Clinical trial results:
26-Week Open-Label Extension Study Evaluating The Safety And Tolerability Of Flexible Doses Of Oral Ziprasidone In Children And Adolescents With Bipolar I Disorder (Most Recent Episode Manic)

Summary

EudraCT number	2020-004088-26
Trial protocol	Outside EU/EEA
Global end of trial date	31 July 2020

Results information

Result version number	v1 (current)
This version publication date	10 February 2021
First version publication date	10 February 2021

Trial information

Trial identification

Sponsor protocol code	A1281201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03768726
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 November 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of oral ziprasidone (20-80 mg BID) during long term, open label administration in children and adolescents with Bipolar I Disorder who participated in Study A1281198.

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	21 December 2018
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: 23
Worldwide total number of subjects	23
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)	3
Adolescents (12-17 years)	20
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who participated in study A1281198 (NCT02075047) and consented for treatment with open label ziprasidone were enrolled in the current study.

Pre-assignment

Screening details:

Study was conducted in the United States from 21-Dec-2018 to 31-July-2020.

Period 1

Period 1 title	Open Label Treatment Phase (26 Weeks)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Double Blind Ziprasidone to Open Label Ziprasidone

Arm description:

Subjects who were on ziprasidone in study A1281198, continued to receive ziprasidone, under double-blind conditions for maximum up to Week 2. Any subject if unable to tolerate the ziprasidone during Week 1 was discontinued from the study. After Week 2 to Week 26, dosing was open label and flexible. Subjects were followed up for 1 Week after last dose.

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	Double Blind Placebo to Open Label Ziprasidone

Arm description:

Subjects who were on placebo in study A1281198,received ziprasidone,under double-blind conditions for maximum up to Week 2,where dose was titrated up to appropriate weight-adjusted target dose per discretion of investigator to maintain optimal efficacy and tolerability.Subjects with weight >=45 kg:target dose range was total daily dose of 120-160 mg/day given in 2 divided doses with food.Subjects with weight <45 kg:target dose range was total daily dose of 60-80 mg/day given in 2 divided doses with food.Subjects who did not tolerate dose of 80 mg/day were allowed to have dose reduction and to continue study treatment at lower dose that was tolerable to them.Minimum permitted dose was 40 mg/day (20 mg BID) for all subjects.Any subject unable to tolerate ziprasidone during Week 1 was discontinued from study.After Week 2 to Week 26,for >=45 kg subjects and after Week 1 to Week 26 for <45 kg subjects,dosing was open label and flexible.Subjects were followed up for 1 Week after last dose.

Arm type	Experimental
Investigational medicinal product name	Ziprasidone
Investigational medicinal product code	CP-88,059-1
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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.

Number of subjects in period 1	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone
Started	10	13
Completed	2	10
Not completed	8	3
Consent withdrawn by subject	3	1
Adverse event, non-fatal	2	2
Withdrawal By Parent/Guardian	2	-
Lost to follow-up	1	-

Period 2

Period 2 title	Follow-Up Phase (1 Week)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Double Blind Ziprasidone to Open Label Ziprasidone

Arm description:

Subjects who were on ziprasidone in study A1281198, continued to receive ziprasidone, under double-blind conditions for maximum up to Week 2. Any subject if unable to tolerate the ziprasidone during Week 1 was discontinued from the study. After Week 2 to Week 26, dosing was open label and flexible. Subjects were followed up for 1 Week after last dose.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Double Blind Placebo to Open Label Ziprasidone

Arm description:

Subjects who were on placebo in study A1281198,received ziprasidone,under double-blind conditions for maximum up to Week 2,where dose was titrated up to appropriate weight-adjusted target dose per discretion of investigator to maintain optimal efficacy and tolerability.Subjects with weight >=45 kg:target dose range was total daily dose of 120-160 mg/day given in 2 divided doses with food.Subjects with weight <45 kg:target dose range was total daily dose of 60-80 mg/day given in 2 divided doses with food.Subjects who did not tolerate dose of 80 mg/day were allowed to have dose reduction and to continue study treatment at lower dose that was tolerable to them.Minimum permitted dose was 40 mg/day (20 mg BID) for all subjects.Any subject unable to tolerate ziprasidone during Week 1 was discontinued from study.After Week 2 to Week 26,for >=45 kg subjects and after Week 1 to Week 26 for <45 kg subjects,dosing was open label and flexible.Subjects were followed up for 1 Week after last dose.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone
Started	2	10
Completed	2	9
Not completed	6	3
Consent withdrawn by subject	2	-
Adverse event, non-fatal	2	2
Withdrawal By Parent/Guardian	1	1
Unspecified	1	-
Joined	6	2
Continued to follow up	6	2

Baseline characteristics

Reporting groups

Reporting group title	Double Blind Ziprasidone to Open Label Ziprasidone

Reporting group description:

Subjects who were on ziprasidone in study A1281198, continued to receive ziprasidone, under double-blind conditions for maximum up to Week 2. Any subject if unable to tolerate the ziprasidone during Week 1 was discontinued from the study. After Week 2 to Week 26, dosing was open label and flexible. Subjects were followed up for 1 Week after last dose.

Reporting group title	Double Blind Placebo to Open Label Ziprasidone

Reporting group description:

Subjects who were on placebo in study A1281198,received ziprasidone,under double-blind conditions for maximum up to Week 2,where dose was titrated up to appropriate weight-adjusted target dose per discretion of investigator to maintain optimal efficacy and tolerability.Subjects with weight >=45 kg:target dose range was total daily dose of 120-160 mg/day given in 2 divided doses with food.Subjects with weight <45 kg:target dose range was total daily dose of 60-80 mg/day given in 2 divided doses with food.Subjects who did not tolerate dose of 80 mg/day were allowed to have dose reduction and to continue study treatment at lower dose that was tolerable to them.Minimum permitted dose was 40 mg/day (20 mg BID) for all subjects.Any subject unable to tolerate ziprasidone during Week 1 was discontinued from study.After Week 2 to Week 26,for >=45 kg subjects and after Week 1 to Week 26 for <45 kg subjects,dosing was open label and flexible.Subjects were followed up for 1 Week after last dose.

Reporting group values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone	Total
Number of subjects	10	13	23
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	1	2	3
Adolescents (12-17 years)	9	11	20
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	14.0	14.2	
standard deviation	± 2.3	± 2.0	-
Sex: Female, Male Units: Subjects			
Female	5	7	12
Male	5	6	11
Race Characteristics Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	1	1	2
White	8	10	18
More than one race	1	1	2
Unknown or Not Reported	0	0	0
Ethnicity Characteristics Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	9	13	22
Unknown or Not Reported	1	0	1

End points

End points reporting groups

Reporting group title	Double Blind Ziprasidone to Open Label Ziprasidone

Reporting group description:

Subjects who were on ziprasidone in study A1281198, continued to receive ziprasidone, under double-blind conditions for maximum up to Week 2. Any subject if unable to tolerate the ziprasidone during Week 1 was discontinued from the study. After Week 2 to Week 26, dosing was open label and flexible. Subjects were followed up for 1 Week after last dose.

Reporting group title	Double Blind Placebo to Open Label Ziprasidone

Reporting group description:

Subjects who were on placebo in study A1281198,received ziprasidone,under double-blind conditions for maximum up to Week 2,where dose was titrated up to appropriate weight-adjusted target dose per discretion of investigator to maintain optimal efficacy and tolerability.Subjects with weight >=45 kg:target dose range was total daily dose of 120-160 mg/day given in 2 divided doses with food.Subjects with weight <45 kg:target dose range was total daily dose of 60-80 mg/day given in 2 divided doses with food.Subjects who did not tolerate dose of 80 mg/day were allowed to have dose reduction and to continue study treatment at lower dose that was tolerable to them.Minimum permitted dose was 40 mg/day (20 mg BID) for all subjects.Any subject unable to tolerate ziprasidone during Week 1 was discontinued from study.After Week 2 to Week 26,for >=45 kg subjects and after Week 1 to Week 26 for <45 kg subjects,dosing was open label and flexible.Subjects were followed up for 1 Week after last dose.

Reporting group title	Double Blind Ziprasidone to Open Label Ziprasidone

Reporting group description:

Subjects who were on ziprasidone in study A1281198, continued to receive ziprasidone, under double-blind conditions for maximum up to Week 2. Any subject if unable to tolerate the ziprasidone during Week 1 was discontinued from the study. After Week 2 to Week 26, dosing was open label and flexible. Subjects were followed up for 1 Week after last dose.

Reporting group title	Double Blind Placebo to Open Label Ziprasidone

Reporting group description:

Subjects who were on placebo in study A1281198,received ziprasidone,under double-blind conditions for maximum up to Week 2,where dose was titrated up to appropriate weight-adjusted target dose per discretion of investigator to maintain optimal efficacy and tolerability.Subjects with weight >=45 kg:target dose range was total daily dose of 120-160 mg/day given in 2 divided doses with food.Subjects with weight <45 kg:target dose range was total daily dose of 60-80 mg/day given in 2 divided doses with food.Subjects who did not tolerate dose of 80 mg/day were allowed to have dose reduction and to continue study treatment at lower dose that was tolerable to them.Minimum permitted dose was 40 mg/day (20 mg BID) for all subjects.Any subject unable to tolerate ziprasidone during Week 1 was discontinued from study.After Week 2 to Week 26,for >=45 kg subjects and after Week 1 to Week 26 for <45 kg subjects,dosing was open label and flexible.Subjects were followed up for 1 Week after last dose.

Primary: 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)[1]

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 hospitalization; 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 took at least 1 dose of study medication in this open-label extension study.

End point type	Primary

End point timeframe:

Day 1 up to 1 week after last dose of study medication (maximum up to 27 weeks)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this end point.

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: subjects				
AEs	7	12		
SAEs	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Abnormalities

End point title	Number of Subjects With Laboratory Abnormalities

End point description:

Hemoglobin(Hg),hematocrit,erythrocytes:<0.8*lower limits of normal(LLN); platelets:<0.5*LLN>1.75*upper limits of normal(ULN);leukocytes(leu),glucose-fasting:<0.6*LLN>1.5*ULN; lymphocytes(lym), lym/leu, neutrophils(neu), neu/leu, protein, albumin, phosphate, free thyroxine, thyroid stimulating hormone:<0.8*LLN>1.2*ULN;basophils (bas), bas/leu, eosinophils(eos), eos/leu, monocytes(mon), mon/leu:>1.2*ULN; bilirubin (total,direct,indirect):>1.5*ULN;aspartate aminotransferase(AT), alanine AT, lactate dehydrogenase, alkaline phosphatase:>3.0*ULN;blood urea nitrogen, creatinine, cholesterol (total,LDL,HDL), triglycerides, Hg A1C:>1.3*ULN;sodium:<0.95*LLN>1.05*ULN;potassium, chloride, calcium, magnesium, bicarbonate:<0.9*LLLN>1.1*ULN;prolactin:>1.1*ULN;creatine kinase:>2.0*ULN;urobilinogen:>=1;Urine-specific gravity:<1.003>1.030, pH:<4.5 >8, glucose,protein,bilirubin,nitrite,leukocyte esterase,ketones:>=1. Safety analysis set. 'Number of

End point type	Secondary

End point timeframe:

Day 1 up to 1 week after last dose of study medication (maximum up to 27 weeks)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	13		
Units: subjects	5	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Physical Examination Abnormalities at Baseline and Week 26

End point title	Number of Subjects With Physical Examination Abnormalities at Baseline and Week 26

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 took at least 1 dose of study medication in this open-label extension study.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: subjects				
Baseline	0	0		
Week 26	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Blood Pressure (BP) at Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit (ET) and Follow-up Visit

End point title	Change From Baseline in Blood Pressure (BP) at Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit (ET) and Follow-up Visit

End point description:

Change from baseline in sitting and standing systolic BP (SBP) and diastolic BP (DBP) in millimeter of mercury (mmHg) was reported. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit (anytime till Week 26), Follow-up Visit (1 week from last dose of study medication, anytime maximum up to Week 27)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: mmHg				
arithmetic mean (standard deviation)				
Sitting SBP, Baseline (n =10, 13)	111.70 (± 13.712)	111.38 (± 11.384)		
Sitting SBP, Change at Week 1 (n =9,12)	2.44 (± 10.944)	-1.00 (± 11.505)		
Sitting SBP, Change at Week 2 (n =7,12)	0.43 (± 6.024)	0.08 (± 10.431)		
Sitting SBP, Change at Week 4 (n =7,12)	3.29 (± 8.036)	-1.83 (± 8.321)		
Sitting SBP, Change at Week 6 (n =6,11)	3.17 (± 6.969)	-3.45 (± 11.903)		
Sitting SBP, Change at Week 10 (n =5,11)	-0.80 (± 9.203)	-3.09 (± 11.674)		
Sitting SBP, Change at Week 14 (n =5,11)	-2.80 (± 9.011)	-7.09 (± 8.949)		
Sitting SBP, Change at Week 18 (n =3,11)	-2.67 (± 8.327)	-0.82 (± 10.852)		
Sitting SBP, Change at Week 22 (n =2,10)	-5.00 (± 1.414)	1.40 (± 11.568)		
Sitting SBP, Change at Week 26/ET (n =8,13)	-0.63 (± 9.620)	-2.23 (± 14.219)		
Sitting SBP, Change at Follow up (n =4,3)	0.75 (± 7.365)	7.67 (± 4.041)		
Standing SBP, Baseline (n =10,13)	113.40 (± 10.690)	111.38 (± 12.738)		
Standing SBP, Change at Week 1 (n =9,11)	-0.67 (± 11.916)	-1.00 (± 8.161)		
Standing SBP, Change at Week 2 (n =7,12)	2.86 (± 13.753)	1.33 (± 12.759)		
Standing SBP, Change at Week 4 (n =7,12)	-1.57 (± 7.138)	2.17 (± 11.707)		
Standing SBP, Change at Week 6 (n =6,11)	1.67 (± 7.230)	-2.00 (± 14.457)		
Standing SBP, Change at Week 10 (n =5,11)	-0.60 (± 9.423)	-2.18 (± 11.391)		
Standing SBP, Change at Week 14 (n =5,11)	-0.80 (± 9.039)	-4.55 (± 6.933)		
Standing SBP, Change at Week 18 (n =3,11)	-2.67 (± 8.327)	-1.73 (± 13.342)		
Standing SBP, Change at Week 22 (n =2,10)	-7.00 (± 7.071)	5.40 (± 13.006)		
Standing SBP, Change at Week 26/ET(n =8,12)	-3.38 (± 7.230)	-5.33 (± 12.010)		
Standing SBP, Change at Follow up (n =4, 2)	-5.50 (± 8.544)	2.50 (± 4.950)		
Sitting DBP, Baseline (n =10,13)	71.00 (± 7.688)	72.00 (± 9.256)		
Sitting DBP, Change at Week 1 (n =9,12)	0.67 (± 10.794)	-1.67 (± 9.633)		
Sitting DBP, Change at Week 2 (n =7, 12)	-4.14 (± 3.185)	0.17 (± 8.376)		
Sitting DBP, Change at Week 4 (n =7, 12)	0.14 (± 6.768)	-2.17 (± 10.744)		

Sitting DBP, Change at Week 6 (n =6, 11)	-0.83 (± 8.183)	1.00 (± 13.176)		
Sitting DBP, Change at Week 10 (n =5,11)	-3.40 (± 4.393)	-7.09 (± 10.387)		
Sitting DBP, Change at Week 14 (n =5, 11)	-6.20 (± 6.058)	-3.91 (± 10.094)		
Sitting DBP, Change at Week 18 (n =3,11)	-2.67 (± 3.786)	0.27 (± 15.186)		
Sitting DBP, Change at Week 22 (n =2,10)	-5.50 (± 2.121)	-1.30 (± 9.019)		
Sitting DBP, Change at Week 26/ET (n =8,13)	-2.50 (± 6.302)	-2.46 (± 10.548)		
Sitting DBP, Change at Follow up (n =4,3)	-1.75 (± 13.175)	-1.67 (± 8.145)		
Standing DBP, Baseline (n =10, 13)	73.90 (± 6.402)	74.85 (± 4.930)		
Standing DBP, Change at Week 1 (n =9, 11)	-1.00 (± 7.483)	-4.45 (± 6.654)		
Standing DBP, Change at Week 2 (n =7, 12)	-4.14 (± 3.132)	-0.33 (± 4.924)		
Standing DBP, Change at Week 4 (n =7,12)	-3.14 (± 7.625)	-2.67 (± 10.465)		
Standing DBP, Change at Week 6 (n =6, 11)	-1.17 (± 5.776)	-2.82 (± 7.910)		
Standing DBP, Change at Week 10 (n =5, 11)	0.40 (± 5.941)	-4.36 (± 7.215)		
Standing DBP, Change at Week 14 (n =5, 11)	-3.00 (± 3.317)	-4.09 (± 7.516)		
Standing DBP, Change at Week 18 (n =3,11)	-5.33 (± 3.055)	-0.91 (± 12.136)		
Standing DBP, Change at Week 22 (n =2,10)	0.00 (± 5.657)	-4.30 (± 10.646)		
Standing DBP, Change at Week 26/ET (n =8, 12)	-0.50 (± 4.408)	-4.33 (± 8.700)		
Standing DBP, Change at Follow-up (n =4, 2)	-7.75 (± 10.905)	-3.00 (± 2.828)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pulse Rate at Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit (ET) and Follow-up Visit

End point title	Change From Baseline in Pulse Rate at Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit (ET) and Follow-up Visit

End point description:

Change from baseline pulse rate in beats per minute was reported in sitting and standing positions. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit (anytime till Week 26), Follow-up Visit (1 week from last dose of study medication, anytime maximum up to Week 27)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: beats per minute				
arithmetic mean (standard deviation)				
Sitting, Baseline (n =10, 13)	77.90 (± 9.678)	73.38 (± 11.701)		
Sitting, Change at Week 1 (n =9, 12)	0.78 (± 8.969)	2.00 (± 9.254)		
Sitting, Change at Week 2 (n =7, 12)	0.00 (± 6.758)	8.08 (± 11.782)		
Sitting, Change at Week 4 (n =7, 12)	-3.29 (± 7.365)	2.00 (± 9.789)		
Sitting, Change at Week 6 (n =6, 11)	-1.17 (± 7.139)	2.00 (± 10.954)		
Sitting, Change at Week 10 (n =5, 11)	3.40 (± 11.261)	0.18 (± 14.098)		
Sitting, Change at Week 14 (n =5, 11)	-3.00 (± 14.799)	-0.91 (± 13.308)		
Sitting, Change at Week 18 (n =3, 11)	-0.33 (± 8.622)	1.09 (± 10.606)		
Sitting, Change at Week 22 (n =2, 10)	-12.00 (± 8.485)	4.30 (± 12.056)		
Sitting, Change at Week 26/ET (n =8, 13)	-2.50 (± 11.452)	-2.69 (± 8.5787)		
Sitting, Change at Follow-up (n =4, 3)	-2.50 (± 9.469)	2.67 (± 12.858)		
Standing, Baseline (n =9, 12)	80.00 (± 11.303)	83.08 (± 13.554)		
Standing, Change at Week 1 (n =8, 11)	2.75 (± 9.270)	1.09 (± 11.709)		
Standing, Change at Week 2 (n =6, 11)	5.33 (± 7.528)	7.18 (± 12.131)		
Standing, Change at Week 4 (n =6, 11)	2.67 (± 10.270)	1.27 (± 17.641)		
Standing, Change at Week 6 (n =5, 10)	-3.00 (± 6.000)	0.70 (± 13.857)		
Standing, Change at Week 10 (n =4, 10)	6.00 (± 10.066)	-0.20 (± 12.017)		
Standing, Change at Week 14 (n =5, 10)	-2.20 (± 13.236)	-6.00 (± 10.914)		
Standing, Change at Week 18 (n =3, 10)	-2.00 (± 6.928)	2.30 (± 13.639)		
Standing, Change at Week 22 (n =2, 10)	-10.00 (± 2.828)	2.50 (± 12.095)		
Standing, Change at Week 26/ET (n =7, 12)	2.86 (± 14.381)	-0.33 (± 10.680)		
Standing, Change at Follow-up (n =3, 2)	-3.33 (± 4.619)	-1.00 (± 21.213)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Height and Waist Circumference at Week 6, 26/ Early Termination Visit (ET) and Follow-up Visit

End point title	Change From Baseline in Height and Waist Circumference at Week 6, 26/ Early Termination Visit (ET) and Follow-up 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 took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 6, 26/Early Termination (anytime till Week 26), Follow-up Visit (1 week from last dose of study medication, anytime maximum up to Week 27)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: cm				
arithmetic mean (standard deviation)				
Height, Baseline (n =10, 13)	159.82 (± 10.182)	161.69 (± 11.996)		
Height, Change at Week 6 (n =6, 11)	0.27 (± 0.455)	0.77 (± 0.984)		
Height, Change at Week 26/ET (n =7, 13)	2.04 (± 1.938)	0.55 (± 1.535)		
Height, Change at Follow-up (n =3, 3)	0.90 (± 1.562)	2.42 (± 1.413)		
Waist Circumference, Baseline (n 10, 13)	78.89 (± 11.278)	80.23 (± 13.981)		
Waist Circumference, Change at Week 6 (n =6, 11)	-0.94 (± 2.483)	2.23 (± 7.527)		
Waist Circumference,Change at Week 26/ET(n =7,13)	-1.02 (± 2.278)	1.29 (± 4.210)		
Waist Circumference, Change at Follow-up (n =3, 3)	-6.40 (± 13.777)	2.01 (± 3.778)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Weight at Week 6, 26/ Early Termination Visit and Follow-up Visit

End point title	Change From Baseline in Body Weight at Week 6, 26/ Early Termination Visit and Follow-up Visit

End point description:

Change from baseline in body weight in kilogram (kg) was reported. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 6, 26/Early Termination (anytime till Week 26), Follow-up Visit (1 week from last dose of study medication, anytime maximum up to Week 27)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: kg				
arithmetic mean (standard deviation)				
Baseline (n =10, 13)	57.76 (± 17.634)	62.40 (± 19.375)		
Change at Week 6 (n =6, 11)	0.82 (± 1.343)	0.78 (± 2.530)		
Change at Week 26/Early Termination (n =7, 13)	1.62 (± 2.528)	2.33 (± 4.431)		
Change at Follow-up (n =3, 3)	1.47 (± 1.629)	4.68 (± 2.639)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Mass Index (BMI) at Week 6, 26/Early Termination Visit and Follow-up Visit

End point title	Change From Baseline in Body Mass Index (BMI) at Week 6, 26/Early Termination Visit and Follow-up 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 took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 6, 26/Early Termination (anytime till Week 26), Follow-up Visit (1 week from last dose of study medication, anytime maximum up to Week 27)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: kg/m^2				
arithmetic mean (standard deviation)				
Baseline (n =10, 13)	22.31 (± 5.081)	23.37 (± 4.709)		
Change at Week 6 (n =6, 11)	0.38 (± 0.519)	0.91 (± 2.234)		

Change at Week 26/Early Termination (n =7, 13)	0.19 (± 0.954)	0.78 (± 1.800)		
Change at Follow-up (n =3, 3)	0.35 (± 0.589)	1.54 (± 1.447)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Mass Index (BMI) Z-score at Week 6, 26/Early Termination Visit and Follow-up Visit

End point title	Change From Baseline in Body Mass Index (BMI) Z-score at Week 6, 26/Early Termination Visit and Follow-up 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 took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 6, 26/Early Termination (anytime till Week 26), Follow-up Visit (1 week from last dose of study medication, anytime maximum up to Week 27)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =10, 13)	0.58 (± 1.187)	1.06 (± 0.852)		
Change at Week 6 (n =6, 11)	0.12 (± 0.122)	-0.02 (± 0.511)		
Change at Week 26/Early Termination (n =7, 13)	0.21 (± 0.747)	0.11 (± 0.506)		
Change at Follow-up (n =3, 3)	0.01 (± 0.207)	0.26 (± 0.330)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Heart Rate at Day 1, Week 1, 2, 4, 6, 14, 22, 26/Early Termination Visit and Follow-up Visit

End point title	Change From Baseline in Heart Rate at Day 1, Week 1, 2, 4, 6, 14, 22, 26/Early Termination Visit and Follow-up Visit

End point description:

Change from baseline in heart rate in beats per minute was reported. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows. "99999" signifies that standard deviation was not estimable as only 1 subject was evaluable at specified instances.

End point type	Secondary

End point timeframe:

Baseline (Baseline visit in the double-blind study A1281198), Day 1 (last measurement from A1281198), Week 1, 2, 4, 6, 14, 22, 26/ET (anytime till Week 26), Follow-up Visit (1 week from last dose of study medication, anytime maximum up to Week 27)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: beats per minute				
arithmetic mean (standard deviation)				
Baseline (n =10, 13)	77.8 (± 9.19)	71.5 (± 14.12)		
Change at Day 1 (n =8, 12)	-4.0 (± 9.40)	-1.2 (± 9.09)		
Change at Week 1 (n =9, 12)	-2.0 (± 19.24)	0.4 (± 16.12)		
Change at Week 2 (n =7, 12)	7.4 (± 16.69)	5.0 (± 16.28)		
Change at Week 4 (n =7, 12)	-7.3 (± 8.08)	0.4 (± 13.20)		
Change at Week 6 (n =6, 11)	-5.0 (± 13.04)	-3.9 (± 14.49)		
Change at Week 14 (n =5, 11)	-0.6 (± 15.22)	-2.6 (± 15.23)		
Change at Week 22 (n =2, 10)	-5.0 (± 0.00)	0.3 (± 16.99)		
Change at Week 26/Early Termination (n =8, 13)	-7.8 (± 12.33)	-3.0 (± 8.69)		
Change at Follow-up (n =1, 1)	-15.0 (± 99999)	-13.0 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Electrocardiogram (ECG) Parameters at Day 1, Week 1, 2, 4, 6, 14, 22, 26/Early Termination Visit (ET) and Follow-up Visit

End point title	Change From Baseline in Electrocardiogram (ECG) Parameters at Day 1, Week 1, 2, 4, 6, 14, 22, 26/Early Termination Visit (ET) and Follow-up Visit

End point description:

Change from baseline in PR interval, QT interval corrected using the Bazett's correction (QTcB), QT interval corrected using the Fridericia's formula (QTcF), QT interval, RR interval, QRS duration in millisecond (msec) was reported. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows. "99999" signifies that standard deviation was not estimable as only 1 subject was evaluable at specified instances.

End point type	Secondary

End point timeframe:

Baseline (Baseline visit in the double-blind study A1281198), Day 1 (last measurement from A1281198), Week 1, 2, 4, 6, 14, 22, 26/ET (anytime till Week 26), Follow-up Visit (1 week from last

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: msec				
arithmetic mean (standard deviation)				
PR interval, Baseline (n =10, 13)	145.3 (± 14.77)	148.5 (± 14.47)		
PR interval, Change at Day 1 (n =8, 12)	1.0 (± 9.07)	0.4 (± 10.25)		
PR interval, Change at Week 1 (n =9, 12)	3.6 (± 14.17)	-2.6 (± 9.17)		
PR interval, Change at Week 2 (n =7, 12)	-4.6 (± 9.22)	2.3 (± 11.69)		
PR interval, Change at Week 4 (n =7, 12)	3.0 (± 5.16)	1.1 (± 10.17)		
PR interval, Change at Week 6 (n =6, 11)	0.0 (± 12.60)	4.0 (± 10.89)		
PR interval, Change at Week 14 (n =5, 11)	-6.8 (± 4.87)	-2.0 (± 9.42)		
PR interval, Change at Week 22 (n =2, 10)	12.5 (± 17.68)	1.7 (± 9.25)		
PR interval, Change at Week 26/ET (n =8, 13)	-0.3 (± 7.76)	-0.9 (± 12.70)		
PR interval, Change at Follow-up (n =1, 1)	-3.0 (± 99999)	17.0 (± 99999)		
QTcB interval, Baseline (n =10, 13)	415.8 (± 16.13)	412.4 (± 18.87)		
QTcB interval, Change at Day 1 (n =8, 12)	1.0 (± 13.31)	2.2 (± 15.72)		
QTcB interval, Change at Week 1 (n =9, 12)	1.2 (± 18.34)	15.6 (± 21.74)		
QTcB interval, Change at Week 2 (n =7, 12)	6.4 (± 17.58)	11.4 (± 24.01)		
QTcB interval, Change at Week 4 (n =7, 12)	-7.4 (± 9.36)	2.9 (± 18.81)		
QTcB interval, Change at Week 6 (n =6, 11)	9.0 (± 23.04)	0.2 (± 27.75)		
QTcB interval, Change at Week 14 (n =5, 11)	-5.0 (± 21.30)	3.9 (± 24.20)		
QTcB interval, Change at Week 22 (n =2, 10)	19.0 (± 8.49)	8.9 (± 30.94)		
QTcB interval, Change at Week 26/ET (n =8, 13)	3.0 (± 26.88)	2.5 (± 21.43)		
QTcB interval, Change at Follow-up (n =1, 1)	-14.0 (± 99999)	-5.0 (± 99999)		
QTcF interval, Baseline (n =10, 13)	398.5 (± 14.80)	401.8 (± 18.57)		
QTcF interval, Change at Day 1 (n =8, 12)	3.8 (± 13.36)	2.3 (± 11.40)		
QTcF interval, Change at Week 1 (n =9, 12)	3.0 (± 12.65)	14.0 (± 13.74)		
QTcF interval, Change at Week 2 (n =7, 12)	-0.3 (± 15.30)	5.8 (± 13.98)		

QTcF interval, Change at Week 4 (n =7, 12)	-1.3 (± 13.90)	1.3 (± 12.87)		
QTcF interval, Change at Week 6 (n =6, 11)	12.5 (± 17.21)	3.2 (± 18.94)		
QTcF interval, Change at Week 14 (n =5, 11)	-4.6 (± 10.01)	6.2 (± 12.62)		
QTcF interval, Change at Week 22 (n =2, 10)	23.5 (± 7.78)	7.0 (± 21.21)		
QTcF interval, Change at Week 26/ET (n =8, 13)	10.6 (± 16.77)	4.3 (± 17.51)		
QTcF interval, Change at Follow-up (n =1, 1)	0.0 (± 99999)	6.0 (± 99999)		
QT interval, Baseline (n =10, 13)	366.3 (± 21.79)	382.8 (± 35.86)		
QT interval, Change at Day 1 (n =8, 12)	9.6 (± 22.88)	2.2 (± 17.17)		
QT interval, Change at Week 1 (n =9, 12)	7.8 (± 37.06)	10.8 (± 29.55)		
QT interval, Change at Week 2 (n =7, 12)	-11.4 (± 32.93)	-4.1 (± 26.25)		
QT interval, Change at Week 4 (n =7, 12)	10.4 (± 25.34)	-2.1 (± 25.98)		
QT interval, Change at Week 6 (n =6, 11)	20.5 (± 26.71)	9.0 (± 25.65)		
QT interval, Change at Week 14 (n =5, 11)	-3.4 (± 20.70)	10.6 (± 21.47)		
QT interval, Change at Week 22 (n =2, 10)	34.0 (± 5.66)	4.1 (± 31.27)		
QT interval, Change at Week 26/ET (n =8, 13)	24.5 (± 18.90)	7.2 (± 20.99)		
QT interval, Change at Follow-up (n =1,1)	23.0 (± 99999)	26.0 (± 99999)		
RR interval, Baseline (n =10, 13)	781.0 (± 95.07)	873.6 (± 171.26)		
RR interval, Change at Day 1 (n =8, 12)	33.6 (± 100.49)	-5.7 (± 102.47)		
RR interval, Change at Week 1 (n =9, 12)	30.7 (± 203.15)	-17.7 (± 187.46)		
RR interval, Change at Week 2 (n =7, 12)	-73.3 (± 161.14)	-61.2 (± 179.08)		
RR interval , Change at Week 4 (n =7, 12)	70.1 (± 86.24)	-26.9 (± 159.35)		
RR interval, Change at Week 6 (n =6, 11)	56.5 (± 152.31)	40.6 (± 173.34)		
RR interval, Change at Week 14 (n =5, 11)	3.6 (± 157.07)	33.2 (± 169.68)		
RR interval, Change at Week 22 (n =2, 10)	69.0 (± 12.73)	-13.7 (± 208.06)		
RR interval, Change at Week 26/ET (n =8, 13)	99.1 (± 165.02)	20.4 (± 111.79)		
RR interval, Change at Follow-up (n =1, 1)	134.0 (± 99999)	134.0 (± 99999)		
QRS duration, Baseline (n =10, 13)	84.4 (± 7.23)	85.8 (± 5.90)		
QRS duration, Change at Day 1 (n =8, 12)	2.1 (± 3.76)	2.8 (± 3.41)		
QRS duration, Change at Week 1 (n =9, 12)	1.0 (± 3.54)	3.8 (± 5.64)		
QRS duration, Change at Week 2 (n =7, 12)	0.1 (± 3.24)	1.7 (± 6.31)		
QRS duration, Change at Week 4 (n =7, 12)	2.0 (± 4.16)	1.5 (± 5.25)		
QRS duration, Change at Week 6 (n =6, 11)	-0.8 (± 3.06)	2.5 (± 5.05)		

QRS duration, Change at Week 14 (n =5, 11)	-1.2 (± 4.15)	2.9 (± 7.30)		
QRS duration, Change at Week 22 (n =2, 10)	1.0 (± 2.83)	-0.3 (± 6.60)		
QRS duration, Change at Week 26/ET (n =8, 13)	3.5 (± 4.54)	3.5 (± 4.93)		
QRS duration, Change at Follow-up (n =1, 1)	-4.0 (± 99999)	11.0 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Simpson-Angus Rating Scale (SARS) Total Score at Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit and Follow-up Visit

End point title	Change From Baseline in Simpson-Angus Rating Scale (SARS) Total Score at Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit and Follow-up Visit

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. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows. Data for this endpoint is reported only for those time points' categories where at least 1 reporting arm had non-zero values.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit (anytime till Week 26), Follow-up Visit (1 week from last dose of study medication, anytime maximum up to Week 27)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =10, 13)	0.4 (± 1.26)	0.0 (± 0.00)		
Change at Week 1 (n =9, 12)	-0.2 (± 0.67)	0.0 (± 0.00)		
Change at Week 2 (n =7, 12)	0.0 (± 0.00)	0.2 (± 0.39)		
Change at Week 4 (n =7, 12)	0.0 (± 0.00)	0.2 (± 0.58)		
Change at Week 6 (n =6, 11)	0.0 (± 0.00)	0.2 (± 0.40)		
Change at Week 26/ Early Termination (n =8, 13)	-0.5 (± 1.41)	0.0 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Barnes Akathisia Rating Scale (BAS): Global Clinical Assessment of Akathisia Subscale Score at Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit and Follow-up Visit

End point title	Change From Baseline in Barnes Akathisia Rating Scale (BAS): Global Clinical Assessment of Akathisia Subscale Score at Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit and Follow-up Visit

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. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit (anytime till Week 26), Follow-up Visit (1 week from last dose of study medication, anytime maximum up to Week 27)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =10, 13)	0.0 (± 0.00)	0.2 (± 0.38)		
Change at Week 1 (n =9, 12)	0.0 (± 0.00)	-0.1 (± 0.29)		
Change at Week 2 (n =7, 12)	0.0 (± 0.00)	0.3 (± 1.07)		
Change at Week 4 (n =7, 12)	0.0 (± 0.00)	0.1 (± 0.29)		
Change at Week 6 (n =6, 11)	0.0 (± 0.00)	-0.2 (± 0.40)		
Change at Week 10 (n =5, 11)	0.0 (± 0.00)	-0.2 (± 0.40)		
Change at Week 14 (n =5, 11)	0.0 (± 0.00)	-0.2 (± 0.40)		
Change at Week 18 (n =3, 11)	0.0 (± 0.00)	-0.2 (± 0.40)		
Change at Week 22 (n =2, 10)	0.0 (± 0.00)	-0.2 (± 0.42)		
Change at Week 26/ Early Termination (n =8, 13)	0.0 (± 0.00)	-0.2 (± 0.38)		
Change at Follow-up (n =2, 3)	0.0 (± 0.00)	-0.3 (± 0.58)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Abnormal Involuntary Movement Scale (AIMS)

- Movement Cluster Score at Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit and Follow-up Visit

End point title	Change From Baseline in Abnormal Involuntary Movement Scale (AIMS) - Movement Cluster Score at Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit and Follow-up Visit

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 12 are questions with No or Yes response. Only the sum of the first 7 items were calculated to evaluate AIMS movement cluster score, giving it a possible score range of 0 (none) to 28 (maximum severity), higher scores indicate greater severity. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows. Data for this endpoint is reported only for those time points' categories where at least 1 reporting arm had non-zero values.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit (anytime till Week 26), Follow-up Visit (1 week from last dose of study medication, anytime maximum up to Week 27)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: units on a scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n =7,12)	0.0 (± 0.00)	0.3 (± 0.87)		
Change at Week 6 (n =6, 11)	0.0 (± 0.00)	0.1 (± 0.30)		

Statistical analyses

No statistical analyses for this end point

Secondary: 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, preparatory acts, suicidal ideation (wish to be dead; non-specific active suicidal thoughts [AST]; active suicidal ideation with any methods [not plan],without intent to act; active suicidal ideation with some intent to act, without specific plan; active suicidal ideation with specific plan and intent; self-injurious behavior,no suicidal intent). Safety analysis set. Here 'n' signifies number of subjects evaluable for each specified rows. Data for this endpoint is reported only for those time points' categories where at least 1 reporting arm had non-zero values.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit (ET, anytime till Week 26), Follow-up Visit (1 week from last dose of study medication, anytime maximum up to Week 27)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: subjects				
Week 6: Wish to be dead (n =6, 11)	0	1		
Week 10: Wish to be dead (n =5, 11)	0	1		
Week 26/ET: Wish to be dead (n =8, 13)	0	1		
Week 26/ET: Non-specific AST (n =8, 13)	0	1		
Week 26/ET: AST With No Plan, Intent (n =8, 13)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Children's Depression Rating Scale (CDRS-R) Total Score at Week 26/Early Termination Visit

End point title	Change From Baseline in Children's Depression Rating Scale (CDRS-R) Total Score at Week 26/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. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Early Termination Visit (anytime till Week 26)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: units on a scale				

arithmetic mean (standard deviation)				
Baseline (n =10, 13)	68.2 (± 16.40)	67.7 (± 13.28)		
Change at Week 26/Early Termination (n =8, 11)	1.6 (± 11.60)	7.2 (± 10.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Young Mania Rating Scale (YMRS) Total Score at Week 1, 2, 6, 14, 22, 26/Early Termination Visit

End point title	Change From Baseline in Young Mania Rating Scale (YMRS) Total Score at Week 1, 2, 6, 14, 22, 26/Early Termination Visit

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. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 1, 2, 6, 14, 22, 26/Early Termination Visit (anytime till Week 26)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =10, 13)	12.7 (± 8.31)	12.0 (± 5.46)		
Change at Week 1 (n =9, 12)	0.6 (± 10.71)	-5.5 (± 6.87)		
Change at Week 2 (n =7, 12)	-3.1 (± 5.90)	-3.4 (± 7.42)		
Change at Week 6 (n =6, 11)	1.3 (± 10.01)	-3.7 (± 7.71)		
Change at Week 14 (n =5, 11)	0.8 (± 8.84)	-5.8 (± 3.95)		
Change at Week 22 (n =2, 10)	0.5 (± 9.19)	-4.0 (± 7.29)		
Change at Week 26/Early Termination (n =8, 13)	-1.9 (± 4.85)	-6.4 (± 5.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Global Impression of Severity (CGI-S)

Score at Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit

End point title	Change From Baseline in Clinical Global Impression of Severity (CGI-S) Score at Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit

End point description:

CGI-S: 7-point clinician rated scale to assess severity of subject's current illness state; range: 1 (normal or not ill at all) to 7 (among the most extremely ill), higher scores indicated more severity of illness. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 1, 2, 4, 6, 10, 14, 18, 22, 26/Early Termination Visit (anytime till Week 26)

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =10, 13)	2.7 (± 1.25)	2.5 (± 0.97)		
Change at Week 1 (n =9, 12)	0.3 (± 1.12)	-0.3 (± 1.07)		
Chang at Week 2 (n =7, 12)	0.1 (± 1.21)	-0.3 (± 0.98)		
Change at Week 4 (n =7, 12)	0.0 (± 1.00)	-0.2 (± 1.40)		
Change at Week 6 (n =6, 11)	0.5 (± 1.38)	0.0 (± 1.26)		
Change at Week 10 (n =5, 11)	-0.2 (± 0.84)	-0.1 (± 0.83)		
Change at Week 14 (n =5, 11)	0.0 (± 1.00)	-0.5 (± 1.04)		
Change at Week 18 (n =3, 11)	-0.7 (± 1.15)	-0.4 (± 1.12)		
Change at Week 22 (n =2, 10)	-1.0 (± 1.41)	-0.2 (± 1.14)		
Change at Week 26/Early Termination (n =8, 13)	-0.1 (± 1.25)	-0.5 (± 1.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Children's Global Assessment Scale (CGAS) Total Score at Week 26/Early Termination Visit

End point title	Change From Baseline in Children's Global Assessment Scale (CGAS) Total Score at Week 26/Early Termination Visit

End point description:

CGAS: a clinician-rated global assessment item for children based on symptoms and social functioning in home, school, and community settings. Scores on this single item ranged from 1-100 (higher levels indicate greater health), with descriptive anchors for every 10-point interval. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study. Here 'n' signifies number of subjects evaluable for each specified rows.

End point type	Secondary

End point timeframe:

Baseline (Day 1, last measurement from A1281198), Week 26/Early Termination Visit (anytime till Week

End point values	Double Blind Ziprasidone to Open Label Ziprasidone	Double Blind Placebo to Open Label Ziprasidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =10, 13)	68.2 (± 16.40)	67.7 (± 13.28)		
Change at Week 26/Early Termination (n =8, 11)	1.6 (± 11.60)	7.2 (± 10.13)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to 1 week after last dose of study medication (maximum up to 27 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. The safety analysis set included all subjects who took at least 1 dose of study medication in this open-label extension study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Double Blind Placebo to Open Label Ziprasidone

Reporting group description:

Subjects who were on placebo in study A1281198,received ziprasidone,under double-blind conditions for maximum up to Week 2,where dose was titrated up to appropriate weight-adjusted target dose per discretion of investigator to maintain optimal efficacy and tolerability.Subjects with weight >=45 kg:target dose range was total daily dose of 120-160 mg/day given in 2 divided doses with food.Subjects with weight <45 kg:target dose range was total daily dose of 60-80 mg/day given in 2 divided doses with food.Subjects who did not tolerate dose of 80 mg/day were allowed to have dose reduction and to continue study treatment at lower dose that was tolerable to them.Minimum permitted dose was 40 mg/day (20 mg BID) for all subjects.Any subject unable to tolerate ziprasidone during Week 1 was discontinued from study.After Week 2 to Week 26,for >=45 kg subjects and after Week 1 to Week 26 for <45 kg subjects,dosing was open label and flexible.Subjects were followed up for 1 Week after last dose.

Reporting group title	Double Blind Ziprasidone to Open Label Ziprasidone

Reporting group description:

Subjects who were on ziprasidone in study A1281198, continued to receive ziprasidone, under double-blind conditions for maximum up to Week 2. Any subject if unable to tolerate the ziprasidone during Week 1 was discontinued from the study. After Week 2 to Week 26, dosing was open label and flexible. Subjects were followed up for 1 Week after last dose.

Serious adverse events	Double Blind Placebo to Open Label Ziprasidone	Double Blind Ziprasidone to Open Label Ziprasidone	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Psychiatric disorders			
Aggression			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (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 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	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	Double Blind Placebo to Open Label Ziprasidone	Double Blind Ziprasidone to Open Label Ziprasidone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 13 (92.31%)	7 / 10 (70.00%)	
Investigations			
Blood insulin increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Streptococcus test positive			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Ligament injury			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Ligament sprain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Akathisia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	1 / 13 (7.69%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Dystonia			

subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Lethargy			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Memory impairment			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Sedation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Somnolence			
subjects affected / exposed	1 / 13 (7.69%)	3 / 10 (30.00%)	
occurrences (all)	1	4	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 13 (53.85%)	0 / 10 (0.00%)	
occurrences (all)	8	0	
Feeling abnormal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nausea			

subjects affected / exposed	3 / 13 (23.08%)	0 / 10 (0.00%)	
occurrences (all)	4	0	
Vomiting			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Respiratory disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dermatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Hallucination, auditory			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal stiffness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Helicobacter infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Influenza			

subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Pharyngitis streptococcal			
subjects affected / exposed	0 / 13 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 13 (7.69%)	0 / 10 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 February 2019	Protocol summary included trial design and trial treatments were amended.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported