Clinical trial results:
A Phase 3, Multicenter, Four-Week, Randomised, Double-Blind, Placebo-Controlled, Parallel-Group Efficacy And Safety Trial Of Flexible Doses Of Oral Ziprasidone In Children And Adolescents With Bipolar I Disorder (Current Or Most Recent Episode Manic)

Summary

EudraCT number	2020-003972-42
Trial protocol	Outside EU/EEA
Global end of trial date	18 May 2020

Results information

Result version number	v1 (current)
This version publication date	02 December 2020
First version publication date	02 December 2020

Trial information

Trial identification

Sponsor protocol code	A1281198

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02075047
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	24 August 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 May 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of oral ziprasidone compared with placebo in the treatment of children and adolescents aged 10-17 with Bipolar I Disorder (current or most recent episode manic) as measured by the change from baseline to Week 4 in the Young Mania Rating Scale (YMRS) total score. To evaluate the safety and tolerability of oral ziprasidone over 4 weeks in the treatment of children and adolescents with Bipolar I Disorder (current or most recent episode manic).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 May 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 170
Country: Number of subjects enrolled	Ukraine: 1
Worldwide total number of subjects	171
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)	39
Adolescents (12-17 years)	132
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted in the United States and Ukraine. Study started on 23 May 2014 and completed on 18 May 2020. Total 171 subjects were randomised to treatment, of which 86 received investigational product.

Period 1

Period 1 title	Treatment Phase (4 Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Carer, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Ziprasidone

Arm description:

Subjects were randomised to receive ziprasidone capsules orally once daily for 4 weeks. Dose was titrated over the first 7-14 days of treatment, and the stable dose was maintained for remaining treatment period. Subjects with body weight less than 45 kilogram (kg) received 60 to 80 milligram per day (mg/day) and subjects with body weight greater than or equal to (>=) 45 kg received 120-160 mg/day, as per investigator discretion. Subjects after completion or discontinuation of treatment were eligible to enroll in open label extension study A1281201 or were followed-up to 35 days (5 weeks) after last dose in this study.

Arm type	Experimental
Investigational medicinal product name	Ziprasidone
Investigational medicinal product code	CP-88,059-1
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received ziprasidone capsules orally once daily for 4 weeks. Subjects with body weight less than 45 kg received 60 to 80 mg/day and subjects with body weight >=45 kg received 120-160 mg/day.

Arm title	Placebo

Arm description:

Subjects were randomised to receive placebo capsules matched to ziprasidone once daily for 4 weeks. Subjects after completion or discontinuation of treatment were eligible to enroll in open label extension study A1281201 or were followed-up to 35 days (5 weeks) after last dose in this study.

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

Dosage and administration details:

Subjects received placebo capsules matched to ziprasidone daily for 4 weeks.

Number of subjects in period 1	Ziprasidone	Placebo
Started	86	85
Completed	63	75
Not completed	23	10
Screen Failure	1	-
Adverse event, non-fatal	14	4
Withdrawal By Parent/Guardian	4	2
Medication Error Without Associated Adverse Event	1	-
Unspecified	1	1
Lost to follow-up	-	1
Lack of efficacy	2	2

Period 2	
Period 2 title	Follow up Phase (5 Weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms	
Are arms mutually exclusive?	Yes
Arm title	Ziprasidone
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Placebo
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Ziprasidone	Placebo
Started	63	75
Completed	60	72
Not completed	26	13
Screen Failure	1	-
Adverse event, non-fatal	14	4
Withdrawal By Parent/Guardian	7	4

Medication Error Without Associated Adverse Event	1	-
Unspecified	1	2
Lost to follow-up	-	1
Lack of efficacy	2	2
Joined	23	10
Continued to follow up	23	10

Baseline characteristics

Reporting groups	
Reporting group title	Ziprasidone

Reporting group description:

Subjects were randomised to receive ziprasidone capsules orally once daily for 4 weeks. Dose was titrated over the first 7-14 days of treatment, and the stable dose was maintained for remaining treatment period. Subjects with body weight less than 45 kilogram (kg) received 60 to 80 milligram per day (mg/day) and subjects with body weight greater than or equal to (>=) 45 kg received 120-160 mg/day, as per investigator discretion. Subjects after completion or discontinuation of treatment were eligible to enroll in open label extension study A1281201 or were followed-up to 35 days (5 weeks) after last dose in this study.

Reporting group title	Placebo

Reporting group description:

Subjects were randomised to receive placebo capsules matched to ziprasidone once daily for 4 weeks. Subjects after completion or discontinuation of treatment were eligible to enroll in open label extension study A1281201 or were followed-up to 35 days (5 weeks) after last dose in this study.

Reporting group values	Ziprasidone	Placebo	Total
Number of subjects	86	85	171
Age Categorical Units: Subjects			
Children (10-11 years)	23	16	39
Adolescents (12-17 years)	63	69	132
Gender Categorical Units: Subjects			
Female	48	47	95
Male	38	38	76
Race Characteristics Units: Subjects			
White	59	55	114
Black or African American	23	24	47
Asian	1	1	2
Other	3	5	8
Ethnicity Characteristics Units: Subjects			
Hispanic or Latino	12	14	26
Not Hispanic or Latino	74	71	145

End points

End points reporting groups

Reporting group title	Ziprasidone

Reporting group description:

Subjects were randomised to receive ziprasidone capsules orally once daily for 4 weeks. Dose was titrated over the first 7-14 days of treatment, and the stable dose was maintained for remaining treatment period. Subjects with body weight less than 45 kilogram (kg) received 60 to 80 milligram per day (mg/day) and subjects with body weight greater than or equal to (>=) 45 kg received 120-160 mg/day, as per investigator discretion. Subjects after completion or discontinuation of treatment were eligible to enroll in open label extension study A1281201 or were followed-up to 35 days (5 weeks) after last dose in this study.

Reporting group title	Placebo

Reporting group description:

Subjects were randomised to receive placebo capsules matched to ziprasidone once daily for 4 weeks. Subjects after completion or discontinuation of treatment were eligible to enroll in open label extension study A1281201 or were followed-up to 35 days (5 weeks) after last dose in this study.

Reporting group title	Ziprasidone

Reporting group description: -

Reporting group title	Placebo

Reporting group description: -

Primary: Change From Baseline in Young Mania Rating Scale (YMRS) Total Score at Week 4

End point title	Change From Baseline in Young Mania Rating Scale (YMRS) Total Score at Week 4

End point description:

YMRS: an 11-item scale that measured the severity of manic episodes. Four items (irritability, speech, thought content, and disruptive/ aggressive behavior) were rated on a scale from 0 (symptom absent) to 8 (symptom extremely severe). The remaining items were rated on a scale from 0 (symptom absent) to 4 (symptom extremely severe). YMRS total score was sum of score of all 11 items and ranged from 0 (no symptoms) to 60 (extreme severity of symptoms), higher score indicated higher severity of mania. Intent-to-treat (ITT): all randomised subjects who had baseline measurements, took at least 1 dose of study medication (ziprasidone or placebo) and with at least 1 post-baseline visit.

End point type	Primary

End point timeframe:

Baseline, Week 4

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	83		
Units: units on a scale				
least squares mean (standard error)	-16.51 (± 1.15)	-12.29 (± 1.10)		

Statistical analyses

Statistical analysis title	Change at Week 4

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Mixed models analysis
Parameter estimate	Difference in least square (LS) mean
Point estimate	-4.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.14
upper limit	-1.32
Variability estimate	Standard error of the mean
Dispersion value	1.47

Secondary: Change From Baseline in Clinical Global Impression of Severity (CGI-S) Score at Weeks 1, 2, 3, and 4

End point title	Change From Baseline in Clinical Global Impression of Severity (CGI-S) Score at Weeks 1, 2, 3, and 4

End point description:

CGI-S: 7-point clinician rated scale to assess severity of subject's current illness state; range: 1 (normal - not ill at all) to 7 (among the most extremely ill), higher scores indicated more severity of illness. ITT population included all randomised subjects who had baseline measurements, took at least 1 dose of study medication (ziprasidone or placebo) and with at least 1 post-baseline visit.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 2, 3, 4

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	83		
Units: units on a scale				
least squares mean (standard error)				
Change at Week 1	-0.91 (± 0.10)	-0.47 (± 0.10)		
Change at Week 2	-1.13 (± 0.12)	-0.91 (± 0.12)		
Change at Week 3	-1.53 (± 0.13)	-1.14 (± 0.13)		
Change at Week 4	-1.59 (± 0.14)	-1.32 (± 0.14)		

Statistical analyses

Statistical analysis title	Change at Week 1

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Change at Week 2

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.174
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Change at Week 3

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a

covariate along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.024
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	-0.05
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Change at Week 4

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.138
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.19

Secondary: Change From Baseline in the Young Mania Rating Scale (YMRS) Total Score at Weeks 1, 2, and 3

End point title	Change From Baseline in the Young Mania Rating Scale (YMRS) Total Score at Weeks 1, 2, and 3

End point description:

YMRS: an 11-item scale that measured the severity of manic episodes. Four items (irritability, speech, thought content, and disruptive/ aggressive behavior) were rated on a scale from 0 (symptom absent) to 8 (symptom extremely severe). The remaining items were rated on a scale from 0 (symptom absent) to 4 (symptom extremely severe). YMRS total score was sum of score of all 11 items and ranged from 0 (no symptoms) to 60 (extreme severity of symptoms), higher score indicated higher severity of mania. ITT population included all randomised subjects who had baseline measurements, took at least 1 dose of

study medication (ziprasidone or placebo) and with at least 1 post-baseline visit.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 2, 3

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	83		
Units: units on a scale				
least squares mean (standard error)				
Change at Week 1	-11.43 (± 0.94)	-5.58 (± 0.93)		
Change at Week 2	-13.70 (± 1.02)	-9.53 (± 1.01)		
Change at Week 3	-16.79 (± 1.04)	-11.17 (± 1.01)		

Statistical analyses

Statistical analysis title	Change at Week 1

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.

Comparison groups	Placebo v Ziprasidone
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-5.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.16
upper limit	-3.54
Variability estimate	Standard error of the mean
Dispersion value	1.17

Statistical analysis title	Change at Week 2

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo

Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-4.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.74
upper limit	-1.59
Variability estimate	Standard error of the mean
Dispersion value	1.3

Statistical analysis title	Change at Week 3

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-5.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.21
upper limit	-3.04
Variability estimate	Standard error of the mean
Dispersion value	1.31

Secondary: Clinical Global Impression of Improvement (CGI-I) Scores at Weeks 1, 2, 3, and 4

End point title	Clinical Global Impression of Improvement (CGI-I) Scores at Weeks 1, 2, 3, and 4

End point description:

CGI-I: 7-point clinician rated scale which rates the subject’s improvement or worsening from baseline, ranging from 1 (very much improved) to 7 (very much worse), higher scores indicate less improvement. ITT population included all randomised subjects who had baseline measurements, took at least 1 dose of study medication (ziprasidone or placebo) and with at least 1 post-baseline visit.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 2, 3, 4

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	83		
Units: units on a scale				
least squares mean (standard error)				
Week 1	2.89 (± 0.11)	3.41 (± 0.11)		
Week 2	2.75 (± 0.12)	2.89 (± 0.12)		
Week 3	2.42 (± 0.12)	2.68 (± 0.12)		
Week 4	2.30 (± 0.13)	2.64 (± 0.13)		

Statistical analyses

Statistical analysis title	Change at Week 1

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	-0.26
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Change at Week 2

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo

Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.349
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Change at Week 3

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.103
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Change at Week 4

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo

Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.17

Other pre-specified: Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An AE was any untoward medical occurrence in a subject who received study medication without regard to possibility of causal relationship to it. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/ incapacity; congenital anomaly. AEs included both serious and all non-serious AEs. The safety analysis set included all subjects who were randomised and took at least 1 dose of study medication (ziprasidone or placebo).

End point type	Other pre-specified

End point timeframe:

Screening up to maximum of 35 days after administration of the final dose of study medication (maximum up to 11 weeks)

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	85		
Units: subjects				
AEs	67	50		
SAEs	3	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Columbia Classification Algorithm of Suicide Assessment (C-CASA) Categorization Mapped From Columbia-Suicide Severity Rating Scale (C-SSRS)

End point title	Number of Subjects With Columbia Classification Algorithm of

	Suicide Assessment (C-CASA) Categorization Mapped From Columbia-Suicide Severity Rating Scale (C-SSRS)

End point description:

C-SSRS: a measure used to identify and assess subjects at risk for suicide. It is a semi-structured interview that captures the occurrence, severity, and frequency of suicide-related thoughts and behaviors. C-SSRS items were mapped to the following C-CASA categories: completed suicide, attempted suicide (actual attempt; aborted attempt; interrupted attempt), non-suicidal self-injurious behavior (SIB), preparatory acts, suicidal ideation (wish to be dead; non-specific active suicidal thoughts [AST]; active suicidal ideation [ASI] with any methods [not plan], without intent to act; ASI with some intent to act, without specific plan; ASI with specific plan and intent; SIB, no suicidal intent). ITT population included all randomised subjects who had baseline measurements, took at least 1 dose of study medication (ziprasidone or placebo) and with at least 1 post-baseline visit. "n" = number of subjects evaluable for specified categories.

End point type	Other pre-specified

End point timeframe:

Screening (maximum up to 14 days before Day 1), Baseline (Day 1), Week 1, 2, 3, 4, Early termination Visit (ET = anytime till Week 4), Follow up Visit (FW = anytime from last dose of study drug up to 35 days till Week 11)

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	83		
Units: Subjects				
Screening (n =85, 83): Completed Suicide	0	0		
Screening (n =85, 83): Actual Attempt	5	3		
Screening (n =85, 83): Aborted Attempt	0	0		
Screening (n =85, 83): Interrupted Attempt	0	1		
Screening (n =85, 83): Non-Suicidal SIB	10	5		
Screening (n =85, 83): Preparatory Acts	0	1		
Screening (n =85, 83): Wish To Be Dead	25	25		
Screening (n =85, 83): Non-specific AST	16	13		
Screening (n =85, 83): ASI with no plan, intent	0	0		
Screening (n=85, 83): ASI with no plan,some intent	0	0		
Screening (n =85, 83): ASI with plan, intent	0	0		
Screening (n =85, 83): SIB, no intent	0	0		
Baseline (n =85, 83): Completed Suicide	0	0		
Baseline (n =85, 83): Actual Attempt	0	0		
Baseline (n =85, 83): Aborted Attempt	0	0		
Baseline (n =85, 83): Interrupted Attempt	0	0		
Baseline (n =85, 83): Non-Suicidal SIB	0	0		
Baseline (n =85, 83): Preparatory Acts	0	0		
Baseline (n =85, 83): Wish To Be Dead	1	0		
Baseline (n =85, 83): Non-specific AST	0	0		
Baseline (n=85, 83): ASI with no plan, intent	4	7		

Baseline (n=85,83): ASI with no plan,some intent	2	3		
Baseline (n =85, 83): ASI with plan, intent	4	3		
Baseline (n =85,83): SIB, no intent	0	0		
Week 1 (n =78, 83): Completed Suicide	0	0		
Week 1 (n =78, 83): Actual Attempt	0	0		
Week 1 (n =78, 83): Aborted Attempt	0	0		
Week 1 (n =78, 83): Interrupted Attempt	0	0		
Week 1 (n =78, 83): Non-Suicidal SIB	0	0		
Week 1 (n =78, 83): Preparatory Acts	0	0		
Week 1 (n =78, 83): Wish To Be Dead	0	1		
Week 1 (n =78, 83): Non-specific AST	0	0		
Week 1 (n =78, 83): ASI with no plan, intent	0	0		
Week 1 (n =78, 83): ASI with no plan, some intent	0	0		
Week 1 (n =78, 83): ASI with plan, intent	0	0		
Week 1(n =78, 83): SIB, no intent	0	0		
Week 2 (n =67, 78): Completed Suicide	0	0		
Week 2 (n =67, 78): Actual Attempt	0	0		
Week 2 (n =67, 78): Aborted Attempt	0	0		
Week 2 (n =67, 78): Interrupted Attempt	0	0		
Week 2 (n =67, 78): Non-Suicidal SIB	0	0		
Week 2 (n =67, 78): Preparatory Acts	0	0		
Week 2 (n =67, 78): Wish To Be Dead	0	0		
Week 2 (n =67, 78): Non-specific AST	0	0		
Week 2 (n =67, 78): ASI with no plan, intent	0	0		
Week 2 (n =67, 78): ASI with no plan, some intent	0	0		
Week 2 (n =67, 78): ASI with plan, intent	0	0		
Week 2(n =67, 78): SIB, no intent	0	0		
Week 3 (n =64, 75): Completed Suicide	0	0		
Week 3 (n =64, 75): Actual Attempt	0	0		
Week 3 (n =64, 75): Aborted Attempt	0	0		
Week 3 (n =64, 75): Interrupted Attempt	0	0		
Week 3 (n =64, 75): Non-Suicidal SIB	0	0		
Week 3 (n =64, 75): Preparatory Acts	0	0		
Week 3 (n =64, 75): Wish To Be Dead	0	0		
Week 3 (n =64, 75): Non-specific AST	0	0		
Week 3 (n =64, 75): ASI with no plan, intent	0	0		
Week 3 (n =64, 75): ASI with no plan, some intent	0	0		
Week 3 (n =64, 75): ASI with plan, intent	0	0		
Week 3 (n =64, 75): SIB, no intent	0	0		
Week 4 (n =63, 75): Completed Suicide	0	0		
Week 4 (n =63, 75): Actual Attempt	0	0		
Week 4 (n =63, 75): Aborted Attempt	0	0		

Week 4 (n =63, 75): Interrupted Attempt	0	0		
Week 4 (n =63, 75): Non-Suicidal SIB	1	0		
Week 4 (n =63, 75): Preparatory Acts	0	0		
Week 4 (n =63, 75): Wish To Be Dead	2	0		
Week 4 (n =63, 75): Non-specific AST	1	0		
Week 4 (n =63, 75): ASI with no plan, intent	0	0		
Week 4 (n =63, 75): ASI with no plan, some intent	0	0		
Week 4 (n =63, 75): ASI with plan, intent	0	0		
Week 4 (n =63, 75): SIB, no intent	0	0		
ET (n =21, 5): Completed Suicide	0	0		
ET (n =21, 5): Actual Attempt	0	0		
ET (n =21, 5): Aborted Attempt	0	0		
ET (n =21, 5): Interrupted Attempt	0	0		
ET (n =21, 5): Non-Suicidal SIB	0	0		
ET (n =21, 5): Preparatory Acts	0	0		
ET (n =21, 5): Wish To Be Dead	1	0		
ET (n =21, 5): Non-specific AST	1	0		
ET (n =21, 5): ASI with no plan, intent	1	0		
ET (n =21, 5): ASI with no plan, some intent	0	0		
ET (n =21, 5): ASI with plan, intent	0	0		
ET (n =21, 5): SIB, no intent	0	0		
FW (n =62, 64): Completed Suicide	0	0		
FW (n =62, 64): Actual Attempt	1	0		
FW (n =62, 64): Aborted Attempt	0	0		
FW (n =62, 64): Interrupted Attempt	0	0		
FW (n =62, 64): Non-Suicidal SIB	0	0		
FW (n =62, 64): Preparatory Acts	0	0		
FW (n =62, 64): Wish To Be Dead	2	0		
FW (n =62, 64): Non-specific AST	0	0		
FW (n =62, 64): ASI with no plan, intent	0	0		
FW (n =62, 64): ASI with no plan, some intent	0	0		
FW (n =62, 64): ASI with plan, intent	0	0		
FW (n =62, 64): SIB, no intent	0	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects who Took At least 1 Concomitant Medication and Concomitant Non-Drug Treatments/Procedures

End point title	Number of Subjects who Took At least 1 Concomitant Medication and Concomitant Non-Drug Treatments/Procedures

End point description:

Concomitant medications or treatments were those prescription and over-the-counter drugs and supplements or non drug treatment/procedures that a study subject had taken along with the study medication as per investigator's discretion. The safety analysis set included all subjects who were

randomised and took at least 1 dose of study medication (ziprasidone or placebo).

End point type	Other pre-specified

End point timeframe:

Screening up to Week 5

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	85		
Units: subjects				
Concomitant Medication	55	47		
Concomitant Non-Drug Treatments/Procedures	6	7		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Laboratory Abnormalities

End point title	Number of Subjects With Laboratory Abnormalities

End point description:

Hematology-hemoglobin(Hg),hematocrit,erythrocytes(ery)<0.8*LLN,ery mean corpuscular volume <0.9*LLN>1.1*ULN,platelets<0.5*LLN>1.75*ULN,leukocytes(leu)<0.6*LLN>1.5*ULN,lymphocytes(lym) ,lym/leu,neutrophils(neu),neu/leu<0.8*LLN>1.2*ULN,basophils (bas),bas/leu,eosinophils(eos),eos/leu, monocytes(mon),mon/leu>1.2*ULN;Clinical chemistry bilirubin:total,direct,indirect>1.5*ULN, aspartate aminotransferase(AT),alanine AT,gamma glutamyl transferase,lactate dehydrogenase,alkaline phosphatase>3.0*ULN,protein,albumin<0.8*LLN>1.2*ULN,blood urea nitrogen,creatinine>1.3*ULN, urate>1.2*ULN,HDL<0.8*LLN;LDL>1.2*ULN cholesterol(CH),sodium<0.95*LLN>1.05*ULN,potassium, chloride,calcium,magnesium,bicarbonate<0.9*LLLN>1.1*ULN,phosphate,free thyroxine,thyroid stimulating hormone<0.8*LLN>1.2*ULN,prolactin>1.1*ULN,glucose<0.6*LLN>1.5*ULN,HgA1C,CH, triglycerides>1.3*ULN,creatine kinase>2.0*ULN;Urinalysis-specific gravity<1.003>1.030,pH<4.5 >8,urine glucose,protein,Hg,ketones:>=1.Safety set.N=subjects evaluable.

End point type	Other pre-specified

End point timeframe:

Screening up to Week 5

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	83		
Units: Subjects	50	62		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Physical Examination Abnormalities

End point title	Number of Subjects With Physical Examination Abnormalities

End point description:

Parameters assessed for physical examination included: oral/tympanic temperature, general appearance, skin, head, ears, eyes, nose, throat, heart, lungs, breasts (if medically indicated), abdomen, external genitalia [if medically indicated], extremities, back/spinal system, lymph nodes or worsening of medical history conditions. Abnormality in physical examination was at the investigator's discretion. The safety analysis set included all subjects who were randomised and took at least 1 dose of study medication (ziprasidone or placebo).

End point type	Other pre-specified

End point timeframe:

Screening up to Week 4

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	85		
Units: Subjects	4	5		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Blood Pressure at Week 1, 2, 3, 4, Early Termination Visit and Follow-up Visit

End point title	Change From Baseline in Blood Pressure at Week 1, 2, 3, 4, Early Termination Visit and Follow-up Visit

End point description:

Change from baseline in sitting and standing systolic blood pressure (SBP) and diastolic blood pressure (DBP) in millimeter of mercury (mmHg) was reported. The safety analysis set included all subjects who were randomised and took at least 1 dose of study medication (ziprasidone or placebo). Here 'n' signifies number of subjects evaluable for each specified category.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 1, 2, 3, 4, Early termination Visit (ET = anytime till Week 4), Follow up Visit (FW = anytime from last dose of study drug up to 35 days till Week 11)

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	85		
Units: millimeter of mercury				
arithmetic mean (standard deviation)				
Sitting SBP, Baseline (n = 86, 85)	110.5 (± 9.84)	110.9 (± 11.45)		
Sitting SBP, Change at Week 1 (n = 78, 83)	0.7 (± 6.90)	0.2 (± 8.71)		

Sitting SBP, Change at Week 2 (n = 67, 78)	0.2 (± 9.65)	0.1 (± 9.26)		
Sitting SBP, Change at Week 3 (n = 64, 75)	-0.7 (± 10.12)	-0.6 (± 8.93)		
Sitting SBP, Change at Week 4 (n = 63, 75)	-0.7 (± 10.60)	-2.2 (± 10.39)		
Sitting SBP, Change at ET (n = 20, 5)	0.7 (± 7.87)	6.4 (± 5.90)		
Sitting SBP, Change at FW (n = 21, 22)	-1.4 (± 12.44)	-2.2 (± 8.35)		
Standing SBP, Baseline (n = 86, 85)	110.7 (± 9.53)	112.0 (± 10.16)		
Standing SBP, Change at Week 1 (n = 78, 83)	0.8 (± 7.67)	-2.5 (± 10.38)		
Standing SBP, Change at Week 2 (n = 67, 78)	0.1 (± 9.13)	-1.8 (± 9.71)		
Standing SBP, Change at Week 3 (n = 64, 75)	-0.1 (± 9.68)	-1.8 (± 9.71)		
Standing SBP, Change at Week 4 (n = 63, 75)	-0.8 (± 9.50)	-2.5 (± 10.77)		
Standing SBP, Change at ET (n = 20, 5)	-2.1 (± 10.14)	5.6 (± 13.58)		
Standing SBP, Change at FW (n = 21, 22)	-4.9 (± 11.86)	-4.4 (± 10.01)		
Sitting DBP, Baseline (n = 86, 85)	68.8 (± 7.99)	70.3 (± 7.94)		
Sitting DBP, Change at Week 1 (n = 78, 83)	0.7 (± 7.72)	-1.5 (± 8.49)		
Sitting DBP, Change at Week 2 (n = 67, 78)	1.0 (± 9.76)	-0.6 (± 9.40)		
Sitting DBP, Change at Week 3 (n = 64, 75)	0.2 (± 9.36)	0.1 (± 8.03)		
Sitting DBP, Change at Week 4 (n = 63, 75)	1.1 (± 8.18)	-0.6 (± 10.22)		
Sitting DBP, Change at ET (n = 20, 5)	-1.8 (± 9.65)	2.0 (± 8.46)		
Sitting DBP, Change at FW (n = 21, 22)	2.7 (± 8.64)	1.7 (± 6.75)		
Standing DBP, Baseline (n = 86, 85)	70.3 (± 6.98)	72.3 (± 7.91)		
Standing DBP, Change at Week 1 (n = 78, 83)	1.5 (± 7.40)	-1.6 (± 8.46)		
Standing DBP, Change at Week 2 (n = 67, 78)	-0.1 (± 7.83)	-1.7 (± 8.75)		
Standing DBP, Change at Week 3 (n = 64, 75)	-1.1 (± 7.91)	-1.6 (± 10.27)		
Standing DBP, Change at Week 4 (n = 63, 75)	1.0 (± 7.76)	-0.5 (± 9.83)		
Standing DBP, Change at ET (n = 20, 5)	1.3 (± 10.22)	1.6 (± 7.60)		
Standing DBP, Change at FW (n = 21, 22)	1.2 (± 8.41)	-2.1 (± 12.89)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Pulse Rate at Week 1, 2, 3, 4, Early Termination Visit and Follow-up Visit

End point title	Change From Baseline in Pulse Rate at Week 1, 2, 3, 4, Early Termination Visit and Follow-up Visit

End point description:

Change from baseline in pulse rate in (beats per minute) was reported in sitting and standing positions. The safety analysis set included all subjects who were randomised and took at least 1 dose of study

medication (ziprasidone or placebo). Here 'n' signifies number of subjects evaluable for each specified category.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 1, 2, 3, 4, Early termination Visit (ET = anytime till Week 4), Follow up Visit (FW = anytime from last dose of study drug up to 35 days till Week 11)

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	85		
Units: beats per minute				
arithmetic mean (standard deviation)				
Sitting, Baseline (n = 86, 85)	79.1 (± 12.58)	75.8 (± 9.80)		
Sitting, Change at Week 1 (n = 78, 83)	-0.9 (± 11.24)	-2.0 (± 9.40)		
Sitting, Change at Week 2 (n = 67, 78)	-2.4 (± 11.75)	1.5 (± 8.82)		
Sitting, Change at Week 3 (n = 64, 75)	-0.5 (± 12.79)	2.3 (± 10.61)		
Sitting, Change at Week 4 (n = 63, 75)	-2.3 (± 11.49)	-0.2 (± 10.30)		
ET: Sitting (n = 20, 5)	3.5 (± 14.02)	1.6 (± 7.02)		
FW: Sitting (n = 21, 22)	2.0 (± 11.32)	3.1 (± 11.73)		
Standing, Baseline (n = 86, 85)	84.6 (± 12.23)	83.3 (± 10.95)		
Standing, Change at Week 1 (n = 78, 83)	2.1 (± 10.77)	-2.2 (± 10.18)		
Standing, Change at Week 2 (n = 67, 78)	-0.4 (± 12.25)	1.9 (± 10.19)		
Standing, Change at Week 3 (n = 64, 75)	1.4 (± 13.54)	2.6 (± 11.70)		
Standing, Change at Week 4 (n = 63, 75)	-0.7 (± 11.77)	-0.6 (± 12.83)		
ET: Standing (n = 20, 5)	7.9 (± 13.98)	-6.2 (± 21.12)		
FW: Standing (n = 21, 22)	5.4 (± 10.15)	4.5 (± 11.67)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Height and Waist Circumference at Week 4 and Early Termination Visit

End point title	Change From Baseline in Height and Waist Circumference at Week 4 and Early Termination Visit

End point description:

Change from baseline in height and waist circumference in centimeter (cm) was reported. The safety analysis set included all subjects who were randomised and took at least 1 dose of study medication (ziprasidone or placebo). Here 'n' signifies number of subjects evaluable for each specified category.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 4, Early termination Visit (ET = anytime till Week 4)

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	85		
Units: centimeter				
arithmetic mean (standard deviation)				
Height, Baseline (n = 86, 85)	157.9 (± 10.63)	159.7 (± 11.41)		
Height, Change at Week 4 (n = 63, 75)	0.4 (± 0.60)	0.7 (± 1.77)		
Height, Change at ET (n = 19, 5)	0.2 (± 0.54)	0.5 (± 0.73)		
Waist circumference, Baseline (n = 86, 85)	76.9 (± 12.22)	74.9 (± 10.56)		
Waist circumference, Change at Week 4 (n = 63, 75)	-0.1 (± 2.79)	0.3 (± 3.26)		
Waist circumference, Change at ET (n = 19, 5)	0.4 (± 3.77)	1.0 (± 1.74)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Body Weight at Week 4 and Early Termination Visit

End point title	Change From Baseline in Body Weight at Week 4 and Early Termination Visit

End point description:

Change from baseline in weight in kilogram (kg) was reported. The safety analysis set included all subjects who were randomised and took at least 1 dose of study medication (ziprasidone or placebo). Here 'n' signifies number of subjects evaluable for each specified category.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 4, Early termination Visit (ET = anytime till Week 4)

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	85		
Units: kilogram				
arithmetic mean (standard deviation)				
Baseline (n = 86, 85)	57.5 (± 14.52)	58.0 (± 14.54)		
Change at Week 4 (n = 63, 75)	0.3 (± 1.97)	0.8 (± 2.04)		
Change at ET (n = 19, 5)	-0.3 (± 1.75)	1.0 (± 1.46)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Body Mass Index (BMI) at Week 4 and Early Termination Visit

End point title	Change From Baseline in Body Mass Index (BMI) at Week 4 and Early Termination Visit

End point description:

Change from baseline in BMI in kilogram per meter square (kg/m^2) was reported. The safety analysis set included all subjects who were randomised and took at least 1 dose of study medication (ziprasidone or placebo). Here 'n' signifies number of subjects evaluable for each specified category.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 4, Early termination Visit (ET = anytime till Week 4)

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	85		
Units: kilogram per meter square				
arithmetic mean (standard deviation)				
Baseline (n = 86, 85)	22.8 (± 4.15)	22.5 (± 3.76)		
Change at Week 4 (n = 63, 75)	0.1 (± 0.79)	0.2 (± 0.92)		
Change at ET (n = 19, 5)	-0.3 (± 0.95)	0.3 (± 0.51)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Body Mass Index (BMI) Z-score at Week 4 and Early Termination Visit

End point title	Change From Baseline in Body Mass Index (BMI) Z-score at Week 4 and Early Termination Visit

End point description:

BMI z-score was reported using the Children's Hospital of Philadelphia z-score calculator. Z-score is a statistical measure to describe whether a mean was above or below the standard. A z-score of 0 is equal to the mean and is considered normal. Lower numbers indicate values lower than the mean and higher numbers indicate values higher than the mean. Higher values are indicative of higher BMI. The safety analysis set included all subjects who were randomised and took at least 1 dose of study medication (ziprasidone or placebo). Here 'n' signifies number of subjects evaluable for each specified category.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 4, Early termination Visit (ET = anytime till Week 4)

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	85		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n = 86, 85)	0.8 (± 0.87)	0.7 (± 0.82)		
Change at Week 4 (n = 63, 75)	0.0 (± 0.18)	-0.0 (± 0.24)		
Change at ET (n = 19, 5)	-0.0 (± 0.15)	-0.0 (± 0.22)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Pre-defined Categories of Electrocardiogram (ECG) Findings

End point title	Number of Subjects With Pre-defined Categories of Electrocardiogram (ECG) Findings

End point description:

Pre-defined categories for ECG were: heart rate intervals - QT interval corrected using the Fridericia's formula (QTCF) value greater than or equal to (>=450) millisecond (msec), >=460 msec, >=480 msec, >=500 msec, >=30 msec increase, >=60 msec increase, >=75 msec increase, QT interval corrected using the Bazett's correction (QTCB) value >=450 msec, >=460 msec, >=480 msec, >=500 msec, >=30 msec increase, >=60 msec increase, >=75 msec increase, PR value >=25 percentage increase, QRS value >=25 percentage increase, QT value >=25 percentage increase, RR value >=25 percentage increase, and HR value >=25 percentage increase. The safety analysis set included all subjects who were randomised and took at least 1 dose of study medication (ziprasidone or placebo). Here 'number of subjects analysed' signifies number of subjects who were evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 1, 2, 3, 4, Early termination Visit (anytime till Week 4), Follow up Visit (anytime from last dose of study drug up to 35 days till Week 11)

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	83		
Units: Subjects				
QTcF at >=450 msec	3	1		
QTcF at >=460 msec	1	0		
QTcF at >=480 msec	0	0		
QTcF at >=500 msec	0	0		
QTcF at >=30 msec increase	9	4		
QTcF at >=60 msec increase	0	0		
QTcF at >=75 msec increase	0	0		
QTcB at >=450 msec	14	7		
QTcB at >=460 msec	8	3		
QTcB at >=480 msec	1	0		
QTcB at >=500 msec	0	0		
QTcB at >=30 msec increase	16	7		
QTcB at >=60 msec increase	0	0		

QTcB at >=75 msec increase	0	0		
PR at >=25% increase	0	0		
QRS at >=25% increase	3	1		
QT at >=25% increase	0	0		
RR at >=25% increase	12	14		
HR at >=25% increase	18	9		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Children's Depression Rating Scale (CDRS-R) Total Score at Weeks 1, 2, 3, and 4 and Early Termination Visit

End point title	Change From Baseline in Children's Depression Rating Scale (CDRS-R) Total Score at Weeks 1, 2, 3, and 4 and Early Termination Visit

End point description:

CDRS-R: clinician-rated interview-based scale (with both child and parent or guardian) to assess 17 distinct symptom areas to derive an index of depression severity. Discrepancies between informants responses were resolved by using most impaired rating given by valid informant. Rated on a 7-point scale; range from 1 (no impairment) to 7 (maximum impairment). Higher scores indicated greater impairment. Total score calculated as sum of the 17 items ranged from 1 (no impairment) to 119 (maximum impairment); higher score indicated greater impairment. ITT population included all randomised subjects who had baseline measurements, took at least 1 dose of study medication (ziprasidone or placebo) and with at least 1 post-baseline visit. Here 'number of subjects analysed' signifies number of subjects who were evaluable for this endpoint and 'n' signifies number of subjects evaluable for each specified category.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 1, 2, 3, 4, Early termination Visit (ET = anytime till Week 4)

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	83		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n = 85, 83)	29.0 (± 6.62)	28.3 (± 5.74)		
Change at Week 1 (n = 78, 83)	-2.5 (± 5.78)	-0.8 (± 4.85)		
Change at Week 2 (n = 67, 78)	-2.9 (± 6.31)	-2.4 (± 5.37)		
Change at Week 3 (n = 64, 75)	-3.7 (± 6.39)	-3.3 (± 6.15)		
Change at Week 4 (n = 63, 75)	-3.6 (± 6.53)	-3.8 (± 5.99)		
Change at ET (n = 20, 5)	2.3 (± 10.46)	-1.2 (± 4.60)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Simpson-Angus Rating Scale (SARS) Total Score at Weeks 1, 2, 3, and 4

End point title	Change From Baseline in Simpson-Angus Rating Scale (SARS) Total Score at Weeks 1, 2, 3, and 4

End point description:

SARS: 10-item clinician rated instrument to assess parkinsonian symptoms and related extrapyramidal side effects. All 10 items were anchored on a 5-point scale: range 0 (absence of condition, normal) to 4 (the most extreme form of condition). Total score is sum of individual item scores, ranged from 0 (normal) to 40 (most extreme symptoms and effects); higher score indicates more affected. ITT population included all randomised subjects who had baseline measurements, took at least 1 dose of study medication (ziprasidone or placebo) and with at least 1 post-baseline visit.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 1, 2, 3, 4

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	83		
Units: units on a scale				
least squares mean (standard error)				
Change at Week 1	0.09 (± 0.04)	-0.01 (± 0.04)		
Change at Week 2	0.11 (± 0.05)	-0.00 (± 0.05)		
Change at Week 3	0.11 (± 0.05)	-0.00 (± 0.05)		
Change at Week 4	0.09 (± 0.04)	-0.00 (± 0.04)		

Statistical analyses

Statistical analysis title	Change at Week 1

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Change at Week 2
Statistical analysis description:	
Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.	
Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.124
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.25
Variability estimate	Standard error of the mean
Dispersion value	0.07

Statistical analysis title	Change at Week 3
Statistical analysis description:	
Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.	
Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.084
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	Change at Week 4

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.104
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.05

Other pre-specified: Change From Baseline in Barnes Akathisia Rating Scale (BAS): Global Clinical Assessment of Akathisia Subscale Score at Weeks 1, 2, 3, and 4

End point title	Change From Baseline in Barnes Akathisia Rating Scale (BAS): Global Clinical Assessment of Akathisia Subscale Score at Weeks 1, 2, 3, and 4

End point description:

BAS: clinician rated scale to assess akathisia by determining the degree of subjective restlessness and distress associated with restlessness. First 3 items (objective, subjective, and distress related to restlessness) were rated on a 4-point scale with range 0 (no symptoms) to 3 (maximum severity of symptoms). Item 4, global clinical assessment of akathisia, was rated on a 6-point scale range 0 (no symptoms) to 5 (maximum severity of symptoms); higher score indicates increased severity. ITT population included all randomised subjects who had baseline measurements, took at least 1 dose of study medication (ziprasidone or placebo) and with at least 1 post-baseline visit.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 1, 2, 3, 4

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	83		
Units: units on a scale				
least squares mean (standard error)				
Change at Week 1	-0.01 (± 0.01)	0.02 (± 0.01)		
Change at Week 2	0.04 (± 0.03)	0.04 (± 0.03)		
Change at Week 3	0.01 (± 0.02)	0.01 (± 0.01)		
Change at Week 4	0.01 (± 0.01)	-0.01 (± 0.01)		

Statistical analyses

Statistical analysis title	Change at Week 1
Statistical analysis description:	
Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.	
Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.169
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Change at Week 2
Statistical analysis description:	
Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.	
Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.893
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Change at Week 3
Statistical analysis description:	
Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.	
Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.915
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Change at Week 4
Statistical analysis description:	
Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.	
Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.289
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.01

Other pre-specified: Change From Baseline in Abnormal Involuntary Movement Scale (AIMS) - Movement Cluster Score at Weeks 1, 2, 3, and 4

End point title	Change From Baseline in Abnormal Involuntary Movement Scale (AIMS) - Movement Cluster Score at Weeks 1, 2, 3, and 4

End point description:

AIMS: clinician rated 12-item scale to document occurrences of dyskinesia in subjects, specifically tardive dyskinesia. Items 1 to 10, scored as 0 (none) to 4 (severe); higher score indicates greater severity. Items 11 to 14 are questions with No or Yes response. Only the sum of the first 7 items were calculated to evaluate AIMS movement cluster score with a core range of 0 (none) to 28 (extreme severity); higher score indicates greater severity. ITT population included all randomised subjects who had baseline measurements, took at least 1 dose of study medication (ziprasidone or placebo) and with at least 1 post-baseline visit.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 1, 2, 3, 4

End point values	Ziprasidone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	83		
Units: units on a scale				
least squares mean (standard error)				
Change at Week 1	0.03 (± 0.01)	0.00 (± 0.01)		
Change at Week 2	0.03 (± 0.01)	0.00 (± 0.01)		
Change at Week 3	0.08 (± 0.03)	0.00 (± 0.03)		
Change at Week 4	0.05 (± 0.02)	0.00 (± 0.02)		

Statistical analyses

Statistical analysis title	Change at Week 1

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.145
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Change at Week 2
Statistical analysis description:	
Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.	
Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.148
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Change at Week 3
Statistical analysis description:	
Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.	
Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.082
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.04

Statistical analysis title	Change at Week 4

Statistical analysis description:

Results were obtained from a mixed effects repeated measures analysis of covariance model treatment, visit, visit-by-treatment interaction, and weight category as fixed effects and baseline score as a covariate along with subject as a random effect.

Comparison groups	Ziprasidone v Placebo
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.07
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.02

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Screening up to maximum of 35 days after administration of the final dose of study medication (maximum up to 11 weeks)

Adverse event reporting additional description:

Same event may appear as both AE and SAE. An event may be categorized as serious in 1 subject and non-serious in other, or subject may experience both SAE and non-SAE.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Ziprasidone

Reporting group description:

Subjects were randomised to receive ziprasidone capsules orally once daily for 4 weeks. Dose was titrated over the first 7-14 days of treatment, and the stable dose was maintained for remaining treatment period. Subjects with body weight less than 45 kg received 60 to 80 mg/day and subjects with body weight >=45 kg received 120-160 mg/day, as per investigator discretion. Subjects after completion or discontinuation of treatment were eligible to enroll in open label extension study A1281201 or were followed-up to 35 days (5 weeks) after last dose in this study.

Reporting group title	Placebo

Reporting group description:

Subjects were randomised to receive placebo capsules matched to ziprasidone once daily for 4 weeks. Subjects after completion or discontinuation of treatment were eligible to enroll in open label extension study A1281201 or were followed-up to 35 days (5 weeks) after last dose in this study.

Serious adverse events	Ziprasidone	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 86 (3.49%)	0 / 85 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Sunburn			
subjects affected / exposed	1 / 86 (1.16%)	0 / 85 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 86 (1.16%)	0 / 85 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 86 (1.16%)	0 / 85 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 86 (1.16%)	0 / 85 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 86 (1.16%)	0 / 85 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ziprasidone	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 86 (75.58%)	35 / 85 (41.18%)	
Nervous system disorders			
Akathisia			
subjects affected / exposed	5 / 86 (5.81%)	0 / 85 (0.00%)	
occurrences (all)	5	0	
Dizziness			
subjects affected / exposed	6 / 86 (6.98%)	2 / 85 (2.35%)	
occurrences (all)	7	2	
Headache			
subjects affected / exposed	9 / 86 (10.47%)	8 / 85 (9.41%)	
occurrences (all)	10	9	
Hypersomnia			
subjects affected / exposed	2 / 86 (2.33%)	0 / 85 (0.00%)	
occurrences (all)	2	0	
Sedation			
subjects affected / exposed	8 / 86 (9.30%)	3 / 85 (3.53%)	
occurrences (all)	11	3	
Somnolence			

subjects affected / exposed	27 / 86 (31.40%)	7 / 85 (8.24%)	
occurrences (all)	39	7	
Speech disorder			
subjects affected / exposed	2 / 86 (2.33%)	0 / 85 (0.00%)	
occurrences (all)	2	0	
Tremor			
subjects affected / exposed	2 / 86 (2.33%)	0 / 85 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	19 / 86 (22.09%)	2 / 85 (2.35%)	
occurrences (all)	23	4	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	3 / 86 (3.49%)	1 / 85 (1.18%)	
occurrences (all)	4	2	
Diarrhoea			
subjects affected / exposed	2 / 86 (2.33%)	1 / 85 (1.18%)	
occurrences (all)	2	1	
Nausea			
subjects affected / exposed	12 / 86 (13.95%)	5 / 85 (5.88%)	
occurrences (all)	14	6	
Salivary hypersecretion			
subjects affected / exposed	2 / 86 (2.33%)	0 / 85 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	9 / 86 (10.47%)	3 / 85 (3.53%)	
occurrences (all)	12	6	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 86 (2.33%)	1 / 85 (1.18%)	
occurrences (all)	2	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 86 (0.00%)	4 / 85 (4.71%)	
occurrences (all)	0	4	

Anxiety			
subjects affected / exposed	3 / 86 (3.49%)	0 / 85 (0.00%)	
occurrences (all)	3	0	
Initial insomnia			
subjects affected / exposed	2 / 86 (2.33%)	0 / 85 (0.00%)	
occurrences (all)	2	0	
Insomnia			
subjects affected / exposed	3 / 86 (3.49%)	1 / 85 (1.18%)	
occurrences (all)	4	1	
Irritability			
subjects affected / exposed	2 / 86 (2.33%)	0 / 85 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Joint stiffness			
subjects affected / exposed	2 / 86 (2.33%)	0 / 85 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal stiffness			
subjects affected / exposed	2 / 86 (2.33%)	0 / 85 (0.00%)	
occurrences (all)	2	0	
Myalgia			
subjects affected / exposed	2 / 86 (2.33%)	0 / 85 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 86 (2.33%)	3 / 85 (3.53%)	
occurrences (all)	2	3	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 86 (11.63%)	0 / 85 (0.00%)	
occurrences (all)	10	0	
Increased appetite			
subjects affected / exposed	3 / 86 (3.49%)	1 / 85 (1.18%)	
occurrences (all)	3	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 August 2018	Pregnancy testing was done weekly with no 14 day screening window.
19 February 2019	Language was applied to reflect the FDA agreed upon increase in sample size due to the rater training issue and adding a separate sensitivity analysis of final data set.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported