: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Subscale Scores

End point title	Extension Phase: Change From Baseline in Positive and Negative Syndrome Scale (PANSS) Subscale Scores
End point description:	
<p>The PANSS is a 30-item scale to assess the neuropsychiatric symptoms of schizophrenia. The PANSS provides a total score and scores for 3 subscales, the positive subscale (7 items), the negative subscale (7 items), and the general psychopathology (GP) subscale (16 items), each item scored on a scale of 1 (absent) to 7 (extreme). Positive subscale score ranges from 7 (absent) to 49 (extreme psychopathology), negative subscale score ranges from 7 (absent) to 49 (extreme psychopathology) and general psychopathology subscale score ranges from 16 (absent) to 112 (extreme psychopathology). ITT population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement. Here, 'n' (number analyzed) included all subjects evaluable for specified category.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Week 26, Year 1, 2, 3 and Endpoint (ranging from 0.5 to 9.2 years)	

End point values	Paliperidone Extended Release (ER)			
Subject group type	Reporting group			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Positive: Week 26 (n=605)	-4.6 (± 4.8)			
Positive: Year 1 (n=454)	-4.8 (± 5.3)			
Positive: Year 2 (n=133)	-5.5 (± 5.9)			
Positive: Year 3 (n=56)	-6.2 (± 6.1)			
Positive: Endpoint (n=593)	-4.3 (± 6.3)			
Negative: Week 26 (n=605)	-5.2 (± 5.3)			
Negative: Year 1 (n=454)	-5.6 (± 5.9)			
Negative: Year 2 (n=133)	-6.9 (± 6.5)			
Negative: Year 3 (n=56)	-7.4 (± 7.3)			
Negative: Endpoint (n=593)	-5.4 (± 6.4)			
GP: Week 26 (n=605)	-9.2 (± 8.6)			
GP: Year 1 (n=454)	-9.8 (± 9.5)			
GP: Year 2 (n=133)	-10.4 (± 10.6)			
GP: Year 3 (n=56)	-11.4 (± 11.6)			
GP: Endpoint (n=593)	-8.9 (± 10.9)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Extension Phase: Change From Baseline in Clinical Global Impression-Severity (CGI-S) Score

End point title	Extension Phase: Change From Baseline in Clinical Global Impression-Severity (CGI-S) Score
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End point description:

The CGI-S rating scale assesses the severity of a participant's psychotic condition on a 7-point scale ranging from 1 (not ill) to 7 (extremely severe). ITT population for efficacy included all subjects who received paliperidone ER at least once and provided at least 1 post baseline efficacy measurement. Here, 'n' (number analyzed) included all subjects evaluable for specified category.

End point type	Secondary
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End point timeframe:

Baseline, Week 26, Year 1, 2, 3 and Endpoint (ranging from 0.5 to 9.2 years)

End point values	Paliperidone Extended Release (ER)			
Subject group type	Reporting group			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 26	-0.8 (± 0.9)			
Year 1 (n=454)	-0.8 (± 1.0)			
Year 2 (n=133)	-0.9 (± 1.2)			
Year 3 (n=56)	-1.0 (± 1.2)			
Endpoint (n=593)	-0.7 (± 1.1)			

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 12 years and 10 months

Adverse event reporting additional description:

Intent to Treat (ITT) population for safety included all subjects who received paliperidone ER at least once and provided any post baseline safety information.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1 & 10.0

### Reporting groups

Reporting group title	Paliperidone ER – Main and Modified Extension Phase
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Reporting group description:

Paliperidone ER oral tablet in dose range of 3 to 12 mg per day were continued in Extension phase as per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics due to lack of efficacy, lack of tolerability, lack of compliance or other reasons. Subjects who completed 6 months Core Treatment Phase and choose to continue receiving Paliperidone in Extension Phase (main and modified extension phase) received Paliperidone ER until it is commercially available.

Reporting group title	Paliperidone Extended Release (ER) – Core Treatment Phase
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Reporting group description:

Paliperidone ER tablet in dose range of 3 to 12 milligrams (mg) per day was given orally per Investigator's discretion to subjects who transitioned to Paliperidone ER from other oral antipsychotics due to lack of efficacy, lack of tolerability, lack of compliance or other reasons up to 6 months.

<b>Serious adverse events</b>	Paliperidone ER – Main and Modified Extension Phase	Paliperidone Extended Release (ER) – Core Treatment Phase	
Total subjects affected by serious adverse events			
subjects affected / exposed	80 / 605 (13.22%)	160 / 1811 (8.83%)	
number of deaths (all causes)	3	3	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute Lymphocytic Leukaemia			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Neoplasm Malignant			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Rectal Cancer			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory Collapse			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Appendicectomy			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder Operation			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal Operation			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rehabilitation Therapy			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenectomy			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Stent Placement			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose Vein Operation			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	0 / 605 (0.00%)	2 / 1811 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 605 (0.00%)	2 / 1811 (0.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
Malaise			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organ Failure			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Treatment Noncompliance			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Galactorrhoea			

subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Respiratory, thoracic and mediastinal disorders</b>			
Dyspnoea			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Disorder			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Psychiatric disorders</b>			
Abnormal Behaviour			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Psychosis			
subjects affected / exposed	1 / 605 (0.17%)	2 / 1811 (0.11%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aggression			
subjects affected / exposed	1 / 605 (0.17%)	3 / 1811 (0.17%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitation			
subjects affected / exposed	2 / 605 (0.33%)	3 / 1811 (0.17%)	
occurrences causally related to treatment / all	2 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholism			
subjects affected / exposed	1 / 605 (0.17%)	2 / 1811 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Anxiety			
subjects affected / exposed	7 / 605 (1.16%)	17 / 1811 (0.94%)	
occurrences causally related to treatment / all	1 / 12	3 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety Disorder			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Attention-Seeking Behaviour			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional State			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 605 (0.17%)	4 / 1811 (0.22%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delusion			
subjects affected / exposed	5 / 605 (0.83%)	7 / 1811 (0.39%)	
occurrences causally related to treatment / all	1 / 5	4 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delusional Disorder, Persecutory Type			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed Mood			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			

subjects affected / exposed	3 / 605 (0.50%)	7 / 1811 (0.39%)
occurrences causally related to treatment / all	0 / 4	3 / 8
deaths causally related to treatment / all	0 / 0	0 / 0
Depressive Symptom		
subjects affected / exposed	1 / 605 (0.17%)	2 / 1811 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Disorientation		
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)
occurrences causally related to treatment / all	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Drug Dependence		
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Emotional Disorder		
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Factitious Disorder		
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hallucination		
subjects affected / exposed	4 / 605 (0.66%)	4 / 1811 (0.22%)
occurrences causally related to treatment / all	1 / 6	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Hallucination, Auditory		
subjects affected / exposed	0 / 605 (0.00%)	3 / 1811 (0.17%)
occurrences causally related to treatment / all	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Hypomania		

subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Impulsive Behaviour</b>			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Insomnia</b>			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Mania</b>			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Negative Thoughts</b>			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Panic Attack</b>			
subjects affected / exposed	1 / 605 (0.17%)	2 / 1811 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Paranoia</b>			
subjects affected / exposed	2 / 605 (0.33%)	2 / 1811 (0.11%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Persecutory Delusion</b>			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Psychotic Disorder</b>			

subjects affected / exposed	11 / 605 (1.82%)	43 / 1811 (2.37%)
occurrences causally related to treatment / all	5 / 12	22 / 45
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Restlessness</b>		
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Schizophrenia</b>		
subjects affected / exposed	18 / 605 (2.98%)	28 / 1811 (1.55%)
occurrences causally related to treatment / all	6 / 20	10 / 33
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Schizophrenia, Paranoid Type</b>		
subjects affected / exposed	2 / 605 (0.33%)	9 / 1811 (0.50%)
occurrences causally related to treatment / all	0 / 6	2 / 13
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Self Injurious Behaviour</b>		
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Sleep Disorder</b>		
subjects affected / exposed	0 / 605 (0.00%)	2 / 1811 (0.11%)
occurrences causally related to treatment / all	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Suicidal Ideation</b>		
subjects affected / exposed	3 / 605 (0.50%)	4 / 1811 (0.22%)
occurrences causally related to treatment / all	0 / 4	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Suicide Attempt</b>		
subjects affected / exposed	3 / 605 (0.50%)	9 / 1811 (0.50%)
occurrences causally related to treatment / all	1 / 3	3 / 10
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Tension</b>		

subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Investigations</b>			
<b>Blood Potassium Decreased</b>			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Haematocrit Decreased</b>			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Platelet Count Decreased</b>			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Transaminases Increased</b>			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Weight Decreased</b>			
subjects affected / exposed	2 / 605 (0.33%)	2 / 1811 (0.11%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Weight Increased</b>			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Injury, poisoning and procedural complications</b>			
<b>Alcohol Poisoning</b>			
subjects affected / exposed	2 / 605 (0.33%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ankle Fracture			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus Fracture			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional Overdose			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 605 (0.00%)	2 / 1811 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Aorta Hypoplasia			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac disorders			
Acute Coronary Syndrome			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Failure			
subjects affected / exposed	2 / 605 (0.33%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	

Cardiac Failure Acute			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial Infarction			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Akathisia			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autonomic Nervous System Imbalance			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular Accident			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Disturbance in Attention			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Extrapyramidal Disorder			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokinesia			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychomotor Hyperactivity			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sensory Disturbance			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	3 / 18	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Hernia			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Inguinal Hernia			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis Chronic			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis Acute			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular Damage			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Acne Conglobata			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dermatitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 605 (0.17%) 0 / 1 0 / 0	0 / 1811 (0.00%) 0 / 0 0 / 0	
Urticaria subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 605 (0.17%) 1 / 1 0 / 0	0 / 1811 (0.00%) 0 / 0 0 / 0	
Renal and urinary disorders Renal Failure subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 605 (0.17%) 0 / 1 0 / 0	1 / 1811 (0.06%) 0 / 1 0 / 0	
Musculoskeletal and connective tissue disorders Muscle Rigidity subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 605 (0.17%) 0 / 1 0 / 0	1 / 1811 (0.06%) 0 / 1 0 / 0	
Rhabdomyolysis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 605 (0.00%) 0 / 0 0 / 0	1 / 1811 (0.06%) 0 / 1 0 / 0	
Infections and infestations Abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 605 (0.00%) 0 / 0 0 / 0	1 / 1811 (0.06%) 0 / 1 0 / 0	
Appendicitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 605 (0.00%) 0 / 0 0 / 0	1 / 1811 (0.06%) 0 / 1 0 / 0	
Eczema Herpeticum			

subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gastrointestinal Infection</b>			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Pneumonia</b>			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Pyelonephritis</b>			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Septic Shock</b>			
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Metabolism and nutrition disorders</b>			
<b>Hypokalaemia</b>			
subjects affected / exposed	0 / 605 (0.00%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hyponatraemia</b>			
subjects affected / exposed	0 / 605 (0.00%)	2 / 1811 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hypovolaemia</b>			
subjects affected / exposed	1 / 605 (0.17%)	1 / 1811 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Metabolic Syndrome</b>			

subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Obesity</b>		
subjects affected / exposed	1 / 605 (0.17%)	0 / 1811 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Paliperidone ER – Main and Modified Extension Phase	Paliperidone Extended Release (ER) – Core Treatment Phase	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	270 / 605 (44.63%)	680 / 1811 (37.55%)	
<b>Investigations</b>			
Weight Decreased			
subjects affected / exposed	13 / 605 (2.15%)	15 / 1811 (0.83%)	
occurrences (all)	13	15	
Weight Increased			
subjects affected / exposed	56 / 605 (9.26%)	65 / 1811 (3.59%)	
occurrences (all)	59	66	
<b>Vascular disorders</b>			
Hypertension			
subjects affected / exposed	16 / 605 (2.64%)	23 / 1811 (1.27%)	
occurrences (all)	17	24	
<b>Nervous system disorders</b>			
Akathisia			
subjects affected / exposed	24 / 605 (3.97%)	56 / 1811 (3.09%)	
occurrences (all)	27	60	
Extrapyramidal Disorder			
subjects affected / exposed	30 / 605 (4.96%)	64 / 1811 (3.53%)	
occurrences (all)	38	74	
Headache			
subjects affected / exposed	29 / 605 (4.79%)	65 / 1811 (3.59%)	
occurrences (all)	36	76	

Sedation			
subjects affected / exposed	14 / 605 (2.31%)	27 / 1811 (1.49%)	
occurrences (all)	15	27	
Somnolence			
subjects affected / exposed	34 / 605 (5.62%)	76 / 1811 (4.20%)	
occurrences (all)	43	80	
Tremor			
subjects affected / exposed	21 / 605 (3.47%)	40 / 1811 (2.21%)	
occurrences (all)	22	42	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	22 / 605 (3.64%)	56 / 1811 (3.09%)	
occurrences (all)	25	58	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	16 / 605 (2.64%)	50 / 1811 (2.76%)	
occurrences (all)	16	51	
Psychiatric disorders			
Agitation			
subjects affected / exposed	8 / 605 (1.32%)	37 / 1811 (2.04%)	
occurrences (all)	14	44	
Anxiety			
subjects affected / exposed	52 / 605 (8.60%)	115 / 1811 (6.35%)	
occurrences (all)	72	132	
Depression			
subjects affected / exposed	22 / 605 (3.64%)	66 / 1811 (3.64%)	
occurrences (all)	25	68	
Insomnia			
subjects affected / exposed	61 / 605 (10.08%)	166 / 1811 (9.17%)	
occurrences (all)	79	188	
Sleep Disorder			
subjects affected / exposed	14 / 605 (2.31%)	54 / 1811 (2.98%)	
occurrences (all)	35	73	
Musculoskeletal and connective tissue disorders			
Muscle Rigidity			

subjects affected / exposed occurrences (all)	13 / 605 (2.15%) 14	21 / 1811 (1.16%) 23	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	14 / 605 (2.31%) 21	39 / 1811 (2.15%) 47	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 June 2007	The amendment was issued for following changes. The maximum number of subjects per site was increased to allow larger sites to enroll more than 8 subjects. Inclusion criteria were updated as pregnancy tests were not to be performed for women of non-childbearing potential. Sections were updated based on text of the Summary of Product Characteristics (SmPC) submitted to the European Medicines Agency (EMA). Exclusion criteria were updated to make clear that current or history of substance use or abuse according to Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria was allowed and current or history of substance dependence according to DSM-IV criteria was not allowed. (This was the intention of the original protocol text, but the initial wording could be misunderstood). Concomitant therapy section was updated to allow the use of trihexyphenidyl as in some countries, benztropine mesylate or biperidene are not available, but trihexyphenidyl is. Footnote in the flow chart was reworded to better reflect the adverse events (AEs) to be recorded during the screening visit. As qualification of a clinician or physician was not required, the term "qualified" was deleted from Section 9. The wording in Section 10.2 Withdrawal from the study of the protocol was made consistent with other protocols. Section 16.2.2 was updated to clarify that the investigator financial disclosure form (IFDF) only needs to be collected if required by national law. Writing errors were corrected.
07 August 2007	The amendment was issued for following changes. The INVEGA Summary of Product Characteristics (SmPC), which was approved by the EMA, was added as attachment to the protocol and referred to in the body text to provide investigators with up-to-date medical guidance. In order to make the protocol consistent with the INVEGA SmPC several sections were updated.
27 August 2010	12-mg tablets were made unavailable. The Main Extension Phase was ended with the 'End of Main Extension Phase Visit' as originally described and a Modified Extension Phase was added to start immediately after this 'End of Main Extension Phase Visit'. The assessments during the Modified Extension Phase will be limited to clinical global impression severity (CGI-S) and adverse event (AE) reporting, both on a quarterly basis, and a body weight measurement at the end of the Modified Extension Phase.
01 February 2012	The Time and Events Schedule was updated to reflect the changes in the Modified Extension Phase. Regular Follow-Up Visits Section (Every 6 Months) during Modified Extension Phase was added. The sponsor suggested to have the Modified Extension Phase visits performed every 6 months, instead of every 3 months. As a consequence, CGI-S was performed every 6 months during the Modified Extension Phase.

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.

As this was an open-label, single-group trial, randomization and blinding procedures were not applicable. Comparability of the treatment cohorts was only adjusted for known covariates as subjects were not randomized over treatment cohorts.

Notes: