Clinical trial results:
A Double-blind, Placebo-controlled Study, Followed by an Open-label Extension Study Evaluating the Efficacy and Safety of Risperidone (R064766) in Children and Adolescents with Irritability Associated with Autistic Disorder

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

Summary

EudraCT number	2015-001320-31
Trial protocol	Outside EU/EEA
Global end of trial date	09 October 2014

Results information

Result version number	v2 (current)
This version publication date	21 July 2016
First version publication date	03 June 2015
Version creation reason	• Correction of full data set Review of FDS

Trial information

Trial identification

Sponsor protocol code	RIS-AUT-JPN-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01624675
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Pharmaceutical K.K
Sponsor organisation address	3-5-2 Nishi-kanda, Chiyoda-ku,, Tokyo, Japan, 101-0065
Public contact	Janssen Research and Development, Clinical Registry Group-JB BV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Janssen Research and Development, Clinical Registry Group-JB BV, 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy of risperidone compared with placebo in children and adolescents with irritability associated with autistic disorder.

Protection of trial subjects:

Safety was evaluated based on the following variables: Adverse events; Clinical laboratory tests (hematology and serum chemistry); Vital sign measurements; Physical examinations; ECGs; Drug Induced Extrapyramidal Symptoms Scale questionnaire. Any clinically significant abnormalities persisting at the end of the study/early withdrawal were followed by the investigator until resolution or until a clinically stable endpoint was reached.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 August 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 39
Worldwide total number of subjects	39
EEA total number of subjects	0

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)	28

Adolescents (12-17 years)	11
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted between 28 August 2012 and 9 October 2014 and recruited subjects from 18 study centers in Japan.

Pre-assignment

Screening details:

Thirty-nine subjects were enrolled and randomly assigned to the risperidone group or placebo group (n=18) in double blind period.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Risperidone

Arm description:

Subjects weighing less than 20 kilogram (kg) received risperidone 0.25 milligram per day (mg/day) up to Day 4. On Day 4, dose was titrated in increments of 0.25 mg/day (up to a daily dose of 1.0 mg) at the regular study visit thereafter till Week 8. Subjects weighing greater than or equal to (>=) 20 kg received risperidone 0.5 mg/day up to Day 4. On Day 4, dose was titrated in increments of 0.5 mg per day (up to a daily dose of 2.5 mg) at the regular visit thereafter till Week 8. The maximum daily dose for subjects weighing >= 45 kg was 3.0 mg. For subjects weighing >=45 kg, the maximum daily dose was 3.0 mg.

Arm type	Experimental
Investigational medicinal product name	Risperidone
Investigational medicinal product code	
Other name	Risperdal
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects weighing less than 20 kilogram (kg) received risperidone 0.25 milligram per day (mg/day) up to Day 4. On Day 4, dose was titrated in increments of 0.25 mg/day (up to a daily dose of 1.0 mg) at the regular study visit thereafter till Week 8. Subjects weighing greater than or equal to (>=) 20 kg received risperidone 0.5 mg/day up to Day 4. On Day 4, dose was titrated in increments of 0.5 mg per day (up to a daily dose of 2.5 mg) at the regular visit thereafter till Week 8. For subjects weighing >=45 kg, the maximum daily dose was 3.0 mg.

Arm title	Placebo

Arm description:

Subjects received placebo matching with risperidone from Day 1 up to Week 8.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matching with risperidone from Day 1 up to Week 8.

Arm title	Open Label Risperidone

Arm description:

Subjects who completed the period 1 (either Risperidone Arm or Placebo Arm) and subjects who were eligible as per Investigator's discretion continued to open label period 2. Subjects < 20 kg received risperidone 0.25 mg/day up to Day 4. On Day 4, dose was increased to 0.5 mg/day. Dose was titrated in increments of 0.25 mg/day up to 1.0 mg/Day, at the regular study visit thereafter till Week 48. Subjects weighing >=20 kg received risperidone 0.5 mg/day up to Day 4. On Day 4, dose was increased to 1.0 mg/day. Dose was titrated in increments of 0.5 mg/day up to 2.5 mg/Day, at the regular study visit thereafter till Week 48. The maximum daily dose for subject weighing >=45 kg was 3.0 mg.

Arm type	Experimental
Investigational medicinal product name	Risperidone
Investigational medicinal product code	
Other name	Risperdal
Pharmaceutical forms	Oral solution, Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Subject who completed the period 1 (either Risperidone Arm or Placebo Arm) and participants who were eligible as per Investigator's discretion continued to open label period 2. Participants < 20 kg received risperidone 0.25 mg/day up to Day 4. On Day 4, dose was increased to 0.5 mg/day. Dose was titrated in increments of 0.25 mg/day up to 1.0 mg/Day, at the regular study visit thereafter till Week 48. Participants weighing >=20 kg received risperidone 0.5 mg/day up to Day 4. On Day 4, dose was increased to 1.0 mg/day. Dose was titrated in increments of 0.5 mg/day up to 2.5 mg/Day, at the regular study visit thereafter till Week 48. The maximum daily dose for participant weighing >=45 kg was 3.0 mg.

Number of subjects in period 1	Risperidone	Placebo	Open Label Risperidone
Started	21	18	35
Completed	18	11	26
Not completed	3	7	9
Adverse event, non-fatal	-	-	1
Not Defined	-	-	1
non-compliance with the study drug	-	-	3
Violated Eligibility Criteria	-	-	1
Consent withdrawn by subject	2	-	-
Lack of efficacy	1	7	3

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study (Double Blind+Open label)

Reporting group description: -

Reporting group values	Overall Study (Double Blind+Open label)	Total	
Number of subjects	39	39	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	28	28	
Adolescents (12-17 years)	11	11	
Adults (18-64 years)	0	0	
From 65 to 84 years	0	0	
85 years and over	0	0	
Title for Gender Units: subjects			
Female	9	9	
Male	30	30	

End point values	Risperidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[2]	18[3]		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline	28.2 (± 6.36)	27.5 (± 5.26)		
Change at Endpoint	-9.7 (± 7.29)	-2.8 (± 6.62)		

Notes:

[2] - FAS population

[3] - FAS population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Risperidone v Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [4]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.6
upper limit	-2.6
Variability estimate	Standard error of the mean
Dispersion value	2.23

Notes:

[4] - p-value is analysed by using analysis of covariance (ANCOVA) model including treatment group as a fixed factor and baseline score as a covariate.

Secondary: Change From Baseline in the Aberrant Behavior Checklist−Japanese Version (ABC-J) Irritability Subscale Scores at Week 2, 4 and 6 of Double Blind Phase

End point title	Change From Baseline in the Aberrant Behavior Checklist−Japanese Version (ABC-J) Irritability Subscale Scores at Week 2, 4 and 6 of Double Blind Phase[5]

End point description:

The ABC-J consists of 58 items divided into 5 subscales: Irritability, Lethargy and Social withdrawal, Stereotypic behavior, Hyperactivity/Noncompliance, and Inappropriate speech. Each item scores range from 0 to 3: 0 = No problem, 1 = Mild aberrant behavior, 2 = Moderate aberrant behavior, and 3 = Severe aberrant behavior. Higher scores represent worse condition. Missing data was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Week 2, 4 and 6 of Double-blind Phase

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Risperidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[6]	18[7]		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Week 2	-7.7 (± 8.33)	-1.4 (± 4.07)		
Change at Week 4	-9.5 (± 8.42)	-1.2 (± 5.92)		
Change at Week 6	-9 (± 7.18)	-2.1 (± 6.51)		

Notes:

[6] - FAS population

[7] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Aberrant Behavior Checklist−Japanese Version (ABC-J) Irritability Subscale Scores at Week 2, 4, 8, 16, 24, 32, 40 and 48 of Open label Phase

End point title	Change From Baseline in the Aberrant Behavior Checklist−Japanese Version (ABC-J) Irritability Subscale Scores at Week 2, 4, 8, 16, 24, 32, 40 and 48 of Open label Phase[8]

End point description:

The ABC-J consists of 58 items divided into 5 subscales: Irritability, Lethargy and Social withdrawal, Stereotypic behavior, Hyperactivity/Noncompliance, and Inappropriate speech. Each item scores range from 0 to 3: 0 = No problem, 1 = Mild aberrant behavior, 2 = Moderate aberrant behavior, and 3 = Severe aberrant behavior. Higher scores represent worse condition. Missing data was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 8, 16, 24, 32, 40 and 48 of Open Label Phase

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data was planned to be reported for the specific arms only

End point values	Open Label Risperidone			
Subject group type	Reporting group			
Number of subjects analysed	35[9]			
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline	26.3 (± 8.4)			
Change at Week 2	-9.5 (± 8.32)			
Change at Week 4	-11.7 (± 8.93)			
Change at Week 8	-12.5 (± 9.44)			
Change at Week 16	-12.5 (± 9.9)			
Change at Week 24	-12.6 (± 9.64)			
Change at Week 32	-12.2 (± 9.7)			
Change at Week 40	-13.2 (± 10.19)			
Change at Endpoint (Week 48)	-13.3 (± 10.27)			

Notes:

[9] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Global Impression - Severity (CGI-S) Score at Week 1, 2, 3, 4, 6 and 8 of Double Blind Phase

End point title	Change From Baseline in Clinical Global Impression - Severity (CGI-S) Score at Week 1, 2, 3, 4, 6 and 8 of Double Blind Phase[10]

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 patient. 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 patients". Higher scores indicate worsening. Missing data was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 2, 3, 4, 6 and 8 of Double Blind Phase

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Risperidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[11]	18[12]		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline	4.6 (± 0.81)	4.2 (± 0.55)		
Change at Week 1	0 (± 0.22)	0 (± 0)		
Change at Week 2	-0.1 (± 0.36)	0 (± 0.34)		
Change at Week 3	-0.2 (± 0.4)	0.1 (± 0.58)		
Change at Week 4	-0.2 (± 0.4)	0.1 (± 0.68)		
Change at Week 6	-0.1 (± 0.48)	0.2 (± 0.71)		
Change at Endpoint (Week 8)	-0.1 (± 0.48)	0.2 (± 0.71)		

Notes:

[11] - FAS population

[12] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Global Impression - Severity (CGI-S) Score at Week 1, 2, 3, 4, 8, 16, 24, 32, 40 and 48 of Open-label-Phase

End point title	Change From Baseline in Clinical Global Impression - Severity (CGI-S) Score at Week 1, 2, 3, 4, 8, 16, 24, 32, 40 and 48 of Open-label-Phase[13]

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 patient. 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 patients". Higher scores indicate worsening. Missing data was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 2, 3, 4, 8, 16, 24, 32, 40 and 48 of Open-Label Phase

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Open Label Risperidone			
Subject group type	Reporting group			
Number of subjects analysed	35[14]			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline	4.5 (± 0.85)			
Change at Week 1	-0.3 (± 0.67)			
Change at Week 2	-0.3 (± 0.68)			
Change at Week 3	-0.5 (± 0.78)			
Change at Week 4	-0.7 (± 0.84)			
Change at Week 8	-0.7 (± 0.87)			
Change at Week 16	-0.7 (± 0.87)			
Change at Week 24	-0.7 (± 0.93)			
Change at Week 32	-0.7 (± 0.93)			
Change at Week 40	-0.7 (± 1)			
Change at Endpoint (Week 48)	-0.7 (± 1.04)			

Notes:

[14] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Children's Global Assessment Scale (C-GAS) Score at Week 4 and 8 of Double Blind Phase

End point title	Change From Baseline in Children's Global Assessment Scale (C-GAS) Score at Week 4 and 8 of Double Blind Phase[15]

End point description:

The C-GAS rates the patient's general psychological and social functioning on scores ranging from 1 through 100. Lower scores (range 1-10) mean that the patient needs constant supervision; higher scores (range 91-100) mean that the patient has a superior functioning in all areas. Missing data was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Baseline, Week 4 and 8 of Double Blind Phase

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Risperidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[16]	18[17]		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline	41.9 (± 14.69)	45.4 (± 12.82)		
Change at Week 4	3.8 (± 7.74)	-1.2 (± 6.98)		
Change at endpoint (Week 8)	5.8 (± 7.67)	-1.9 (± 7.22)		

Notes:

[16] - FAS population

[17] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Children's Global Assessment Scale (C-GAS) at Week 4, 8, 16, 24, 32, 40 and 48 of Open Label Phase

End point title	Change From Baseline in Children's Global Assessment Scale (C-GAS) at Week 4, 8, 16, 24, 32, 40 and 48 of Open Label Phase[18]

End point description:

The C-GAS rates the patient's general psychological and social functioning on scores ranging from 1 through 100. Lower scores (range 1-10) mean that the patient needs constant supervision; higher scores (range 91-100) mean that the patient has a superior functioning in all areas. Missing data was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 16, 24, 32, 40 and 48 of Open label Phase

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Open Label Risperidone			
Subject group type	Reporting group			
Number of subjects analysed	35[19]			
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Baseline	42.1 (± 13.88)			
Change at Week 4	7.9 (± 9.19)			
Change at Week 8	9.3 (± 9.67)			
Change at Week 16	10.5 (± 10.78)			
Change at Week 24	10.4 (± 11.17)			
Change at Week 32	10.6 (± 11.94)			
Change at Week 40	10.5 (± 13.69)			
Change at Endpoint (Week 48)	10.6 (± 13.61)			

Notes:

[19] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression−Change (CGI-C) Score at Week 1, 2, 3, 4, 6 and 8 of Double Blind Phase

End point title	Clinical Global Impression−Change (CGI-C) Score at Week 1, 2, 3, 4, 6 and 8 of Double Blind Phase[20]

End point description:

The CGI-C assesses the patient's condition on the basis of the rater's impression, on a 7-point scale ranging from 1 (Very much improved) to 7 (Very much worse). Missing data was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Week 1, 2, 3, 4, 6 and 8 of double blind Phase

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Risperidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[21]	18[22]		
Units: Number of Subjects				
Week 1: Very much improved	0	0		
Week 1: Much improved	1	0		
Week 1: Minimally improved	8	1		
Week 1: No change	12	15		
Week 1: Minimally worse	0	1		
Week 1: Much worse	0	1		
Week 1: Very much worse	0	0		
Week 2: Very much improved	0	0		
Week 2: Much improved	6	0		
Week 2: Minimally improved	8	2		
Week 2: No change	7	11		
Week 2: Minimally worse	0	3		
Week 2: Much worse	0	2		
Week 2: Very much worse	0	0		
Week 3: Very much improved	0	0		
Week 3: Much improved	5	1		
Week 3: Minimally improved	8	3		
Week 3: No change	5	7		
Week 3: Minimally worse	2	0		
Week 3: Much worse	1	7		
Week 3: Very much worse	0	0		
Week 4: Very much improved	0	0		
Week 4: Much improved	6	0		
Week 4: Minimally improved	9	3		
Week 4: No change	5	6		
Week 4: Minimally worse	0	2		
Week 4: Much worse	1	7		
Week 4: Very much worse	0	0		
Week 6: Very much improved	1	0		
Week 6: Much improved	4	0		

Week 6: Minimally improved	9	4		
Week 6: No change	5	5		
Week 6: Minimally worse	1	1		
Week 6: Much worse	1	8		
Week 6: Very much worse	0	0		
Endpoint (Week 8): Very much improved	1	0		
Endpoint (Week 8): Much improved	2	0		
Endpoint (Week 8): Minimally improved	11	5		
Endpoint (Week 8): No change	5	3		
Endpoint (Week 8): Minimally worse	1	2		
Endpoint (Week 8): Much worse	1	8		
Endpoint (Week 8): Very much worse	0	0		

Notes:

[21] - FAS population

[22] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression−Change (CGI-C) at Week 1, 2, 3, 4, 8, 16, 24, 32, 40 and 48 of Open-Label Phase

End point title	Clinical Global Impression−Change (CGI-C) at Week 1, 2, 3, 4, 8, 16, 24, 32, 40 and 48 of Open-Label Phase[23]

End point description:

The CGI-C assesses the patient's condition on the basis of the rater's impression, on a 7-point scale ranging from 1 (Very much improved) to 7 (Very much worse). Missing data was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Week 1, 2, 3, 4, 8, 16, 24, 32, 40 and 48 of Open-Label Phase

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Open Label Risperidone			
Subject group type	Reporting group			
Number of subjects analysed	35[24]			
Units: Number of Subjects				
Week 1: Very much improved	2			
Week 1: Much improved	2			
Week 1: Minimally improved	18			
Week 1: No change	9			
Week 1: Minimally worse	2			
Week 1: Much worse	2			
Week 1: Very much worse	0			
Week 2: Very much improved	2			
Week 2: Much improved	5			
Week 2: Minimally improved	19			
Week 2: No change	7			

Week 2: Minimally worse	2			
Week 2: Much worse	0			
Week 2: Very much worse	0			
Week 3: Very much improved	2			
Week 3: Much improved	9			
Week 3: Minimally improved	17			
Week 3: No change	6			
Week 3: Minimally worse	1			
Week 3: Much worse	0			
Week 3: Very much worse	0			
Week 4: Very much improved	2			
Week 4: Much improved	11			
Week 4: Minimally improved	15			
Week 4: No change	6			
Week 4: Minimally worse	1			
Week 4: Much worse	0			
Week 4: Very much worse	0			
Week 8: Very much improved	1			
Week 8: Much improved	14			
Week 8: Minimally improved	13			
Week 8: No change	5			
Week 8: Minimally worse	2			
Week 8: Much worse	0			
Week 8: Very much worse	0			
Week 16: Very much improved	1			
Week 16: Much improved	12			
Week 16: Minimally improved	16			
Week 16: No change	4			
Week 16: Minimally worse	2			
Week 16: Much worse	0			
Week 16: Very much worse	0			
Week 24: Very much improved	1			
Week 24: Much improved	12			
Week 24: Minimally improved	13			
Week 24: No change	6			
Week 24: Minimally worse	3			
Week 24: Much worse	0			
Week 24: Very much worse	0			
Week 32: Very much improved	0			
Week 32: Much improved	13			
Week 32: Minimally improved	14			
Week 32: No change	4			
Week 32: Minimally worse	4			
Week 32: Much worse	0			
Week 32: Very much worse	0			
Week 40: Very much improved	2			
Week 40: Much improved	11			
Week 40: Minimally improved	12			
Week 40: No change	5			
Week 40: Minimally worse	5			
Week 40: Much worse	0			
Week 40: Very much worse	0			

Endpoint (Week 48): Very much improved	1			
Endpoint (Week 48): Much improved	11			
Endpoint (Week 48): Minimally improved	13			
Endpoint (Week 48): No change	4			
Endpoint (Week 48): Minimally worse	6			
Endpoint (Week 48): Much worse	0			
Endpoint (Week 48): Very much worse	0			

Notes:

[24] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Parent Satisfaction Questionnaire (PSQ): Question 1 at Week 1, 2, 3, 4, 6 and 8 of Double Blind Period

End point title	Parent Satisfaction Questionnaire (PSQ): Question 1 at Week 1, 2, 3, 4, 6 and 8 of Double Blind Period[25]

End point description:

The PSQ evaluates the caregiver's satisfaction with the study drug. Caregivers were requested to answer question (Ques) 1: Overall, how pleased have you been with the current study medication for your child's autistic disorder symptoms. Number of participants at each category for each question were reported. Missing data was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Week 1, 2, 3, 4, 6 and 8 of Double-blind Phase

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Risperidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[26]	18[27]		
Units: Number of subjects				
Week 1: Ques 1: Extremely displeased	0	0		
Week 1: Ques 1: Very displeased	2	2		
Week 1: Ques 1: A bit displeased	3	9		
Week 1: Ques 1: Pleased	13	6		
Week 1: Ques 1: Very pleased	3	1		
Week 1: Ques 1: Extremely pleased	0	0		
Week 2: Ques 1: Extremely displeased	0	1		
Week 2: Ques 1: Very displeased	2	3		
Week 2: Ques 1: A bit displeased	4	9		
Week 2: Ques 1: Pleased	12	5		
Week 2: Ques 1: Very pleased	2	0		
Week 2: Ques 1: Extremely pleased	1	0		
Week 3: Ques 1: Extremely displeased	1	1		
Week 3: Ques 1: Very displeased	0	7		
Week 3: Ques 1: A bit displeased	3	3		

End point values	Risperidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[29]	18[30]		
Units: Number of subjects				
Week 1: Ques 2: A little bit	1	10		
Week 1: Ques 2: Not at all	12	7		
Week 1: Ques 2: Some	3	1		
Week 1: Ques 2: A lot	0	0		
Week 2: Ques 2: Not at all	3	11		
Week 2: Ques 2: A little bit	13	6		
Week 2: Ques 2: Some	4	1		
Week 2: Ques 2: A lot	1	0		
Week 3: Ques 2: Not at all	2	10		
Week 3: Ques 2: A little bit	15	6		
Week 3: Ques 2: Some	4	2		
Week 3: Ques 2: A lot	0	0		
Week 4: Ques 2: Not at all	3	10		
Week 4: Ques 2: A little bit	13	6		
Week 4: Ques 2: Some	5	2		
Week 4: Ques 2: A lot	0	0		
Week 6: Ques 2: Not at all	2	10		
Week 6: Ques 2: A little bit	15	5		
Week 6: Ques 2: Some	4	3		
Week 6: Ques 2: A lot	0	0		
Endpoint (Week 8): Ques 2: Not at all	2	11		
Endpoint (Week 8): Ques 2: A little bit	16	5		
Endpoint (Week 8): Ques 2: Some	3	2		
Endpoint (Week 8): Ques 2: A lot	0	0		

Notes:

[29] - FAS population

[30] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Parent Satisfaction Questionnaire (PSQ): Question 3 at Week 1, 2, 3, 4, 6 and 8 of Double Blind Period

End point title	Parent Satisfaction Questionnaire (PSQ): Question 3 at Week 1, 2, 3, 4, 6 and 8 of Double Blind Period[31]

End point description:

The PSQ evaluates the caregiver's satisfaction with the study drug. Caregivers were requested to answer question (Ques) 3: Would you recommend the current study medication for your child’s symptoms to someone else with same condition. Number of participants at each category for each question were reported. Missing data was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Week 1, 2, 3, 4, 6 and 8 of Double-blind Phase

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Risperidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[32]	18[33]		
Units: Number of subjects				
Week 1: Ques 3: No	1	3		
Week 1: Ques 3: Unsure	17	14		
Week 1: Ques 3: Yes	3	1		
Week 2: Ques 3: No	1	3		
Week 2: Ques 3: Unsure	17	14		
Week 2: Ques 3: Yes	3	1		
Week 3: Ques 3: No	1	5		
Week 3: Ques 3: Unsure	15	10		
Week 3: Ques 3: Yes	5	3		
Week 4: Ques 3: No	1	4		
Week 4: Ques 3: Unsure	16	9		
Week 4: Ques 3: Yes	4	5		
Week 6: Ques 3: No	1	5		
Week 6: Ques 3: Unsure	16	9		
Week 6: Ques 3: Yes	4	4		
Endpoint (Week 8): Ques 3: No	1	5		
Endpoint (Week 8): Ques 3: Unsure	16	8		
Endpoint (Week 8): Ques 3: Yes	4	5		

Notes:

[32] - FAS population

[33] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Parent Satisfaction Questionnaire (PSQ): Question 1 at Week 1, 2, 3, 4, 8, 12, 16, 20, 24, 28, 32, 40 and 42 of Open-label Phase

End point title	Parent Satisfaction Questionnaire (PSQ): Question 1 at Week 1, 2, 3, 4, 8, 12, 16, 20, 24, 28, 32, 40 and 42 of Open-label Phase[34]

End point description:

The PSQ evaluates the caregiver's satisfaction with the study drug. Caregivers were requested to answer question (Ques) 1: Overall, how pleased have you been with the current study medication for your child’s autistic disorder symptoms. Missing data was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Week 1, 2, 3, 4, 8, 12, 16, 20, 24, 28, 32, 40 and 42 of Open-label Phase

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Open Label Risperidone			
Subject group type	Reporting group			
Number of subjects analysed	35[35]			
Units: Number of subjects				
Week 1: Ques 1: Extremely displeased	2			
Week 1: Ques 1: Very displeased	1			
Week 1: Ques 1: A bit displeased	8			
Week 1: Ques 1: Pleased (n=34)	15			
Week 1: Ques 1: Very pleased (n=34)	8			
Week 1: Ques 1: Extremely pleased	1			
Week 2: Ques 1: Extremely displeased	0			
Week 2: Ques 1: Very displeased	2			
Week 2: Ques 1: A bit displeased	9			
Week 2: Ques 1: Pleased	16			
Week 2: Ques 1: Very pleased	7			
Week 2: Ques 1: Extremely pleased	1			
Week 3: Ques 1: Extremely displeased	0			
Week 3: Ques 1: Very displeased	2			
Week 3: Ques 1: A bit displeased	4			
Week 3: Ques 1: Pleased	15			
Week 3: Ques 1: Very pleased	12			
Week 3: Ques 1: Extremely pleased	2			
Week 4: Ques 1: Extremely displeased	0			
Week 4: Ques 1: Very displeased	0			
Week 4: Ques 1: A bit displeased	7			
Week 4: Ques 1: Pleased	16			
Week 4: Ques 1: Very pleased	10			
Week 4: Ques 1: Extremely pleased	2			
Week 8: Ques 1: Extremely displeased	0			
Week 8: Ques 1: Very displeased	1			
Week 8: Ques 1: A bit displeased	5			
Week 8: Ques 1: Pleased	15			
Week 8: Ques 1: Very pleased	10			
Week 8: Ques 1: Extremely pleased	4			
Week 12: Ques 1: Extremely displeased	0			
Week 12: Ques 1: Very displeased	1			
Week 12: Ques 1: A bit displeased	6			
Week 12: Ques 1: Pleased	16			
Week 12: Ques 1: Very pleased	8			
Week 12: Ques 1: Extremely pleased	4			
Week 16: Ques 1: Extremely displeased	0			
Week 16: Ques 1: Very displeased	1			
Week 16: Ques 1: A bit displeased	5			
Week 16: Ques 1: Pleased	19			
Week 16: Ques 1: Very pleased	7			
Week 16: Ques 1: Extremely pleased	3			
Week 20: Ques 1: Extremely displeased	0			
Week 20: Ques 1: Very displeased	1			
Week 20: Ques 1: A bit displeased	7			
Week 20: Ques 1: Pleased	14			
Week 20: Ques 1: Very pleased	10			

Week 20: Ques 1: Extremely pleased	3			
Week 24: Ques 1: Extremely displeased	0			
Week 24: Ques 1: Very displeased	2			
Week 24: Ques 1: A bit displeased	8			
Week 24: Ques 1: Pleased	13			
Week 24: Ques 1: Very pleased	8			
Week 24: Ques 1: Extremely pleased	4			
Week 28: Ques 1: Extremely displeased	0			
Week 28: Ques 1: Very displeased	1			
Week 28: Ques 1: A bit displeased	8			
Week 28: Ques 1: Pleased	12			
Week 28: Ques 1: Very pleased	11			
Week 28: Ques 1: Extremely pleased	3			
Week 32: Ques 1: Extremely displeased	0			
Week 32: Ques 1: Very displeased	2			
Week 32: Ques 1: A bit displeased	6			
Week 32: Ques 1: Pleased	16			
Week 32: Ques 1: Very pleased	8			
Week 32: Ques 1: Extremely pleased	3			
Week 36: Ques 1: Extremely displeased	0			
Week 36: Ques 1: Very displeased	1			
Week 36: Ques 1: A bit displeased	7			
Week 36: Ques 1: Pleased	17			
Week 36: Ques 1: Very pleased	8			
Week 36: Ques 1: Extremely pleased	2			
Week 40: Ques 1: Extremely displeased	0			
Week 40: Ques 1: Very displeased	1			
Week 40: Ques 1: A bit displeased	7			
Week 40: Ques 1: Pleased	14			
Week 40: Ques 1: Very pleased	10			
Week 40: Ques 1: Extremely pleased	3			
Week 44: Ques 1: Extremely displeased	1			
Week 44: Ques 1: Very displeased	1			
Week 44: Ques 1: A bit displeased	5			
Week 44: Ques 1: Pleased	20			
Week 44: Ques 1: Very pleased	6			
Week 44: Ques 1: Extremely pleased	2			
Endpoint (Week 48): Ques 1: Extremely displeased	0			
Endpoint (Week 48: Ques 1: Very displeased)	2			
Endpoint (Week 48: Ques 1: A bit displeased)	6			
Endpoint (Week 48): Ques 1: Pleased (n=26)	15			
Endpoint (Week 48): Ques 1: Very pleased	9			
Endpoint (Week 48: Ques 1): Extremely pleased	3			

Notes:

[35] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Parent Satisfaction Questionnaire (PSQ): Question 2 at Week 1, 2, 3, 4, 8, 12, 16, 20, 24, 28, 32, 40 and 42 of Open-label Phase

End point title	Parent Satisfaction Questionnaire (PSQ): Question 2 at Week 1, 2, 3, 4, 8, 12, 16, 20, 24, 28, 32, 40 and 42 of Open-label Phase[36]

End point description:

The PSQ evaluates the caregiver's satisfaction with the study drug. Caregivers were requested to answer question (Ques) 2: How much has your child benefited from the current study medication for his/her autistic disorder symptoms. Missing data was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Week 1, 2, 3, 4, 8, 12, 16, 20, 24, 28, 32, 40 and 42 of Open-label Phase

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Open Label Risperidone			
Subject group type	Reporting group			
Number of subjects analysed	35[37]			
Units: Number of subject				
Week 1: Ques 2: Not at all	5			
Week 1: Ques 2: A little bit	19			
Week 1: Ques 2: Some	9			
Week 1: Ques 2: A lot	2			
Week 2: Ques 2: Not at all	4			
Week 2: Ques 2: A little bit	19			
Week 2: Ques 2: Some	10			
Week 2: Ques 2: A lot	2			
Week 3: Ques 2: Not at all	5			
Week 3: Ques 2: A little bit	13			
Week 3: Ques 2: Some	13			
Week 3: Ques 2: A lot	4			
Week 4: Ques 2: Not at all	4			
Week 4: Ques 2: A little bit	14			
Week 4: Ques 2: Some	13			
Week 4: Ques 2: A lot	4			
Week 8: Ques 2: Not at all	4			
Week 8: Ques 2: A little bit	12			
Week 8: Ques 2: Some	14			
Week 8: Ques 2: A lot	5			
Week 12: Ques 2: Not at all	4			
Week 12: Ques 2: A little bit	6			
Week 12: Ques 2: Some	11			
Week 12: Ques 2: A lot	4			
Week 16: Ques 2: Not at all	3			
Week 16: Ques 2: A little bit	16			
Week 16: Ques 2: Some	14			
Week 16: Ques 2: A lot	2			

Week 20: Ques 2: Not at all	3			
Week 20: Ques 2: A little bit	14			
Week 20: Ques 2: Some	15			
Week 20: Ques 2: A lot	3			
Week 24: Ques 2: Not at all	4			
Week 24: Ques 2: A little bit	16			
Week 24: Ques 2: Some	12			
Week 24: Ques 2: A lot	3			
Week 28: Ques 2: Not at all	4			
Week 28: Ques 2: A little bit	12			
Week 28: Ques 2: Some	15			
Week 28: Ques 2: A lot	4			
Week 32: Ques 2: Not at all	3			
Week 32: Ques 2: A little bit	18			
Week 32: Ques 2: Some	11			
Week 32: Ques 2: A lot	3			
Week 36: Ques 2: Not at all	2			
Week 36: Ques 2: A little bit	17			
Week 36: Ques 2: Some	13			
Week 36: Ques 2: A lot	3			
Week 40: Ques 2: Not at all	2			
Week 40: Ques 2: A little bit	18			
Week 40: Ques 2: Some	12			
Week 40: Ques 2: A lot	3			
Week 44: Ques 2: Not at all	4			
Week 44: Ques 2: A little bit	17			
Week 44: Ques 2: Some	11			
Week 44: Ques 2: A lot	3			
Endpoint (Week 48): Ques 2: Not at all	3			
Endpoint (Week 48): Ques 2: A little bit	16			
Endpoint (Week 48): Ques 2: Some	13			
Endpoint (Week 48): Ques 2: A lot (n=26)	3			

Notes:

[37] - FAS population

Statistical analyses

No statistical analyses for this end point

Secondary: Parent Satisfaction Questionnaire (PSQ): Question 3 at Week 1, 2, 3, 4, 8, 12, 16, 20, 24, 28, 32, 40 and 42 of Open-label Phase

End point title	Parent Satisfaction Questionnaire (PSQ): Question 3 at Week 1, 2, 3, 4, 8, 12, 16, 20, 24, 28, 32, 40 and 42 of Open-label Phase[38]

End point description:

The PSQ evaluates the caregiver's satisfaction with the study drug. Caregivers were requested to answer question (Ques) 3: Would you recommend the current study medication for your child’s symptoms to someone else with same condition. Number of participants at each category for each question were reported. Missing value was calculated by LOCF method.

End point type	Secondary

End point timeframe:

Week 1, 2, 3, 4, 8, 12, 16, 20, 24, 28, 32, 40 and 42 of Open-label Phase

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data was planned to be reported for the specific arms only

End point values	Open Label Risperidone			
Subject group type	Reporting group			
Number of subjects analysed	35[39]			
Units: Number of subjects				
Week 1: Ques 3: No	2			
Week 1: Ques 3: Unsure	22			
Week 1: Ques 3: Less	11			
Week 2: Ques 3: No	0			
Week 2: Ques 3: Unsure	22			
Week 2: Ques 3: Less	13			
Week 3: Ques 3: No	0			
Week 3: Ques 3: Unsure	20			
Week 3: Ques 3: Less	15			
Week 4: Ques 3: No	0			
Week 4: Ques 3: Unsure	21			
Week 4: Ques 3: Less	14			
Week 8: Ques 3: No	1			
Week 8: Ques 3: Unsure	17			
Week 8: Ques 3: Less	17			
Week 12: Ques 3: No	0			
Week 12: Ques 3: Unsure	18			
Week 12: Ques 3: Less	17			
Week 16: Ques 3: No	1			
Week 16: Ques 3: Unsure	18			
Week 16: Ques 3: Less	16			
Week 20: Ques 3: No	1			
Week 20: Ques 3: Unsure	18			
Week 20: Ques 3: Less	16			
Week 24: Ques 3: No	1			
Week 24: Ques 3: Unsure	18			
Week 24: Ques 3: Less	16			
Week 28: Ques 3: No	2			
Week 28: Ques 3: Unsure	17			
Week 28: Ques 3: Less	16			
Week 32: Ques 3: No	1			
Week 32: Ques 3: Unsure	19			
Week 32: Ques 3: Less	15			
Week 36: Ques 3: No	1			
Week 36: Ques 3: Unsure	20			
Week 36: Ques 3: Less	14			
Week 40: Ques 3: No	1			
Week 40: Ques 3: Unsure	20			
Week 40: Ques 3: Less	14			
Week 44: Ques 3: No	1			
Week 44: Ques 3: Unsure	19			
Week 44: Ques 3: Less	15			

Endpoint (Week 48): Ques 3: No	1			
Endpoint (Week 48): Ques 3: Unsure	17			
Endpoint (Week 48): Ques 3: Less	17			

Notes:

[39] - FAS population

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Week 52

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Risperidone

Reporting group description:

Subjects weighing less than 20 kilogram (kg) received risperidone 0.25 milligram per day (mg/day) up to Day 4. On Day 4, dose was titrated in increments of 0.25 mg/day (up to a daily dose of 1.0 mg) at the regular study visit thereafter till Week 8. Subjects weighing greater than or equal to (>=) received risperidone 0.5 mg/day up to Day 4. On Day 4, dose was titrated in increments of 0.5 mg per day (up to a daily dose of 2.5 mg) at the regular visit thereafter till Week 8.

Reporting group title	Open Label Risperidone

Reporting group description:

Subjects who completed the period 1 (either Risperidone Arm or Placebo Arm) and subjects who were eligible as per Investigator's discretion continued to open label period 2. Subjects < 20 kg received risperidone 0.25 mg/day up to Day 4. On Day 4, dose was increased to 0.5 mg/day. Dose was titrated in increments of 0.25 mg/day at the regular study visit thereafter till Week 48. Subjects weighing >=20 kg received risperidone 0.5 mg/day up to Day 4. On Day 4, dose was increased to 1.0 mg/day. Dose was titrated in increments of 0.5 mg/day at the regular study visit thereafter till Week 48. The maximum daily dose for subject weighing >=45 kg was 3.0 mg.

Reporting group title	Placebo

Reporting group description:

Participants received placebo matching with risperidone from Day 1 up to Week 8.

Serious adverse events	Risperidone	Open Label Risperidone	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	2 / 35 (5.71%)	1 / 18 (5.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Inguinal Hernia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 35 (2.86%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 21 (0.00%)	1 / 35 (2.86%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Tracheobronchitis Mycoplasmal			
subjects affected / exposed	0 / 21 (0.00%)	1 / 35 (2.86%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 21 (0.00%)	0 / 35 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Risperidone	Open Label Risperidone	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 21 (90.48%)	34 / 35 (97.14%)	16 / 18 (88.89%)
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	2 / 21 (9.52%)	0 / 35 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 35 (2.86%)	2 / 18 (11.11%)
occurrences (all)	0	1	2
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 21 (4.76%)	3 / 35 (8.57%)	1 / 18 (5.56%)
occurrences (all)	1	6	1
Epistaxis			
subjects affected / exposed	0 / 21 (0.00%)	2 / 35 (5.71%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Rhinitis Allergic			

subjects affected / exposed	0 / 21 (0.00%)	2 / 35 (5.71%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Upper Respiratory Tract Inflammation			
subjects affected / exposed	0 / 21 (0.00%)	5 / 35 (14.29%)	0 / 18 (0.00%)
occurrences (all)	0	6	0

Drooling			
subjects affected / exposed	2 / 21 (9.52%)	2 / 35 (5.71%)	0 / 18 (0.00%)
occurrences (all)	2	2	0
Epilepsy			
subjects affected / exposed	0 / 21 (0.00%)	2 / 35 (5.71%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	1 / 21 (4.76%)	3 / 35 (8.57%)	0 / 18 (0.00%)
occurrences (all)	1	3	0
Somnolence			
subjects affected / exposed	11 / 21 (52.38%)	17 / 35 (48.57%)	2 / 18 (11.11%)
occurrences (all)	13	19	2
Eye disorders			
Conjunctivitis Allergic			
subjects affected / exposed	1 / 21 (4.76%)	3 / 35 (8.57%)	0 / 18 (0.00%)
occurrences (all)	1	3	0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 21 (4.76%)	2 / 35 (5.71%)	0 / 18 (0.00%)
occurrences (all)	1	3	0
Constipation			
subjects affected / exposed	0 / 21 (0.00%)	5 / 35 (14.29%)	0 / 18 (0.00%)
occurrences (all)	0	5	0
Diarrhoea			
subjects affected / exposed	1 / 21 (4.76%)	2 / 35 (5.71%)	2 / 18 (11.11%)
occurrences (all)	2	2	3
Dental Caries			
subjects affected / exposed	0 / 21 (0.00%)	1 / 35 (2.86%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	0 / 21 (0.00%)	1 / 35 (2.86%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	3 / 21 (14.29%)	6 / 35 (17.14%)	0 / 18 (0.00%)
occurrences (all)	4	9	0
Stomatitis			

subjects affected / exposed	0 / 21 (0.00%)	0 / 35 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hepatic Function Abnormal			
subjects affected / exposed	0 / 21 (0.00%)	1 / 35 (2.86%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 21 (4.76%)	2 / 35 (5.71%)	0 / 18 (0.00%)
occurrences (all)	1	3	0
Renal and urinary disorders			
Enuresis			
subjects affected / exposed	1 / 21 (4.76%)	2 / 35 (5.71%)	2 / 18 (11.11%)
occurrences (all)	1	3	2
Endocrine disorders			
Hyperprolactinaemia			
subjects affected / exposed	0 / 21 (0.00%)	4 / 35 (11.43%)	0 / 18 (0.00%)
occurrences (all)	0	4	0
Infections and infestations			
Adenovirus Infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 35 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 21 (0.00%)	3 / 35 (8.57%)	1 / 18 (5.56%)
occurrences (all)	0	9	2
Conjunctivitis			
subjects affected / exposed	0 / 21 (0.00%)	4 / 35 (11.43%)	0 / 18 (0.00%)
occurrences (all)	0	4	0
Cystitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 35 (2.86%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Influenza			
subjects affected / exposed	1 / 21 (4.76%)	7 / 35 (20.00%)	0 / 18 (0.00%)
occurrences (all)	1	9	0
Gastroenteritis			
subjects affected / exposed	1 / 21 (4.76%)	5 / 35 (14.29%)	1 / 18 (5.56%)
occurrences (all)	1	6	1

Pharyngitis			
subjects affected / exposed	1 / 21 (4.76%)	3 / 35 (8.57%)	1 / 18 (5.56%)
occurrences (all)	1	7	2
Nasopharyngitis			
subjects affected / exposed	2 / 21 (9.52%)	10 / 35 (28.57%)	1 / 18 (5.56%)
occurrences (all)	6	18	1
Streptococcal Infection			
subjects affected / exposed	0 / 21 (0.00%)	2 / 35 (5.71%)	1 / 18 (5.56%)
occurrences (all)	0	2	1
Tonsillitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 35 (2.86%)	1 / 18 (5.56%)
occurrences (all)	0	2	1
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 21 (0.00%)	0 / 35 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Increased Appetite			
subjects affected / exposed	5 / 21 (23.81%)	10 / 35 (28.57%)	0 / 18 (0.00%)
occurrences (all)	6	11	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 May 2012	The original protocol dated 16 May 2012 was amended one time on 25 May 2012, for removal to avoid sampling bias, and addition to the safety analysis section to tabulate the suicide-related adverse events.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported