



Clinical trial results:

A Randomized, Multicenter, Double-Blind, Active-Controlled, Flexible-Dose, Parallel-Group Study of the Efficacy and Safety of Extended Release Paliperidone for the Treatment of Symptoms of Schizophrenia in Adolescent Subjects, 12 to 17 Years of Age

Summary

EudraCT number	2009-014811-11
Trial protocol	ES CZ SK Outside EU/EEA
Global end of trial date	11 June 2012

Results information

Result version number	v2 (current)
This version publication date	29 May 2016
First version publication date	05 February 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	R076477PSZ3003
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01009047
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International NV
Sponsor organisation address	Antwerpseweg 15-17, B-2340 Beerse , Belgium,
Public contact	Clinical Registry Group, Janssen-Cilag International NV, +1 609-730-2436, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International NV, +1 609-730-2436, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000014-PIP01-07
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 June 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 June 2012
Global end of trial reached?	Yes
Global end of trial date	11 June 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the efficacy of paliperidone PR relative to aripiprazole in the treatment of symptoms of schizophrenia in adolescent subjects (aged 12 to 17 years of age, inclusive) at the Week 8 endpoint as measured by the change from baseline in the Positive and Negative Syndrome Scale for Schizophrenia (PANSS) total score.

Protection of trial subjects:

The safety assessments included laboratory measurements (for example, chemistry, hematology, urinalysis, lipid panel, and insulin related tests), body weight, waist circumference, electrocardiograms (ECGs), and physical examination. The Abnormal Involuntary Movement Scale (AIMS), Barnes Akathisia Rating Scale (BARS), and Simpson Angus Rating Scale (SARS) were used to assess extrapyramidal symptoms (EPS) and dyskinesia. The Columbia Suicide Severity Rating Scale (C-SSRS) was administered to assess suicidality. Adverse events and vital signs were monitored throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 November 2009
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	India: 39
Country: Number of subjects enrolled	Romania: 9
Country: Number of subjects enrolled	Russian Federation: 114
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Ukraine: 37
Country: Number of subjects enrolled	United States: 22
Country: Number of subjects enrolled	Spain: 5
Worldwide total number of subjects	227
EEA total number of subjects	15

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	227
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 228 subjects were included in the all randomized analysis set, 227 included in the safety analysis set and 226 in the intent-to-treat analysis set.

Pre-assignment

Screening details:

A total of 41 sites in 7 countries participated in this study including 6 sites in India, 1 site in Romania, 16 sites in Russian Federation, 1 site in Slovakia, 3 sites in Spain, 8 sites in Ukraine, and 6 sites in the United States.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

To maintain the blind, study drug was packaged in blister cards which contained over encapsulated tablets.

Arms

Are arms mutually exclusive?	Yes
Arm title	Paliperidone ER

Arm description:

Paliperidone extended release (ER) was administered as oral capsule at a dose of 6 milligram (mg) for 1 week and then was administered at a dose of either 3, 6 or 9 mg up to Week 26, once daily in the morning.

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

Dosage and administration details:

Paliperidone ER was administered as oral capsule at a dose of 6 milligram (mg) for 1 week and then was administered at a dose of either 3, 6 or 9 mg up to Week 26, once daily in the morning.

Arm title	Aripiprazole
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Arm description:

Aripiprazole was administered as oral capsule at a dose of 2 mg on Days 1 and 2, 5 mg on Days 3 and 4, 10 mg on Days 5, 6 and 7; and then was administered at a dose of either 5 or 10 or 15 mg up to Week 26, once daily in the morning.

Arm type	Experimental
Investigational medicinal product name	Aripiprazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Aripiprazole was administered as oral capsule at a dose of 2 mg on Days 1 and 2, 5 mg on Days 3 and 4, 10 mg on Days 5, 6 and 7; and then was administered as a dose of either 5 or 10 or 15 mg up to Week 26, once daily in the morning.

Number of subjects in period 1	Paliperidone ER	Aripiprazole
Started	113	114
Completed	85	89
Not completed	28	25
Lost To Follow-Up	-	2
Adverse Event	5	-
Other	3	1
Lack Of Efficacy	4	11
Withdrawal Of Consent	16	11

Baseline characteristics

Reporting groups

Reporting group title	Paliperidone ER
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Reporting group description:

Paliperidone extended release (ER) was administered as oral capsule at a dose of 6 milligram (mg) for 1 week and then was administered at a dose of either 3, 6 or 9 mg up to Week 26, once daily in the morning.

Reporting group title	Aripiprazole
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Reporting group description:

Aripiprazole was administered as oral capsule at a dose of 2 mg on Days 1 and 2, 5 mg on Days 3 and 4, 10 on mg Days 5, 6 and 7; and then was administered at a dose of either 5 or 10 or 15 mg up to Week 26, once daily in the morning.

Reporting group values	Paliperidone ER	Aripiprazole	Total
Number of subjects	113	114	227
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	113	114	227
Title for AgeContinuous Units: years			
arithmetic mean	15.3	15.4	
standard deviation	± 1.47	± 1.45	-
Title for Gender Units: subjects			
Female	39	38	77
Male	74	76	150

End points

End points reporting groups

Reporting group title	Paliperidone ER
Reporting group description: Paliperidone extended release (ER) was administered as oral capsule at a dose of 6 milligram (mg) for 1 week and then was administered at a dose of either 3, 6 or 9 mg up to Week 26, once daily in the morning.	
Reporting group title	Aripiprazole
Reporting group description: Aripiprazole was administered as oral capsule at a dose of 2 mg on Days 1 and 2, 5 mg on Days 3 and 4, 10 on mg Days 5, 6 and 7; and then was administered at a dose of either 5 or 10 or 15 mg up to Week 26, once daily in the morning.	

Primary: Change From Baseline in the Positive and Negative Syndrome Scale (PANSS) Total Score at Day 56

End point title	Change From Baseline in the Positive and Negative Syndrome Scale (PANSS) Total Score at Day 56
End point description: The PANSS is a 30-item scale with each item rated on a scale of 1 (absent) to 7 (extreme psychopathology), designed to assess various symptoms of schizophrenia including delusions, grandiosity, blunted affect, poor attention, and poor impulse control. The PANSS total score consists of the sum of all 30 PANSS items and ranges from 30 to 210. Higher scores indicate worsening. The intent-to-treat (ITT) population was used as analysis set which included all randomly assigned participants who received at least 1 dose of double-blind study drug, had both a Baseline measurement and at least 1 Post-Baseline measurement in the double-blind phase. Last observation carried forward (LOCF) method was used.	
End point type	Primary
End point timeframe: Baseline and Day 56	

End point values	Paliperidone ER	Aripiprazole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	114		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	89.6 (± 12.22)	92 (± 12.09)		
Day 56	-19.3 (± 13.8)	-19.8 (± 14.56)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Analysis of covariance (ANCOVA) model with treatment (paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate was used.	
Comparison groups	Paliperidone ER v Aripiprazole

Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.935
Method	ANCOVA
Parameter estimate	L S mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.46
upper limit	3.76
Variability estimate	Standard error of the mean
Dispersion value	1.83

Secondary: Change From Baseline in PANSS Total Score at Day 182

End point title	Change From Baseline in PANSS Total Score at Day 182
End point description:	
<p>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. The ITT population included all randomly assigned participants who received at least 1 dose of double-blind study drug, had both a Baseline measurement and at least 1 Post-Baseline measurement in the double-blind phase. Last observation carried forward (LOCF) method was used.</p>	
End point type	Secondary
End point timeframe:	
Baseline and Day 182	

End point values	Paliperidone ER	Aripiprazole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	114		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	89.6 (± 12.22)	92 (± 12.09)		
Change at Day 182	-25.6 (± 16.88)	-26.8 (± 18.82)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
<p>Analysis of covariance (ANCOVA) model with treatment groups (paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate was used.</p>	
Comparison groups	Paliperidone ER v Aripiprazole

Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.877
Method	ANCOVA
Parameter estimate	L S mean difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.68
upper limit	4
Variability estimate	Standard error of the mean
Dispersion value	2.2

Secondary: Change From Baseline in Marder Factor Negative Symptoms Score at Day 56 and 182

End point title	Change From Baseline in Marder Factor Negative Symptoms Score at Day 56 and 182
End point description:	
The PANSS negative subscale based on marder factor assesses 7 negative-symptoms of schizophrenia. Negative symptoms represent a diminution or loss of normal functions. The symptoms are rated on a 7-point scale, with a range of 7 (absent) to 49 (extreme psychopathology). The ITT population included all randomly assigned participants who received at least 1 dose of double-blind study drug, had both a Baseline measurement and at least 1 Post-Baseline measurement in the double-blind phase. Last observation carried forward (LOCF) method was used.	
End point type	Secondary
End point timeframe:	
Baseline, Day 56 and Day 182	

End point values	Paliperidone ER	Aripiprazole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	114		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	23.2 (± 4.92)	23.3 (± 4.54)		
Change at Day 56	-4.3 (± 4.56)	-4.7 (± 4.61)		
Change at Day 182	-6 (± 5.51)	-6.2 (± 5.84)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Day 56: Analysis of covariance (ANCOVA) model with treatment (paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate was used.	
Comparison groups	Paliperidone ER v Aripiprazole

Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.341
Method	ANCOVA
Parameter estimate	L S mean difference
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	1.59
Variability estimate	Standard error of the mean
Dispersion value	0.5

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Day 182: Analysis of covariance (ANCOVA) model with treatment (paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate was used.	
Comparison groups	Paliperidone ER v Aripiprazole
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.723
Method	ANCOVA
Parameter estimate	LS Mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	1.53
Variability estimate	Standard error of the mean
Dispersion value	0.66

Secondary: Change From Baseline in Other Marder Factors Scores at Day 56 and 182	
End point title	Change From Baseline in Other Marder Factors Scores at Day 56 and 182
End point description:	
The subscales based on marder factors are: positive symptoms, disorganised thoughts factor, uncontrolled hostility/excitement factor, and anxiety/depression factor. The symptoms are rated on a 7-point scale, with a range of 8 to 56 for positive symptoms, 7 to 49 for disorganized thoughts and 4 to 28 for Uncontrolled hostility/excitement and anxiety/depression. Higher score indicate worsening.	
End point type	Secondary
End point timeframe:	
Baseline, Day 56 and 182	

End point values	Paliperidone ER	Aripiprazole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	114		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Positive symptoms	24.6 (± 4.08)	24.9 (± 4.32)		
Change at Day 56: Positive symptoms	-6.1 (± 4.96)	-5.6 (± 4.83)		
Change at Day 182: Positive symptoms	-7.8 (± 5.82)	-7.8 (± 6.03)		
Baseline: Negative symptoms	23.2 (± 4.92)	23.3 (± 4.54)		
Change at Day 56: Negative symptoms	-4.3 (± 4.56)	-4.7 (± 4.61)		
Change at Day 182: Negative symptoms	-6 (± 5.51)	-6.2 (± 5.84)		
Baseline: Disorganized thoughts	21.4 (± 4.4)	22.1 (± 3.86)		
Change at Day 56: Disorganized thoughts	-4 (± 3.34)	-4.1 (± 3.4)		
Change at Day 182: Disorganized thoughts	-5.5 (± 4.18)	-5.7 (± 4.46)		
Baseline: Uncontrolled hostility	10.7 (± 3.19)	11.7 (± 3.48)		
Change at Day 56: Uncontrolled hostility	-2.5 (± 2.67)	-2.9 (± 3.05)		
Change at Day 182: Uncontrolled hostility	-3.2 (± 3.11)	-3.8 (± 3.97)		
Baseline: Anxiety/depression	9.7 (± 3.17)	10 (± 3.26)		
Change at Day 56: Anxiety/depression	-2.4 (± 3.08)	-2.6 (± 2.81)		
Change at Day 182: Anxiety/depression	-3 (± 3.29)	-3.2 (± 3.17)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Change at Day 56: Positive Symptoms - ANCOVA model with treatment groups (paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate.	
Comparison groups	Paliperidone ER v Aripiprazole
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.351
Method	ANCOVA

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Change at Day 182: Positive Symptoms - ANCOVA model with treatment groups (paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate was used.	
Comparison groups	Paliperidone ER v Aripiprazole

Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.691
Method	ANCOVA

Statistical analysis title	Statistical Analysis 3
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Statistical analysis description:

Change at Day 56: Disorganized thoughts - ANCOVA model with treatment groups (paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate was used.

Comparison groups	Paliperidone ER v Aripiprazole
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.965
Method	ANCOVA

Statistical analysis title	Statistical Analysis 4
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Statistical analysis description:

Change at Day 182: Disorganized thoughts - ANCOVA model with treatment groups (paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate was used.

Comparison groups	Paliperidone ER v Aripiprazole
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.766
Method	ANCOVA

Statistical analysis title	Statistical Analysis 5
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Statistical analysis description:

Change at Day 56: Uncontrolled hostility/ excitement - ANCOVA model with treatment groups (paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate was used.

Comparison groups	Paliperidone ER v Aripiprazole
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.984
Method	ANCOVA

Statistical analysis title	Statistical Analysis 6
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Statistical analysis description:

Change at Day 182: Uncontrolled Hostility/ Excitement - ANCOVA model with treatment groups

(paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate was used.

Comparison groups	Paliperidone ER v Aripiprazole
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.985
Method	ANCOVA

Statistical analysis title	Statistical Analysis 7
Statistical analysis description: Change at Day 56: Anxiety/ depression - ANCOVA model with treatment groups (paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate.	
Comparison groups	Paliperidone ER v Aripiprazole
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.803
Method	ANCOVA

Statistical analysis title	Statistical Analysis 8
Statistical analysis description: Change at Day 182: Anxiety/ depression - ANCOVA model with treatment groups (paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate.	
Comparison groups	Paliperidone ER v Aripiprazole
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.745
Method	ANCOVA

Secondary: Change From Baseline in Other PANSS Factors and Subscales at Day 56 and 182

End point title	Change From Baseline in Other PANSS Factors and Subscales at Day 56 and 182
End point description: The PANSS provides a total score (sum of the scores of all 30 items) and scores for 3 subscales, the positive subscale (7 items), the negative subscale (7 items), and the general psychopathology subscale (16 items), each rated on a scale of 1 (absent) to 7 (extreme).	
End point type	Secondary
End point timeframe: Baseline, Day 56 and 182	

End point values	Paliperidone ER	Aripiprazole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	114		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Positive Subscale	21.5 (± 4.14)	22.5 (± 4.26)		
Change at Day 56: Positive Subscale	-6.4 (± 4.54)	-6.2 (± 4.91)		
Change at Day 182: Positive Subscale	-8 (± 5.16)	-8.3 (± 6.09)		
Baseline: Negative Subscale	23.8 (± 4.55)	24.2 (± 4.32)		
Change at Day 56: Negative Subscale	-4.2 (± 4.25)	4.5 (± 4.25)		
Change at Day 182: Negative Subscale	-5.7 (± 5.15)	-6.1 (± 5.47)		
Baseline: General Psychopathology	44.3 (± 7.47)	45.3 (± 7.01)		
Change at Day 56: General Psychopathology	-8.7 (± 7.35)	-9.1 (± 7.25)		
Change at Day 182: General Psychopathology	-11.9 (± 9.02)	-12.4 (± 9.41)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinical Stability

End point title	Number of Participants With Clinical Stability
End point description:	
Clinical stability is defined as a decrease of 20 percent or more from Baseline in PANSS total score and CGI-S score less than or equal to 4 at Days 56 and 182, no hospitalizations due to psychiatric illness and no emergence of clinically significant suicidal or homicidal ideation during the maintenance phase.	
End point type	Secondary
End point timeframe:	
Day 56 and 182	

End point values	Paliperidone ER	Aripiprazole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	114		
Units: participants	58	68		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Generalized Cochran- Mantel- Haenszel test for row mean score differences controlling for country was used.	
Comparison groups	Paliperidone ER v Aripiprazole

Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.296
Method	Cochran-Mantel-Haenszel

Secondary: Change From Baseline in Clinical Global Impression - Severity (CGI-S) Score at Days 56 and 182

End point title	Change From Baseline in Clinical Global Impression - Severity (CGI-S) Score at Days 56 and 182
End point description: The CGI-S rating scale is a 7-point global assessment that measures the Clinician's impression of the severity of illness exhibited by a participant. A rating of 1 is equivalent to "Normal, not at all ill" and a rating of 7 is equivalent to "Among the most extremely ill participants". Higher scores indicate worsening.	
End point type	Secondary
End point timeframe: Baseline, Day 56 and 182	

End point values	Paliperidone ER	Aripiprazole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	114		
Units: units on a scale				
median (full range (min-max))				
Baseline	4 (3 to 6)	4 (3 to 6)		
Change at Day 56	-1 (-4 to 0)	-1 (-3 to 1)		
Change at Day 182	-1 (-4 to 1)	-1 (-4 to 1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Change at Day 56: ANCOVA model on ranks with treatment groups (paliperidone ER, aripiprazole) and country as factors, and baseline value (unranked) as a covariate was used.	
Comparison groups	Aripiprazole v Paliperidone ER
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.843
Method	ANCOVA

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

Change at Day 182: ANCOVA model on ranks with treatment groups (paliperidone ER, aripiprazole) and country as factors, and baseline value (unranked) as a covariate was used.

Comparison groups	Paliperidone ER v Aripiprazole
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.914
Method	ANCOVA

Secondary: Change From Baseline in Personal and Social Performance (PSP) Scores at Day 56 and 182

End point title	Change From Baseline in Personal and Social Performance (PSP) Scores at Day 56 and 182
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End point description:

The PSP scale assesses degree of a participants' dysfunction within 4 domains of behavior: socially useful activities, personal and social relationships, self-care, and disturbing and aggressive behavior. The results of the assessment are converted to a numerical score to rate degree of difficulty (1=absent to 6=very severe) in each of the 4 domains. Based on 4 domains there will be 1 total score (total score ranges from 1 to 100, divided into 10 equal intervals). Participants with score of 71 to 100 have mild degree of difficulty; from 31 to 70, varying degrees of disability; less than or equal to 30, functioning so poorly as to require intensive supervision.

End point type	Secondary
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End point timeframe:

Baseline, Day 56 and Day 182

End point values	Paliperidone ER	Aripiprazole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	114		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	49.8 (± 10.32)	49.2 (± 10.21)		
Change at Day 56	12.2 (± 11.72)	12.2 (± 10.17)		
Change at Day 182	17.1 (± 14.46)	17.1 (± 14.03)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Change at Day 56: Analysis of covariance (ANCOVA) model with treatment groups(paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate was used

Comparison groups	Paliperidone ER v Aripiprazole
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Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.895
Method	ANCOVA
Parameter estimate	L S mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.34
upper limit	2.67
Variability estimate	Standard error of the mean
Dispersion value	1.27

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Change at Day 182: Analysis of covariance (ANCOVA) model with treatment groups (paliperidone ER, aripiprazole) and country as factors, and baseline value as a covariate was used.	
Comparison groups	Paliperidone ER v Aripiprazole
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.705
Method	ANCOVA
Parameter estimate	L S mean difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.64
upper limit	3.89
Variability estimate	Standard error of the mean
Dispersion value	1.66

Secondary: Number of Participants With PANSS Response	
End point title	Number of Participants With PANSS Response
End point description:	
The PANSS is a 30-item scale with each item rated on a scale of 1 (absent) to 7 (extreme psychopathology), designed to assess various symptoms of schizophrenia including delusions, grandiosity, blunted affect, poor attention, and poor impulse control. The PANSS total score consists of the sum of all 30 PANSS items and ranges from 30 to 210. Participants with PANSS response were defined as those who achieved greater than or equal to 20 percent or higher reduction from Baseline in the PANSS total score at Day 56 and 182.	
End point type	Secondary
End point timeframe:	
Day 56 and 182	

End point values	Paliperidone ER	Aripiprazole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	114		
Units: participants				
Day 56	76	87		
Day 182	86	93		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Day 56: Generalized Cochran-Mantel-Haenszel test for row mean score differences was used.	
Comparison groups	Paliperidone ER v Aripiprazole
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.119
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Day 182: Generalized Cochran-Mantel-Haenszel test for row mean score differences was used.	
Comparison groups	Paliperidone ER v Aripiprazole
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.444
Method	Cochran-Mantel-Haenszel

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 26

Adverse event reporting additional description:

The safety population included all randomly assigned participants who received at least 1 dose of double-blind study drug. A total of 113 participants in the paliperidone ER group and 114 participants in the aripiprazole group received at least 1 dose of double-blind study medication and were included in the safety analysis set.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.0
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Reporting groups

Reporting group title	Aripiprazole
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Reporting group description:

Aripiprazole will be administered as oral capsule at a dose of 2 mg on Days 1 and 2, 5 mg on Days 3 and 4, 10 mg Days 5, 6 and 7; and then will be administered as a dose of either 5 or 10 or 15 mg up to Week 26, once daily in the morning.

Reporting group title	Paliperidone ER
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Reporting group description:

Paliperidone ER will be administered as oral capsule at a dose of 6 milligram (mg) for 1 week and then will be administered at a dose of either 3, 6 or 9 mg up to Week 26, once daily in the morning.

Serious adverse events	Aripiprazole	Paliperidone ER	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 114 (6.14%)	7 / 113 (6.19%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 114 (0.88%)	1 / 113 (0.88%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			

subjects affected / exposed	1 / 114 (0.88%)	1 / 113 (0.88%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia, paranoid type			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	4 / 114 (3.51%)	1 / 113 (0.88%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sinusitis			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (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: 0 %

Non-serious adverse events	Aripiprazole	Paliperidone ER	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	75 / 114 (65.79%)	87 / 113 (76.99%)	
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	2 / 114 (1.75%)	1 / 113 (0.88%)	
occurrences (all)	2	2	
Asthenia			
subjects affected / exposed	1 / 114 (0.88%)	6 / 113 (5.31%)	
occurrences (all)	1	7	
Feeling jittery			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	1	0	
Gait disturbance			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Irritability			
subjects affected / exposed	1 / 114 (0.88%)	1 / 113 (0.88%)	
occurrences (all)	1	1	
Thirst			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	1 / 114 (0.88%)	2 / 113 (1.77%)	
occurrences (all)	1	2	
Social circumstances			
Sexual activity increased			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Erectile dysfunction			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	

Galactorrhoea subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1	2 / 113 (1.77%) 3	
Epididymitis subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1	0 / 113 (0.00%) 0	
Gynaecomastia subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	1 / 113 (0.88%) 1	
Menstruation irregular subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	1 / 113 (0.88%) 1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	2 / 113 (1.77%) 2	
Nasal congestion subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	1 / 113 (0.88%) 1	
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	1 / 113 (0.88%) 1	
Sinus congestion subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1	0 / 113 (0.00%) 0	
Psychiatric disorders			
Abnormal dreams subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1	1 / 113 (0.88%) 1	
Aggression subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	1 / 113 (0.88%) 1	
Agitation subjects affected / exposed occurrences (all)	2 / 114 (1.75%) 2	1 / 113 (0.88%) 1	
Anxiety			

subjects affected / exposed	3 / 114 (2.63%)	5 / 113 (4.42%)
occurrences (all)	3	6
Depression		
subjects affected / exposed	2 / 114 (1.75%)	3 / 113 (2.65%)
occurrences (all)	2	4
Dyssomnia		
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)
occurrences (all)	1	0
Hallucination		
subjects affected / exposed	0 / 114 (0.00%)	2 / 113 (1.77%)
occurrences (all)	0	3
Libido decreased		
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	1
Hostility		
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)
occurrences (all)	1	0
Insomnia		
subjects affected / exposed	9 / 114 (7.89%)	6 / 113 (5.31%)
occurrences (all)	12	9
Nervousness		
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	1
Mood swings		
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)
occurrences (all)	1	0
Nightmare		
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)
occurrences (all)	1	0
Psychogenic pain disorder		
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	1
Restlessness		
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	1
Schizophrenia		

subjects affected / exposed	10 / 114 (8.77%)	3 / 113 (2.65%)	
occurrences (all)	12	5	
Psychotic disorder			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	1	0	
Social avoidant behaviour			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Suicidal ideation			
subjects affected / exposed	0 / 114 (0.00%)	2 / 113 (1.77%)	
occurrences (all)	0	2	
Suicide attempt			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 114 (0.88%)	1 / 113 (0.88%)	
occurrences (all)	1	1	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Blood glucose			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	2 / 114 (1.75%)	0 / 113 (0.00%)	
occurrences (all)	2	0	
Blood triglycerides increased			

subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	1	0	
Gastric pH decreased			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Hepatic enzyme increased			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
High density lipoprotein decreased			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	3 / 114 (2.63%)	0 / 113 (0.00%)	
occurrences (all)	4	0	
Weight increased			
subjects affected / exposed	7 / 114 (6.14%)	12 / 113 (10.62%)	
occurrences (all)	7	14	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 114 (0.00%)	2 / 113 (1.77%)	
occurrences (all)	0	2	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Ventricular extrasystoles			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	2 / 114 (1.75%)	3 / 113 (2.65%)	
occurrences (all)	3	4	
Nervous system disorders			
Akathisia			
subjects affected / exposed	9 / 114 (7.89%)	13 / 113 (11.50%)	
occurrences (all)	10	13	
Disturbance in attention			

subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)
occurrences (all)	1	0
Dizziness		
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	1
Drooling		
subjects affected / exposed	2 / 114 (1.75%)	0 / 113 (0.00%)
occurrences (all)	2	0
Dysarthria		
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	1
Dyskinesia		
subjects affected / exposed	1 / 114 (0.88%)	1 / 113 (0.88%)
occurrences (all)	1	1
Extrapyramidal disorder		
subjects affected / exposed	2 / 114 (1.75%)	3 / 113 (2.65%)
occurrences (all)	2	3
Dystonia		
subjects affected / exposed	3 / 114 (2.63%)	1 / 113 (0.88%)
occurrences (all)	3	1
Grimacing		
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)
occurrences (all)	1	0
Headache		
subjects affected / exposed	5 / 114 (4.39%)	12 / 113 (10.62%)
occurrences (all)	6	18
Lethargy		
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)
occurrences (all)	0	2
Hypersomnia		
subjects affected / exposed	0 / 114 (0.00%)	2 / 113 (1.77%)
occurrences (all)	0	2
Hypokinesia		
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)
occurrences (all)	1	0
Paraesthesia		

subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	1 / 113 (0.88%) 1	
Parkinsonism subjects affected / exposed occurrences (all)	3 / 114 (2.63%) 4	2 / 113 (1.77%) 2	
Psychomotor hyperactivity subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 2	0 / 113 (0.00%) 0	
Sedation subjects affected / exposed occurrences (all)	3 / 114 (2.63%) 4	6 / 113 (5.31%) 6	
Tremor subjects affected / exposed occurrences (all)	11 / 114 (9.65%) 12	12 / 113 (10.62%) 13	
Somnolence subjects affected / exposed occurrences (all)	12 / 114 (10.53%) 13	12 / 113 (10.62%) 14	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1	0 / 113 (0.00%) 0	
Eosinophilia subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	1 / 113 (0.88%) 1	
Monocytopenia subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1	0 / 113 (0.00%) 0	
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 2	5 / 113 (4.42%) 7	
Eye disorders Accommodation disorder subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 2	0 / 113 (0.00%) 0	
Eye pruritus			

subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Blepharospasm			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Lacrimation increased			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Oculogyric crisis			
subjects affected / exposed	0 / 114 (0.00%)	3 / 113 (2.65%)	
occurrences (all)	0	4	
Photophobia			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	0 / 114 (0.00%)	3 / 113 (2.65%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 114 (1.75%)	0 / 113 (0.00%)	
occurrences (all)	2	0	
Abdominal pain			
subjects affected / exposed	1 / 114 (0.88%)	1 / 113 (0.88%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	2 / 114 (1.75%)	1 / 113 (0.88%)	
occurrences (all)	2	1	
Constipation			
subjects affected / exposed	0 / 114 (0.00%)	2 / 113 (1.77%)	
occurrences (all)	0	3	
Eructation			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	

Flatulence			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	7 / 114 (6.14%)	4 / 113 (3.54%)	
occurrences (all)	8	4	
Salivary hypersecretion			
subjects affected / exposed	2 / 114 (1.75%)	5 / 113 (4.42%)	
occurrences (all)	2	6	
Vomiting			
subjects affected / exposed	1 / 114 (0.88%)	8 / 113 (7.08%)	
occurrences (all)	1	9	
Toothache			
subjects affected / exposed	1 / 114 (0.88%)	1 / 113 (0.88%)	
occurrences (all)	1	1	
Tongue disorder			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Dermatitis			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	1	0	
Alopecia			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Dermatitis allergic			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	2	0	
Pruritus			

subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1	0 / 113 (0.00%) 0	
Rash subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	1 / 113 (0.88%) 2	
Seborrhoea subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1	0 / 113 (0.00%) 0	
Seborrhoeic dermatitis subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1	0 / 113 (0.00%) 0	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	1 / 113 (0.88%) 1	
Musculoskeletal and connective tissue disorders Arthritis reactive subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	1 / 113 (0.88%) 1	
Muscle rigidity subjects affected / exposed occurrences (all)	3 / 114 (2.63%) 4	7 / 113 (6.19%) 8	
Muscle tightness subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	2 / 113 (1.77%) 2	
Back pain subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	2 / 113 (1.77%) 3	
Neck pain subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1	0 / 113 (0.00%) 0	
Musculoskeletal stiffness subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1	1 / 113 (0.88%) 1	
Trismus			

subjects affected / exposed occurrences (all)	0 / 114 (0.00%) 0	1 / 113 (0.88%) 1	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	1 / 114 (0.88%)	2 / 113 (1.77%)	
occurrences (all)	1	2	
Hordeolum			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis viral			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	2 / 114 (1.75%)	1 / 113 (0.88%)	
occurrences (all)	2	1	
Nasopharyngitis			
subjects affected / exposed	5 / 114 (4.39%)	5 / 113 (4.42%)	
occurrences (all)	5	6	
Respiratory tract infection			
subjects affected / exposed	2 / 114 (1.75%)	0 / 113 (0.00%)	
occurrences (all)	2	0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	2 / 114 (1.75%)	0 / 113 (0.00%)	
occurrences (all)	2	0	
Tooth abscess			
subjects affected / exposed	0 / 114 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	

Sinusitis			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	1	0	
Viral infection			
subjects affected / exposed	1 / 114 (0.88%)	1 / 113 (0.88%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 114 (0.88%)	1 / 113 (0.88%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 114 (5.26%)	2 / 113 (1.77%)	
occurrences (all)	6	2	
Glucose tolerance impaired			
subjects affected / exposed	0 / 114 (0.00%)	2 / 113 (1.77%)	
occurrences (all)	0	2	
Hyperglycaemia			
subjects affected / exposed	1 / 114 (0.88%)	0 / 113 (0.00%)	
occurrences (all)	1	0	
Impaired fasting glucose			
subjects affected / exposed	0 / 114 (0.00%)	2 / 113 (1.77%)	
occurrences (all)	0	2	
Increased appetite			
subjects affected / exposed	2 / 114 (1.75%)	2 / 113 (1.77%)	
occurrences (all)	3	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported