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PROPRIETARY DRUG NAME® / GENERIC DRUG NAME: Geodon® / Zeldox® / Ziprasidone hydrochloride

PROTOCOL NO.: A1281148

PROTOCOL TITLE: A Sixteen-Week, Multi-Center, Open-Label Study Evaluating the Safety, Tolerability, and Efficacy of Switching From Quetiapine to Ziprasidone in Subjects Diagnosed With Schizophrenia or Schizoaffective Disorder

Study Centers: Thirty-five centers took part in the study and enrolled subjects: 23 in the United States; 3 in Brazil; 4 in Germany; 1 in Spain; and 2 each in Greece and Turkey.

Study Initiation Date and Final Completion Date: 14 November 2006 to 31 March 2009

Phase of Development: Phase 4

Study Objectives: The primary objective of this study was to evaluate change in weight, as a result of switching to ziprasidone, in subjects who failed to achieve a satisfactory clinical response to quetiapine due to lack of efficacy or poor tolerability.

The secondary objectives of this study were to evaluate the effect on additional safety parameters (glucose and lipid metabolism) and efficacy parameters.

Additional secondary objectives were:

- To evaluate the overall psychopathology using the Positive and Negative Symptoms of Schizophrenia (PANSS).
- To evaluate global clinical severity of symptoms using the Clinical Global Impression-Severity Scale (CGI-S).
- To evaluate global clinical improvement of symptoms using the Clinical Global Impression-Improvement Scale (CGI-I).
- To evaluate depression using the Calgary Depression Scale for Schizophrenia (CDSS).
- To evaluate functioning related to cognitive performance using the Schizophrenia Cognition Rating Scale (ScoRS).
- To evaluate global functioning using the Global Assessment of Function Scale (GAF).

- To evaluate subject treatment satisfaction using Treatment Satisfaction Questionnaire for Medication (TSQM).

- To evaluate the pharmacogenomic basis for ziprasidone treatment responsiveness.

Safety and Tolerability

Movement Disorder symptoms were measured using the Abnormal Involuntary Movement Scale (AIMS).

Laboratory measures were monitored and included fasting lipid profile (total cholesterol), high-density lipoprotein (HDL) low-density lipoprotein, (LDL) and triglycerides, glycosylated hemoglobin (HbA_{1c}) and fasting glucose and insulin.

The circumference measurement of the waist and hip was followed to evaluate any changes from Baseline.

Safety outcome measures included monitoring vital signs, electrocardiogram (ECG), physical examination, and laboratory testing, as well as monitoring adverse events (AEs), serious adverse events (SAEs), and discontinuations due to AEs.

METHODS

Study Design: This was a 16-week open-label, flexible-dose study, with a 16-week follow-up (for a total of 32 weeks) in subjects with a Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) diagnosis of schizophrenia or schizoaffective disorder, who failed to achieve a satisfactory clinical response to quetiapine due to lack of efficacy or poor tolerability. Subjects participated in a 16-week follow-up period after they completed the 16-week treatment phase. The schedule of activities conducted during the study is summarized Table 1.

Table 1. Schedule of Activities

	Screening V1	Baseline V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	Follow-Up V14
	W 1	W 0	W 2	W 4	W 6	W 8	W 10	W 12	W 14	W 16	W 20	W 24	W 28	W 32[a]
Informed consent	X													
Medical/ psychological/ social history	X													
Demographics	X													
Inclusion/ exclusion criteria	X													
Physical examination	X									X				X
Pharmacogenetic sampling		X[b]												
Laboratory tests	X	X			X			X		X	X	X	X	X
Urine drug screen	X													
Serum pregnancy test	X													
Electrocardigram	X	X			X					X				X
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Waist/ hip circumference	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Height	X													
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PANSS		X	X		X					X				X
CGI-S and CGI-I[c]		X	X	X	X	X	X	X	X	X				X
GAF		X	X		X					X				X
SCoRS		X			X					X				X
CDSS		X	X		X					X				X
AIMS		X			X					X				X
TSQM		X								X				X
AE assessment	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Drug accountability/ dosing		X	X	X	X	X	X	X	X	X	X	X	X	X
Dispensing record		X	X	X	X	X	X	X	X	X	X	X	X	
Subject summary														X

AE = adverse event; AIMS = abnormal involuntary movement scale; CDSS = calgary depression scale for schizophrenia; CGI-I = clinical global impression-improvement; CGI-S = clinical global impression-severity; GAF = global assessment of function scale; IEC = independent ethics committee; IRB = institutional review board; PANSS = positive and negative syndrome scales; SCoRS = schizophrenia cognition rating scale; TSQM = treatment satisfaction questionnaire for medication; V = visit; W = week.

a. These assessments were to be completed at the subject's final visit, regardless of completion status.

b. Subject to IRB/IEC approval.

c. CGI-I was recorded at Visit 3.

Number of Subjects (Planned and Analyzed): It was planned to screen approximately 350 subjects to enroll at least 250 subjects. A total of 340 subjects were screened for this study; 241 subjects were enrolled and treated with ziprasidone. Data for the 241 enrolled and treated subjects was analyzed.

Diagnosis and Main Criteria for Inclusion: Male or female subjects between 18 and 55 years of age with a primary diagnosis of schizophrenia, any subtype, or schizoaffective disorder as defined in DSM-IV-TR and with normal vital signs, physical examination, ECG, and laboratory findings at the time of consent, were eligible to be enrolled in the study.

Subjects were required to have been treated with oral doses of quetiapine, consistent with medical practice, at a minimum of 300 mg per day for at least 3 months and should have failed to respond to quetiapine due to lack of efficacy or intolerable side effects.

Study Treatment: Study treatment was administered in an open-label fashion. All study medication was provided in either bottles or blister cards that were adequately labeled to indicate their contents, either 20 mg or 60 mg. At all study visits, the subject was given commercial bottles/blister cards, in doses of both 20 mg and 60 mg, to allow for sufficient medication regardless of the prescribed dose.

Note: Ziprasidone had to be used in compliance with its local prescribing information, which was to be reviewed to ensure that appropriate subjects were enrolled in the study. An overview of study drug administration is presented in Table 2.

Table 2. Overview of Study Drug Administration

Drug	Days –28 to Screening	Day 0 (Baseline)	Days 1-112	Days 113–225
Ziprasidone	No Drug	Study Enrollment – Medication dispensed	Subjects started at 40 mg BID fixed dose on days 1-3, 60 mg BID on days 4-7, and 80 mg BID on day 8. Dosing was flexible between 40-80 mg BID (adjustable up to 40 mg daily/week) for the remainder of the 16-week treatment phase.	Flexible dosing continued throughout the follow-up phase between 40-80 mg BID (adjustable up to 40 mg daily/week) for the remainder of the 16-week follow-up phase.
Quetiapine	Quetiapine dose was maintained through Screening.	Quetiapine dose will be maintained through Day 7.	Quetiapine dose was reduced by 100-200 mg/day every 2 days thereafter until discontinued (based on clinical state and Investigator judgment). Quetiapine should have been discontinued within 2 weeks of study Baseline (Day 14).	

BID = twice a day.

Efficacy and Safety Endpoints:

Primary Endpoint

- Change in weight (kg) at Week 16

Secondary Efficacy Endpoints

- PANSS total score and positive and negative subscale scores
- CGI-I change from CGI-S
- CDSS
- SCoRS
- GAF
- TSQM

Secondary Safety Endpoints

- Fasting lipid profile (total cholesterol)
- HDL, LDL, and triglycerides
- HbA_{1c}
- Fasting glucose and insulin
- Waist and hip circumference
- AIMS
- Spontaneously reported AEs during the study
    - Subjects reporting any AE during the study
    - Subjects reporting a mild, moderate, or severe AE during the study
    - Subjects discontinuing due to an AE during the study
- Subjects who develop clinically significant abnormalities in blood chemistries, hematologies, or ECG parameters during the study

Safety Evaluations: Safety evaluations included monitoring vital signs, weight, waist and hip circumference, ECGs, physical examinations, and laboratory assessments, movement

disorder assessment using AIMS, as well as monitoring AEs, SAEs, and discontinuations due to AEs.

Statistical Methods: Safety Population: The safety analysis set included all enrolled subjects who took at least 1 dose of study medication.

Intent-to-treat (ITT) Population: All enrolled subjects, with Baseline and at least 1 post Baseline efficacy evaluation were included in this population.

The primary analysis and all safety analyses were done on the safety population. Efficacy analysis was done on the ITT population.

The primary analysis was conducted on the safety variable, change in weight (kg) at Week 16 (with last observation carried forward [LOCF]) from Baseline. A negative value for the change from Baseline weight (kg) at Week 16 indicated a decrease from the Baseline weight at Week 16. A 1-sided, 95% upper confidence interval (CI) was constructed on the mean change from Baseline weight at Week 16, to infer whether there was a significant decrease in weight (ie, a 95% upper confidence bound <0 would indicate a statistically significant decrease in weight).

In addition to the primary analysis, the safety variable, change in weight from Baseline to Week 6 was also calculated and summarized using a 1-sided 95% CI. This was considered a secondary analysis.

For the secondary efficacy endpoints, PANSS, CGI-S, CDSS, SCoRS, GAF, and TSQM, 2-sided 95% CIs were computed on the change from Baseline score. For the CGI-I, only raw data was planned to be presented and summarized. In addition, CGI response (a subject was considered a "responder" if the CGI-I score ≤2) was derived and analyzed.

The Abnormal Involuntary Movement disorder symptom parameter, from the AIMS, was analyzed in the same manner as the secondary efficacy parameters.

Laboratory measures were monitored, specifically, fasting lipid profile (total cholesterol, HDL, LDL, triglycerides), HbA_{1c}, fasting glucose, and insulin and summarized appropriately.

Additional safety data including AEs, other laboratory values, ECG, physical examination, and vital signs data were subjected to clinical review and summarized by appropriate descriptive statistics. Weight, waist, and hip circumference were also followed to evaluate any changes from Baseline.

RESULTS

Subject Disposition and Demography: Of the 340 subjects screened for this study, 241 subjects were assigned to study treatment and were treated with ziprasidone. The subject disposition for overall, Weeks 1–16, and for subjects who entered the follow-up period, Weeks 17–32 is summarized in Table 3.

Table 3. Subject Disposition and Subjects Analyzed

Subject Disposition	Number (%) of Subjects Ziprasidone Evaluation Groups		
	Overall Study	Weeks 1–16	Subjects Who Entered Follow-up (Weeks 17–32)
Screened (N=340)			
Assigned to study treatment	241	241	132
Treated	241	241	132
Completed	100 (41.5)	132 (54.8)	100 (75.8)
Discontinued	141 (58.5)	109 (45.2)	32 (24.2)
Deaths	1 (0.4)	1 (0.4)	0
Related to study drug	39 (16.2)	34 (14.1)	5 (3.8)
Adverse event	20 (8.3)	18 (7.5)	2 (1.5)
Laboratory abnormality	3 (1.2)	3 (1.2)	0
Lack of efficacy	13 (5.4)	11 (4.6)	2 (1.5)
Other	3 (1.2)	2 (0.8)	1 (0.8)
Not related to study drug	101 (41.9)	74 (30.7)	27 (20.5)
Adverse event	19 (7.9)	15 (6.2)	4 (3.0)
Laboratory abnormality	1 (0.4)	1 (0.4)	6 (4.5)
Lost to follow-up[a]	21 (8.7)	15 (6.2)	7 (5.3)
Other[b]	30 (12.4)	23 (9.5)	10 (7.6)
Subject no longer willing to participate in study	30 (12.4)	20 (8.3)	0
Analyzed for safety			
Adverse events	224 (92.9)	224 (92.9)	124 (93.9)
Laboratory data	207 (85.9)	205 (85.1)	132 (100)

N = number of subjects.

a. Lost to follow up: example of reasons included subject did not show up for visits; subject moved out of state, subjects could not be reached and did not respond to messages.

b. Other: example of reasons included subject moved out of state, inability to adhere to protocol, study terminated by sponsor.

The demographic characteristics in the treated population are summarized in Table 4.

Table 4. Demographic Characteristics

Demographic Characteristics	Male	Female	Total
Number of Subjects	**130**	**111**	**241**
Age (years)			
<18	0	0	0
18-44	78 (60.0)	62 (55.9)	140 (58.1)
45-64	52 (40.0)	49 (44.1)	101 (41.9)
>=65	0	0	0
Mean	41.9	41.1	41.5
SD	9.6	9.7	9.6
Range	18-60	18-56	18-60
Race, n (%)			
White	87 (66.9)	65 (58.6)	152 (63.1)
Black	34 (26.2)	44 (39.6)	78 (32.4)
Asian	1 (0.8)	0	1 (0.4)
Other	8 (6.2)	2 (1.8)	10 (4.1)
Weight (kg)			
Mean	92.9	85.1	89.3
SD	25.8	23.7	25.1
Range	56.7-210.9	46.7-199.0	46.7-210.9
Height (cm)			
Mean	175.5	163.0	169.7
SD	9.0	7.0	10.2
Range	126.0-198.1	137.2-181.0	126.0-198.1

n = number of subjects in specified category; SD = standard deviation.

Efficacy Results:

Primary Endpoint

Change in Weight (kg) at Week 16: Based on the results of the primary analysis, at Week 16 (LOCF), there was a small but statistically significant weight change of −0.73 kg (ie, 1-sided 95% upper confidence bound = −0.33 <0 indicating a statistically significant decrease in weight at Week 16 compared to Baseline). The summary of change from Baseline weight by week is presented in Table 5.

During the course of this study, the participation of 1 study center was terminated due to Good Clinical Practices non-compliance. Data from this study site are included in the safety and efficacy analyses. As a sensitivity check for the analysis of the primary variable of interest (change from Baseline weight to Week 16 LOCF), this analysis was repeated excluding the data from the closed-out site. Results from this sensitivity analysis were found to be generally consistent with the primary analysis results that included the closed-out site.

Table 5. Summary of Change From Baseline Weight (kg) by Week — Safety Population

Parameter	Baseline Values	Ziprasidone											
		Study Visits											
		W2	W4	W6	W8	W10	W12	W14	W16	W20	W24	W28	W32
N	241	229	199	182	167	130	146	119	133	125	110	106	103
Mean	89.4	90.2	89.2	89.1	88.5	89.7	88.6	88.8	88.3	89.1	87.7	88.3	89.1
SD	25.07	25.31	24.72	25.24	25.77	24.52	25.94	24.69	26.84	27.00	26.59	26.64	27.17
Median	85.0	85.7	84.4	84.1	83.0	85.8	84.6	86.1	84.4	85.7	84.8	85.6	86.8
Range	46.7, 211.4	46.7, 212.3	45.8, 198.3	46.3, 199.0	45.8, 199.4	48.8, 190.5	43.9, 201.2	49.2, 191.4	44.8, 196.4	45.0, 199.7	49.3, 200.5	47.3, 199.4	47.5, 204.8
Change From Baseline													
N	-	229	199	182	167	130	146	119	133	125	110	106	103
Mean	-	0.07	-0.07	-0.34	-0.33	-0.49	-1.02	-0.90	-1.09	-0.82	-1.39	-1.26	-1.25
SD	-	1.803	2.092	2.340	2.770	3.195	3.344	3.571	3.918	5.149	4.946	5.441	6.028
Median	-	0.09	0.00	-0.23	-0.30	-0.86	-1.12	-1.00	-0.90	-0.46	-0.81	-1.07	-0.80
Range	-	-10.30, 4.54	-9.10, 7.26	-9.00, 7.25	-7.10, 9.07	-8.70, 10.61	-10.90, 9.08	-12.25, 9.53	-13.16, 9.53	-14.52, 30.84	-17.24, 11.11	-18.60, 13.61	-19.96, 14.79
One-Sided 95% upper CI		0.26	0.17	-0.05	0.03	-0.03	-0.56	-0.36	-0.53	-0.05	-0.60	-0.38	-0.26
Last Observation Carried Forward Week 16[a]													
N	-	-	-	-	-	-	-	-	231	-	-	-	-
Mean	-	-	-	-	-	-	-	-	89.3	-	-	-	-
SD	-	-	-	-	-	-	-	-	25.47	-	-	-	-
Median	-	-	-	-	-	-	-	-	85.0	-	-	-	-
Range	-	-	-	-	-	-	-	-	44.8, 212.3	-	-	-	-
Change From Baseline to Last Observation Carried Forward Week 16[a]													
N	-	-	-	-	-	-	-	-	231	-	-	-	-
Mean	-	-	-	-	-	-	-	-	-0.73	-	-	-	-
SD	-	-	-	-	-	-	-	-	3.725	-	-	-	-
Median	-	-	-	-	-	-	-	-	-0.19	-	-	-	-
Range	-	-	-	-	-	-	-	-	-13.16, 9.53	-	-	-	-
One-Sided 95% Upper CI		-		-	-	-	-	-	-0.33	-	-	-	-

CI = confidence interval; N = number of subjects; SD = standard deviation; W = week.

a. Primary analysis

Secondary Efficacy Endpoints

PANSS Total Score and Positive and Negative Subscale Scores: Results for the Baseline and change from Baseline PANSS total scores, positive symptom subscale scores and negative symptom subscale scores obtained at each study visit (ITT population) are summarized in Table 6.

Table 6. PANSS Scores at Baseline and Change From Baseline

Parameter	Ziprasidone (N=232)														
	Baseline Values			Week 2			Week 6			Week 16			Week 32 / Follow-up		
	Pos	Neg	Total	Pos	Neg	Total	Pos	Neg	Total	Pos	Neg	Total	Pos	Neg	Total
Baseline															
N	232	232	232	230	230	230	192	192	191	144	144	144	111	111	111
Mean	19.3	19.3	78.1	18.1	18.9	75.3	17	18.4	71.9	16	17.8	68.0	14.4	16.7	62.7
SD	5.56	5.9	17.62	5.79	5.7	17.17	5.65	5.66	17.11	5.43	5.8	17.76	4.87	5.38	14.79
Median	19	19	78.0	17.5	19	75.5	16	18	71.0	16	18	66.0	14	17	61.0
Range	7.0, 35.0	7.0, 40.0	38.0, 149.0	7.0, 36.0	7.0, 37.0	33.0, 129.0	7.0, 33.0	7.0, 34.0	32.0, 124.0	7.0, 31.0	7.0, 35.0	30.0, 118.0	7.0, 30.0	7.0, 31.0	30.0, 101.0
Change From Baseline															
N				230	230	230	192	192	191	144	144	144	111	111	111
Mean				-1.21	-0.4	-2.84	-2.28	-1.07	-6.48	-3.3	-1.67	-10.22	-4.98	-2.99	-15.93
SD				2.96	3.031	8.948	4.227	4.133	13.909	4.658	4.147	15.027	4.803	4.489	14.136
Median				-1	0	-2.00	-2	-1	-5.00	-3	-1	-8.00	-5	-2	-13.00
Range				-12.00, 8.00	-12.00, 10.00	-33.00, 26.00	-19.00, 13.00	-18.00, 16.00	-70.00, 49.00	-17.00, 8.00	-16.00, 9.00	-62.00, 32.00	-15.00, 9.00	-15.00, 9.00	-58.00, 18.00
95% CI				-1.60, -0.83	-0.79, -0.01	-4.01, -1.68	-2.88, -1.67	-1.66, -0.48	-8.46, -4.49	-4.07, -2.53	-2.36, -0.99	-12.70, -7.75	-5.89, -4.08	-3.84, -2.15	-18.59, -13.27
Last Observation Carried Forward Week 16															
N										231	231	231			
Mean										16.9	18.4	71.6			
SD										5.91	5.81	18.22			
Median										16	18	71.0			
Range										7.0, 34.0	7.0, 35.0	30.0, 124.0			
Change From Baseline to Last Observation Carried Forward Week 16															
N										231	231	231			
Mean										-2.43	-0.92	-6.61			
SD										4.634	4.373	15.306			
Median										-2	-1	-5.00			
Range										-19.00, 9.00	-16.00, 16.00	-62.00, 44.00			
95% CI										-3.03, -1.83	-1.48, -0.35	-8.59, -4.63			

CI = confidence interval; N = number of subjects; Neg = negative subscale score; PANSS = positive and negative syndrome scale; Pos = positive subscale score; SD = standard deviation.

CGI-S and CGI-I: The CGI-S score by week and the change from Baseline at each visit is summarized in Table 7. During the study, mean CGI-S scores decreased relative to Baseline at each visit.

For the CGI-I score at each visit using observed case (OC) analysis for the ITT population, scores decreased relative to Baseline at each visit from a mean (standard deviation) Week 2 score of 3.7 (0.90) to 2.4 (0.88), indicating global improvement according to clinical impression. At Week 16 (LOCF), the mean score was 3.2 (95% CI: 3.02, 3.34); at Week 32 / Follow-up, the mean score was 2.4 (95% CI: 2.27, 2.60).

Table 7. Clinical Global Impression-Severity Score at Baseline and Change From Baseline

Parameter	Ziprasidone (N=232)									
	Baseline Values	W2	W4	W6	W8	W10	W12	W14	W16	W32
N	232	229	200	183	169	130	146	119	135	111
Mean	4.1	4.0	3.8	3.7	3.6	3.4	3.4	3.3	3.3	3.1
SD	0.76	0.79	0.76	0.80	0.86	0.83	0.88	0.75	0.87	0.70
Median	4.0	4.0	4.0	4.0	4.0	3.0	3.0	3.0	3.0	3.0
Range	2.0, 6.0	1.0, 6.0	2.0, 6.0	2.0, 6.0	1.0, 6.0	1.0, 6.0	1.0, 6.0	1.0, 5.0	1.0, 6.0	2.0, 5.0
Change From Baseline										
N	-	229	200	183	169	130	146	119	135	111
Mean	-	-0.12	-0.36	-0.44	-0.50	-0.62	-0.66	-0.75	-0.76	-0.92
SD	-	0.407	0.610	0.699	0.733	0.730	0.865	0.826	0.868	0.822
Median	-	0.00	0.00	0.00	0.00	0.00	-1.00	-1.00	-1.00	-1.00
Range	-	-2.00, 1.00	-2.00, 1.00	-3.00, 2.00	-3.00, 1.00	-3.00, 1.00	-3.00, 2.00	-3.00, 1.00	-3.00, 1.00	-3.00, 1.00
95% CI	-	-0.17, -0.06	-0.45, -0.27	-0.54, -0.34	-0.61, -0.39	-0.74, -0.49	-0.81, -0.52	-0.90, -0.60	-0.90, -0.61	-1.07, -0.76
Last Observation Carried Forward Week 16										
N	-	-	-	-	-	-	-	-	231	-
Mean	-	-	-	-	-	-	-	-	3.6	-
SD	-	-	-	-	-	-	-	-	0.96	-
Median	-	-	-	-	-	-	-	-	4.0	-
Range	-	-	-	-	-	-	-	-	1.0, 6.0	-
Change From Baseline to Last Observation Carried Forward Week 16										
N	-	-	-	-	-	-	-	-	231	-
Mean	-	-	-	-	-	-	-	-	-0.47	-
SD	-	-	-	-	-	-	-	-	0.848	-
Median	-	-	-	-	-	-	-	-	0.00	-
Range	-	-	-	-	-	-	-	-	-3.00, 2.00	-
One-Sided 95% Upper CI	-	-	-	-	-	-	-	-	-0.58, -0.36	-

CI = confidence interval; N = number of subjects; SD = standard deviation; W = week.

CDSS: The CDSS scores decreased relative to Baseline at each visit. Results of this scale evaluating depression in subjects with schizophrenia indicated an improvement in symptoms (Table 8).

Table 8. CDSS Total Score at Baseline and Change From Baseline—Each Visit and LOCF at Week 16

Parameter	Ziprasidone (N=232)				
	Baseline	Week 2	Week 6	Week 16	Week 32 / Follow-Up
N	232	230	192	144	111
Mean	6.0	5.3	4.4	3.4	3.0
SD	4.57	4.62	4.33	3.36	3.45
Median	5.5	5.0	3.0	3.0	2.0
Range	0.0, 23.0	0.0, 23.0	0.0, 20.0	0.0, 15.0	0.0, 16.0
Change From Baseline					
N	-	230	192	144	111
Mean	-	-0.71	-1.71	-2.55	-3.15
SD	-	3.072	4.299	4.364	4.727
Median	-	0.00	-1.00	-2.00	-3.00
Range	-	-9.00, 9.00	-18.00, 13.00	-20.00, 9.00	-20.00, 6.00
95% CI	-	-1.11, -0.31	-2.32, -1.10	-3.27, -1.83	-4.04, -2.26
Last Observation Carried Forward Week 16					
N	-	-	-	231	-
Mean	-	-	-	4.5	-
SD	-	-	-	4.44	-
Median	-	-	-	3.0	-
Range	-	-	-	0.0, 20.0	-
Change From Baseline to Last Observation Carried Forward Week 16					
N	-	-	-	231	-
Mean	-	-	-	-1.58	-
SD	-	-	-	4.526	-
Median	-	-	-	-1.00	-
Range	-	-	-	-20.00, 10.00	-
95% CI	-	-	-	-2.16, -0.99	-

CDSS = calgary depression scale for schizophrenia; CI = confidence interval; LOCF = last observation carried forward; N = number of subjects; SD = standard deviation.

GAF: There was an overall improvement in the global functioning, as evidenced by increased GAF scores relative to Baseline at each visit. The GAF score at Baseline and change from Baseline is summarized in Table 9.

Table 9. GAF Score at Baseline and Change From Baseline to Endpoint

Parameter	Ziprasidone (N=232)				
	Baseline	Week 2	Week 6	Week 16	Week 32 / Follow-Up
N	232	229	192	145	111
Mean	50.1	51.8	54.5	57.6	62.3
SD	10.59	10.41	11.09	13.14	12.53
Median	50	51	55	60	61
Range	21.0, 85.0	20.0, 85.0	21.0, 95.0	21.0, 95.0	25.0, 90.0
Change From Baseline					
N		229	192	145	111
Mean		1.7	4.91	7.88	12.32
SD		5.758	8.739	11.029	11.816
Median		0	4	6	10
Range		-33.00, 25.00	-20.00, 35.00	-17.00, 40.00	-26.00, 50.00
95% CI		0.95, 2.45	3.66, 6.15	6.07, 9.69	10.10, 14.55
Last Observation Carried Forward Week 16					
N				230	
Mean				55.4	
SD				12.37	
Median				55	
Range				20.0, 95.0	
Change From Baseline to Last Observation Carried Forward Week 16					
N				230	
Mean				5.27	
SD				10.626	
Median				4	
Range				-33.00, 40.00	
95% CI				3.89, 6.65	

CI = confidence interval; GAF = global assessment of function; N = number of subjects; SD = standard deviation.

TSQM: The subscale results for TSQM-effectiveness, side effect, convenience, and global satisfaction at Baseline and change from Baseline are summarized in Table 10.

Table 10. TSQM-Effectiveness, Side Effect, Convenience, and Global Satisfaction Scores at Baseline and Change From Baseline

Parameter	Ziprasidone (N=232)											
	Baseline				Week 16				Week 32/Follow-Up			
	EFF	SE	CON	GS	EFF	SE	CON	GS	EFF	SE	CON	GS
N	219	209	218	217	181	175	183	183	107	104	108	108
Mean	50.6	58.6	65.4	49.2	60.1	76.3	71.1	63	70.3	85.9	74.2	71.4
SD	21.47	29.8	21.14	24.37	25.6	29.19	18.52	28.76	20.22	22.79	16.1	21.1
Median	50	56.3	66.7	50	66.7	93.8	66.7	71.4	72.2	100	72.2	78.6
Range	0.0, 100.0	0.0, 100.0	0.0, 100.0	0.0, 100.0	0.0, 100.0	0.0, 100.0	0.0, 100.0	0.0, 100.0	5.6, 100.0	0.0, 100.0	16.7, 100.0	0.0, 100.0
Change From Baseline												
N	-	-	-	-	178	167	180	179	103	97	105	104
Mean	-	-	-	-	10.49	18.49	6.45	15.32	20.5	31.44	9.63	24.24
SD	-	-	-	-	30.662	42.883	23.63	36.304	25.388	33.408	21.52	29.884
Median	-	-	-	-	11.11	12.5	5.56	14.29	22.22	31.25	11.11	28.57
Range	-	-	-	-	-83.33, 100.00	-93.75, 100.00	-66.67, 94.44	-71.43, 100.00	-38.89, 83.33	-62.50, 93.75	-44.44, 66.67	-57.14, 100.00
95% CI	-	-	-	-	5.95, 15.02	11.94, 25.04	2.98, 9.93	9.97, 20.68	15.53, 25.46	24.71, 38.18	5.46, 13.79	18.43, 30.06
LOCF Week 16												
N	-	-	-	-	181	175	183	183	-	-	-	-
Mean	-	-	-	-	60.1	76.3	71.1	63	-	-	-	-
SD	-	-	-	-	25.6	29.19	18.52	28.76	-	-	-	-
Median	-	-	-	-	66.7	93.8	66.7	71.4	-	-	-	-
Range	-	-	-	-	0.0, 100.0	0.0, 100.0	0.0, 100.0	0.0, 100.0	-	-	-	-
Change From Baseline to LOCF Week 16												
N	-	-	-	-	178	167	180	179	-	-	-	-
Mean	-	-	-	-	10.49	18.49	6.45	15.32	-	-	-	-
SD	-	-	-	-	30.662	42.883	23.63	36.304	-	-	-	-
Median	-	-	-	-	11.11	12.5	5.56	14.29	-	-	-	-
Range	-	-	-	-	-83.33, 100.00	-93.75, 100.00	-66.67, 94.44	-71.43, 100.00	-	-	-	-
95% CI	-	-	-	-	5.95, 15.02	11.94, 25.04	2.98, 9.93	9.97, 20.68	-	-	-	-

CI = confidence interval; CON = convenience; EFF = effectiveness; GS = global satisfaction; LOCF = last observation carried forward; N = number of subjects; SE = side effect; SD = standard deviation.

Cognitive Function: Overall, there was a significant improvement in the cognitive functioning, as SCoRS total scores decreased relative to Baseline for OCs at each visit. The SCoRS total score and global rating at Baseline and change from Baseline are summarized in Table 11.

Table 11. SCoRS Total Score and Global Rating at Baseline and Change From Baseline

Parameter	Ziprasidone (N=232)							
	Baseline		Week 6		Week 16		Week 36	
	TS	GR	TS	GR	TS	GR	TS	GR
N	229	229	170	168	138	138	150	148
Mean	39.9	5.1	37.2	4.4	36.1	4	35.4	4.3
SD	10.94	1.92	9.76	1.73	9.96	1.79	9.64	1.98
Median	39	5	37	4	35	4	34	4
Range	20.0, 72.0	1.0, 9.0	20.0, 62.0	1.0, 8.0	20.0, 61.0	1.0, 9.0	20.0, 64.0	1.0, 9.0
Change From Baseline								
N	-	-	169	167	137	137	150	147
Mean	-	-	-3.57	-0.65	-4.61	-1.02	-4.62	-1.01
SD	-	-	7.958	1.443	7.981	1.708	9.199	1.712
Median	-	-	-3	-1	-4	-1	-3	-1
Range	-	-	-48.00, 15.00	-5.00, 4.00	-34.00, 26.00	-5.00, 4.00	-33.00, 17.00	-5.00, 3.00
95% CI	-	-	-4.78, -2.37	-0.87, -0.43	-5.95, -3.26	-1.31, -0.73	-6.10, -3.14	-1.29, -0.73
LOCF Week 16								
N	-	-	-	-	170	170	-	-
Mean	-	-	-	-	36.5	4.1	-	-
SD	-	-	-	-	10.36	1.83	-	-
Median	-	-	-	-	35	4	-	-
Range	-	-	-	-	20.0, 61.0	1.0, 9.0	-	-
Change From Baseline to LOCF Week 16								
N	-	-	-	-	169	169	-	-
Mean	-	-	-	-	-4.21	-0.88	-	-
SD	-	-	-	-	8.961	1.643	-	-
Median	-	-	-	-	-4	-1	-	-
Range	-	-	-	-	-48.00, 26.00	-5.00, 4.00	-	-
95% CI	-	-	-	-	-5.57, -2.85	-1.13, -0.63	-	-

CI = confidence interval; GR = global rating; LOCF = last observation carried forward; N = number of subjects; SCoRS = schizophrenia cognition rating scale; SD = standard deviation; TS = total score.

Safety Results:

Secondary Safety Endpoints

Fasting Lipid Profile (Total Cholesterol): Total cholesterol levels at Baseline and changes from Baseline are summarized in Table 12. Throughout the study, cholesterol levels were lower at each study visit.

Table 12. Total Cholesterol at Baseline and Change From Baseline

Parameter	Ziprasidone (N=241)							
	Baseline	**W 6**	**W 12**	**W 16**	**W 20**	**W 24**	**W 28**	**W 32 / Follow-Up**
N	240	216	146	131	121	107	106	104
Mean	198.4	192.1	189.7	189	195.2	191.5	188.4	189.9
SD	42.26	39.26	34.76	33.38	39.02	36.95	35	39.03
Median	192	188	185.5	188	189.2	186	182	187
Min/Max	(111.0, 384.0)	(76.0, 316.6)	(93.0, 311.0)	(117.0, 292.0)	(119.0, 359.1)	(108.1, 312.7)	(112.0, 316.6)	(98.0, 301.2)
Change From Baseline								
N		201	140	128	119	103	102	94
Mean		-7.7	-2.6	-3.0	1.7	-2.4	-5.7	-6.6
SD		28.36	33.02	31.14	36.25	30.56	31.35	33.68
Median		-7.7	-1.5	-4	1	-3.0	-7.5	-5
Min/Max		(-118.0, 76.0)	(-96.0, 120.0)	(-78.0, 124.0)	(-77.0, 135.0)	(-79.0, 105.0)	(-115.0, 72.0)	(-102.0, 71.0)
95% CI		-11.62, -3.73	-8.15, 2.88	-8.48, 2.41	-4.83, 8.33	-8.37, 3.57	-11.87, 0.45	-13.46, 0.33

CI = confidence interval; Max = maximum; Min = minimum; N = number of subjects; SD = standard deviation; W = week.

HDL, LDL and Triglycerides: For HDL, there was a small increase from Baseline, with a mean change at Week 32 / Follow-up of 1.0 mg/dL (95% CI: -0.61, 2.66). For LDL, the levels decreased throughout the study; with the most notable change at Week 32. For triglycerides, the results also indicated a decrease in values. The HDL, LDL, and triglycerides at Baseline and change from Baseline are summarized in Table 13.

Table 13. HDL, LDL, and Triglycerides at Baseline and Change From Baseline

Parameter	Ziprasidone (N=241)		
	HDL (mg/dL)	LDL (mg/dL)	Triglycerides (mg/dL)
Baseline			
N	240	232	240
Mean	50.5	114.8	173.7
SD	13.01	34.85	124.21
Median	48.5	111.0	136.0
Min/Max	(26.0, 105.0)	(55.0, 258.7)	(35.0, 911.0)
Week 6			
N	217	206	217
Mean	51.0	109.8	165.9
SD	14.43	34.77	112.85
Median	49.0	106.5	139.0
Min/Max	(22.0, 128.0)	(21.0, 235.5)	(35.0, 795.0)
Change From Baseline to Week 6			
N	202	186	202
Mean	0.6	-6.4	-11.8
SD	9.20	22.46	99.79
Median	0.0	-7.0	0.0
Min/Max	(-19.3, 60.0)	(-69.5, 71.0)	(-738.0, 252.0)
95% CI	-0.71, 1.84	-9.69, -3.19	-25.62, 2.07
Week 12			
N	145	140	145
Mean	49.3	109.5	163.7
SD	12.48	31.77	111.71
Median	48.0	103.0	130.0
Min/Max	(23.0, 94.0)	(46.0, 227.8)	(38.0, 729.0)
Change From Baseline to Week 12			
N	139	134	139
Mean	-0.0	-2.1	1.7
SD	9.05	27.44	91.03
Median	0.0	-2.9	-3.0
Min/Max	(-34.0, 54.0)	(-81.0, 93.0)	(-401.0, 497.0)
95% CI	-1.55, 1.48	-6.82, 2.55	-13.53, 17.01
Week 16			
N	131	127	131
Mean	49.7	110.2	153.2
SD	12.80	27.10	105.71
Median	47.0	110.0	126.0
Min/Max	(23.0, -106.0)	(50.0, 185.3)	(39.0, 831.0)
Change From Baseline to Week 16			
N	128	123	128
Mean	-0.2	-2.5	-1.6
SD	9.32	25.66	84.58
Median	0.0	-1.0	5.5
Min/Max	(-37.0, 38.0)	(-81.0, 77.0)	(-357.0, 304.0)
95% CI	-1.82, 1.44	-7.07, 2.09	-16.44, 13.15
Week 20			
N	119	116	120
Mean	50.2	112.4	164.7
SD	12.66	31.95	110.12
Median	48.0	109.1	130.0
Min/Max	(27.0, 97.0)	(54.1, 247.1)	(41.0, 802.0)
Change From Baseline to Week 20			
N	117	113	118
Mean	0.7	-0.2	2.5
SD	8.42	30.50	86.28
Median	1.0	-2.0	6.0

Table 13. HDL, LDL, and Triglycerides at Baseline and Change From Baseline

Parameter	Ziprasidone (N=241)		
	HDL (mg/dL)	LDL (mg/dL)	Triglycerides (mg/dL)
Min/Max	(-24.0, 23.0)	(-77.0, 110.0)	(-315.0, 275.0)
95% CI	-0.80, 2.29	-5.88, 5.49	-13.19, 18.27
Week 24			
N	107	104	107
Mean	49.8	109.6	164.2
SD	13.11	31.87	93.84
Median	47.0	105.1	141.6
Min/Max	(21.0, 114.0)	(42.5, 231.7)	(46.0, 485.0)
Change From Baseline to Week 24			
N	103	99	103
Mean	0.6	-3.4	1.9
SD	9.63	25.86	80.98
Median	0.0	0.0	7.0
Min/Max	(-27.0, 40.0)	(-75.0, 77.0)	(-298.0, 316.0)
95% CI	-1.30, 2.47	-8.59, 1.72	-13.88, 17.77
Week 28			
N	106	102	106
Mean	49.7	107.2	163.1
SD	12.19	30.97	113.77
Median	48.0	106.0	126.0
Min/Max	(25.0, 94.0)	(32.0, 243.2)	(41.0, 689.0)
Change From Baseline to Week 28			
N	102	98	102
Mean	0.6	-5.6	0.2
SD	8.48	24.70	86.24
Median	0.0	-6.0	8.0
Min/Max	(-23.0, 24.0)	(-66.0, -62.0)	(-336.0, 270.0)
95% CI	-1.08, 2.25	-10.53, -0.62	-16.69, 17.19
Week 32 / Follow-up			
N	104	100	104
Mean	49.4	108.2	165.3
SD	12.28	35.64	125.85
Median	48.0	106.5	136.5
Min/Max	(23.2, 88.0)	(21.0, 224.0)	(45.0, 974.0)
Change from Baseline to Week 32 / Follow-up			
N	94	90	94
Mean	1.0	-7.8	4.3
SD	8.00	31.51	92.10
Median	1.0	-7.0	0.0
Min/Max	(-16.0, 25.0)	(-92.7, 81.0)	(-255.0, -447.0)
95% CI	-0.61, 2.66	-14.43, -1.23	-14.52, 23.21

CI = confidence interval; HDL = high-density lipoprotein; LDL = low-density lipoprotein; Max = maximum; Min = minimum; N = number of subjects; SD = standard deviation.

HbA_{1c}: There were no meaningful changes in HbA_{1c} during the study. The HbA_{1c} at Baseline and changes from Baseline are summarized in Table 14.

Table 14. HbA_{1c} (%) at Baseline and Change From Baseline

Parameter	Ziprasidone (N=241)							
	Baseline	W 6	W 12	W 16	W 20	W 24	W 28	W 32 / Follow-Up
N	240	214	144	131	119	106	106	102
Mean	5.6	5.7	5.6	5.7	5.6	5.7	5.8	5.7
SD	0.83	1.01	0.94	1.06	1.09	1.22	1.28	1.31
Median	5.5	5.5	5.5	5.5	5.5	5.4	5.6	5.5
Min/Max	(3.1, 11.1)	(3.1, 13.6)	(3.4, 13.0)	(3.5, 13.8)	(3.4, 14.1)	(3.6, 15.2)	(3.3, 14.4)	(3.4, 15.1)
Change From Baseline								
N	-	201	138	127	117	102	102	93
Mean	-	0.0	0.0	0.1	0.0	0.0	0.1	0.0
SD	-	0.41	0.38	0.44	0.45	0.56	0.69	0.56
Median	-	0.0	0.0	0.0	-0.1	-0.1	0.0	0.0
Min/Max	-	(-2.6, 2.5)	(-1.6, 1.9)	(-1.6, 2.7)	(-0.8, 3.0)	(-1.0, 4.1)	(-0.9, 4.9)	(-1.3, 3.9)
95% CI	-	-0.04, 0.07	-0.03, 0.10	-0.02, 0.14	-0.07, 0.09	-0.09, 0.13	-0.03, 0.24	-0.09, 0.14

CI = confidence interval; HbA_{1c} = glycosylated hemoglobin; Max = maximum; Min = minimum; N = number of subjects; SD = standard deviation.

Fasting Glucose and Insulin: The fasting glucose and insulin at Baseline and changes from Baseline are summarized in Table 15.

Several protocol violations during the study may have affected the weight and metabolic outcome analysis for the ITT population in this study. Relevant violations were inclusion of subjects with diabetes mellitus (n=19) or subject taking insulin (n=1), and subjects not fasting when the laboratory samples were taken (n=8).

Table 15. Fasting Glucose and Insulin at Baseline and Change From Baseline

Parameter	Ziprasidone (N=241)	
	Fasting Glucose (mg/dL)	Insulin (MCIU/mL)
Baseline		
N	240	236
Mean	97.8	484.7
SD	30.89	607.56
Median	92.0	311.7
Min/Max	(46.9, 325.0)	(45.6, 4644.9)
Week 6		
N	216	201
Mean	102.1	502.5
SD	40.11	596.05
Median	93.7	323.7
Min/Max	(59.0, 405.0)	(38.4, 5114.9)
Change From Baseline to Week 6		
N	201	183
Mean	3.3	8.2
SD	26.73	828.25
Median	0.0	33.6
Min/Max	(-87.0, 152.0)	(-4357.2, 4913.5)
95% confidence interval	-0.44, 6.99	-112.64, 128.97
Week 12		
N	146	140
Mean	101.6	565.1
SD	28.15	694.22
Median	94.0	338.1
Min/Max	(67.0, 283.0)	(52.8, 4326.0)
Change From Baseline to Week 12		
N	140	132
Mean	5.8	66.8
SD	25.79	930.03
Median	3.0	22.8
Min/Max	(-76.0, 117.0)	(-4342.8, 3601.8)
95% confidence interval	1.45, 10.07	-93.30, 226.97
Week 16		
N	131	124
Mean	97.6	564.5
SD	19.34	726.33
Median	94.0	297.4
Min/Max	(59.0, 182.0)	(38.4, 4167.7)
Change From Baseline to Week 16		
N	128	118
Mean	3.0	134.8
SD	17.84	851.28
Median	2.5	27.6
Min/Max	(-42.0, 65.0)	(-4539.4, 2947.1)
95% confidence interval	-0.09, 6.15	-20.43, 289.98
Week 20		
N	121	114
Mean	98.3	530.0
SD	24.78	697.47
Median	94.0	327.3
Min/Max	(62.0, 232.0)	(52.8, 4268.4)
Change From Baseline to Week 20		
N	119	109
Mean	3.6	127.0
SD	19.69	683.93
Median	0.0	24.0

Table 15. Fasting Glucose and Insulin at Baseline and Change From Baseline

Parameter	Ziprasidone (N=241)	
	Fasting Glucose (mg/dL)	Insulin (MCIU/mL)
Min/Max	(-36.0, 110.0)	(-1906.4, 3894.4)
95% confidence interval	0.07, 7.22	-2.82, 256.88
Week 24		
N	107	105
Mean	99.2	471.2
SD	31.41	533.91
Median	92.0	280.6
Min/Max	(49.0, 334.0)	(31.2, 3503.5)
Change From Baseline to Week 24		
N	103	99
Mean	4.4	66.0
SD	30.25	573.95
Median	0.0	4.8
Min/Max	(-55.0, 212.0)	(-1242.2, 3124.6)
95% confidence interval	-1.47, 10.35	-48.49, 180.45
Week 28		
N	106	98
Mean	103.4	547.7
SD	35.29	708.93
Median	97.2	334.5
Min/Max	(25.0, 284.0)	(26.4, 4733.7)
Change from Baseline to Week 28		
N	102	92
Mean	8.2	159.0
SD	30.51	736.93
Median	3.0	22.8
Min/Max	(-69.0, 148.0)	(-1494.0, 4009.5)
95% confidence interval	2.25, 14.24	6.41, 311.64
Week 32 / Follow-up		
N	104	99
Mean	99.2	559.8
SD	20.73	845.21
Median	93.5	314.1
Min/Max	(71.0, 190.0)	(60.0, 6254.0)
Change From Baseline to Week 32 / Follow-up		
N	94	88
Mean	4.2	130.8
SD	17.10	844.26
Median	2.5	39.6
Min/Max	(-32.0, 91.0)	(-1952.0, 5191.7)
95% confidence interval	0.71, 7.71	-48.11, 309.65

Max = maximum; Min = minimum; N = number of subjects; SD = standard deviation.

Waist and Hip Circumference: Overall, the mean waist circumference was 103.2 cm at Baseline and 101.3 cm at Week 32 / Follow-up, with a mean change of -1.2 cm. The mean hip circumference was 109.8 cm at Baseline and 108.6 cm at Week 32 / Follow-up, with a mean change of -1.4 cm. The waist and hip circumference at Baseline and change from Baseline are summarized in Table 16.

Table 16. Waist and Hip Circumference at Baseline and Change From Baseline

Parameter	Ziprasidone (N=241)	
	Waist Circumference (cm)	Hip Circumference (cm)
Baseline		
N	240	236
Mean	103.2	109.8
SD	23.13	22.40
Median	101.6	107.5
Min/Max	(67.3, 322.6)	(72.4, 325.1)
Week 2		
N	228	224
Mean	104.4	110.1
SD	23.45	22.86
Median	101.6	108.0
Min/Max	(68.0, 322.6)	(73.7, 325.1)
Change From Baseline to week 2		
N	227	223
Mean	0.5	0.0
SD	3.54	3.61
Median	0.0	0.0
Min/Max	(-14.0, 15.0)	(-15.2, 26.0)
95% confidence interval	0.06, 0.98	-0.44, 0.51
Week 4		
N	199	195
Mean	103.3	109.8
SD	23.78	23.82
Median	101.6	107.0
Min/Max	(64.8, 320.0)	(66.0, 325.1)
Change From Baseline to week 4		
N	198	194
Mean	0.2	0.1
SD	3.88	5.41
Median	0.0	0.0
Min/Max	(-10.5, 20.3)	(-15.9, 49.5)
95% confidence interval	-0.35, 0.73	-0.70, 0.83
Week 6		
N	182	180
Mean	102.0	108.7
SD	18.67	17.85
Median	100.3	106.8
Min/Max	(62.9, 170.2)	(65.4, 175.3)
Change From Baseline to Week 6		
N	181	178
Mean	-1.4	-1.6
SD	15.13	15.47
Median	0.0	0.0
Min/Max	(-196.6, 19.8)	(-198.1, 29.0)
95% confidence interval	-3.61, 0.83	-3.90, 0.67
Week 8		
N	167	167
Mean	101.4	107.9
SD	18.65	17.72
Median	99.1	105.0
Min/Max	(62.9, 162.6)	(66.0, 170.2)
Change From Baseline to Week 8		
N	166	164
Mean	-1.6	-1.7
SD	15.80	16.47
Median	0.0	0.0

Table 16. Waist and Hip Circumference at Baseline and Change From Baseline

Parameter	Ziprasidone (N=241)	
	Waist Circumference (cm)	Hip Circumference (cm)
Min/Max	(-195.6, 26.7)	(-197.1, 28.0)
95% confidence interval	-4.03, 0.81	-4.28, 0.80
Week 10		
N	130	130
Mean	101.9	107.9
SD	18.46	17.37
Median	99.1	106.0
Min/Max	(69.9, 154.9)	(74.9, 167.6)
Change From Baseline to Week 10		
N	129	130
Mean	-2.1	-2.2
SD	18.05	18.27
Median	0.0	0.0
Min/Max	(-198.6, 20.1)	(-199.1, 30.0)
95% confidence interval	-5.29, 1.00	-5.37, 0.97
Week 12		
N	146	146
Mean	101.6	108.1
SD	18.34	17.57
Median	99.4	106.0
Min/Max	(68.6, 177.8)	(76.2, 182.9)
Change From Baseline to Week 12		
N	145	143
Mean	-2.3	-2.4
SD	16.81	17.12
Median	-1.0	-0.6
Min/Max	(-195.6, 19.9)	(-196.1, 29.0)
95% confidence interval	-5.02, 0.50	-5.21, 0.45
Week 14		
N	119	119
Mean	101.3	107.9
SD	18.25	17.25
Median	100.3	106.7
Min/Max	(66.7, 152.4)	(74.3, 167.6)
Change From Baseline to Week 14		
N	118	119
Mean	-2.8	-2.7
SD	18.20	18.73
Median	-1.0	-0.8
Min/Max	(-193.6, 12.7)	(-197.1, 28.0)
95% confidence interval	-6.16, 0.48	-6.10, 0.70
Week 16		
N	133	133
Mean	100.6	107.3
SD	19.27	17.75
Median	98.0	104.1
Min/Max	(64.5, 160.0)	(73.7, 167.6)
Change From Baseline to Week 16		
N	132	131
Mean	-2.9	-3.0
SD	17.53	18.21
Median	-1.3	-0.0
Min/Max	(-194.6, 14.0)	(-199.1, 27.0)
95% confidence interval	-5.93, 0.11	-6.20, 0.10
Week 20		
N	125	125

Table 16. Waist and Hip Circumference at Baseline and Change From Baseline

Parameter	Ziprasidone (N=241)	
	Waist Circumference (cm)	Hip Circumference (cm)
Mean	100.4	107.3
SD	20.23	18.62
Median	98.0	106.7
Min/Max	(43.2, 162.6)	(49.3, 170.2)
Change From Baseline to Week 20		
N	124	123
Mean	-3.7	-3.9
SD	19.11	19.94
Median	-0.6	-1.0
Min/Max	(-196.6, 12.7)	(-198.1, 13.0)
95% confidence interval	-7.06, -0.27	-7.44, -0.32
Week 24		
N	110	110
Mean	101.1	107.3
SD	20.79	17.96
Median	98.0	106.7
Min/Max	(64.8, 188.0)	(72.4, 172.7)
Change From Baseline to Week 24		
N	109	108
Mean	-0.4	-1.5
SD	12.84	5.39
Median	-0.6	0.0
Min/Max	(-15.5, 119.4)	(-21.6, 12.0)
95% confidence interval	-2.85, 2.03	-2.52, -0.46
Week 28		
N	106	106
Mean	101.1	108.3
SD	19.11	17.78
Median	99.0	106.1
Min/Max	(69.9, 163.8)	(75.6, 168.9)
Change From Baseline to Week 28		
N	105	104
Mean	-3.1	-3.6
SD	19.53	20.00
Median	-1.3	0.0
Min/Max	(-192.6, 19.1)	(-197.1, 14.0)
95% confidence interval	-6.92, 0.64	-7.51, 0.27
Week 32 / Follow-up		
N	103	103
Mean	101.3	108.6
SD	20.36	19.07
Median	99.1	106.7
Min/Max	(68.6, 190.5)	(74.9, 203.2)
Change From Baseline to Week 32 / Follow-up		
N	102	101
Mean	-1.2	-1.4
SD	6.80	6.39
Median	0.0	0.0
Min/Max	(-25.4, 17.8)	(-22.9, 27.9)
95% confidence interval	-2.50, 0.17	-2.66, -0.14

CI = confidence interval; Max = maximum; Min = minimum; N = number of subjects; SD = standard deviation.

AIMS: According to the results, there was no worsening from Baseline in involuntary movement with ziprasidone treatment administered for 32 weeks. The AIMS mean score at Baseline and change from Baseline are summarized in Table 17.

Table 17. AIMS Total Score at Baseline and Change From Baseline

Parameter	Ziprasidone (N=241)			
	Baseline	Week 6	Week 16	Week 32 / Follow-Up
Baseline				
N	241	218	144	111
Mean	0.7	0.7	0.6	0.2
SD	2.13	1.82	1.8	0.61
Median	0	0	0	0
Range	0.0, 17.0	0.0, 12.0	0.0, 17.0	0.0, 5.0
Change From Baseline				
N	-	218	144	111
Mean	-	0.01	0.05	-0.22
SD	-	1.976	2.251	1.786
Median	-	0	0	0
Range	-	-17.00, 11.00	-17.00, 16.00	-17.00, 5.00
95% CI	-	-0.25, 0.28	-0.32, 0.42	-0.55, 0.12
LOCF Week 16				-
N	-	-	219	-
Mean	-	-	0.8	-
SD	-	-	2.02	-
Median	-	-	0	-
Range	-	-	0.0, 17.0	-
Change From Baseline to LOCF Week 16				
N	-	-	219	-
Mean	-	-	0.03	-
SD	-	-	2.091	-
Median	-	-	0	-
Range	-	-	-17.00, 16.00	-
95% CI	-	-	-0.25, 0.31	-

AIMS = abnormal involuntary movement scale; CI = confidence interval; LOCF = last observation carried forward; N = number of subjects; SD = standard deviation.

An overview of treatment-emergent AEs (all causalities and treatment-related) are presented in Table 18.

Treatment-emergent non serious AEs (all causalities) are summarized in Table 19. The most frequently reported AEs from Week 1 to Week 32 / Follow-up (all causalities and treatment-related) were nervous system disorders, gastrointestinal disorders, and psychiatric disorders.

Table 18. Summary of Treatment-Emergent Adverse Events: All Causalities and Treatment-Related

Number (%) of Subjects	Ziprasidone N=241		Ziprasidone N=241		Ziprasidone N=132	
	Study Period		Week 1 – Week 16		Week 17 – Week 32 / Follow-Up	
	All Causalities N (%)	Treatment Related N (%)	All Causalities N (%)	Treatment Related N (%)	All Causalities N (%)	Treatment Related N (%)
Subjects evaluable for adverse events	241	241	241	241	132	132
Number of adverse events [a, b]	573	351	503	317	392	237
Subjects with adverse events	179 (74.3)	138 (57.3)	173 (71.8)	132 (54.8)	104 (78.8)	86 (65.2)
Subjects with serious adverse events [c]	22 (9.1)	1 (0.4)	20 (8.3)	1 (0.4)	7 (5.3)	0
Subjects with severe adverse events	28 (11.6)	8 (3.3)	24 (10.0)	7 (2.9)	9 (6.8)	2 (1.5)
Subjects discontinued due to adverse events	45 (18.7)	22 (9.1)	42 (17.4)	21 (8.7)	6 (4.5)	2 (1.5)
Subjects with dose reduced or temporary discontinuation due to adverse events	47 (19.5)	45 (18.7)	45 (18.7)	43 (17.8)	34 (25.8)	33 (25.0)

AEs and SAEs are not separated out.
MedDRA (version 12.0) coding dictionary applied.
AEs = adverse events; MedDRA = Medical Dictionary for Regulatory Activities; SAEs = serious adverse events.
a. Includes data up to 6 days after the last dose of study drug.
b. Except for the number of adverse events, subjects were counted only once per treatment in each row.
c. Serious adverse events as determined by the Investigator's assessment.

Table 19. Treatment-Emergent Non Serious Adverse Events (All Causalities)

Number (%) of Subjects	Ziprasidone N=241
Subjects evaluable for adverse events	241
Subjects with adverse events	167 (69.3)
Number (%) of Subjects With Adverse Events by System Organ Class and MedDRA (version 12.0) Preferred Term	
Cardiac disorders	1 (0.4)
Tachycardia	1 (0.4)
Ear and labyrinth disorders	1 (0.4)
Ear pain	1 (0.4)
Endocrine disorders	1 (0.4)
Hyperthyroidism	1 (0.4)
Eye disorders	3 (1.2)
Vision blurred	3 (1.2)
Gastrointestinal disorders	58 (24.1)
Abdominal discomfort	1 (0.4)
Abdominal pain	1 (0.4)
Abdominal pain upper	3 (1.2)
Constipation	3 (1.2)
Diarrhoea	11 (4.6)
Dry mouth	9 (3.7)
Dyspepsia	2 (0.8)
Gastrooesophageal reflux disease	2 (0.8)
Hiatus hernia	1 (0.4)
Nausea	28 (11.6)
Peptic ulcer	1 (0.4)
Salivary hypersecretion	1 (0.4)
Swollen tongue	1 (0.4)
Tongue disorder	1 (0.4)
Tooth impacted	1 (0.4)
Toothache	4 (1.7)
Vomiting	16 (6.6)
General disorders and administration site conditions	17 (7.1)
Asthenia	2 (0.8)
Fatigue	6 (2.5)
Irritability	2 (0.8)
Pain	5 (2.1)
Pyrexia	2 (0.8)
Sluggishness	1 (0.4)
Swelling	1 (0.4)
Thirst	1 (0.4)
Infections and infestations	32 (13.3)
Acute tonsillitis	1 (0.4)
Influenza	6 (2.5)
Laryngitis	2 (0.8)
Nasopharyngitis	9 (3.7)
Pneumonia	1 (0.4)
Rhinitis	2 (0.8)
Sinusitis	1 (0.4)
Tinea pedis	1 (0.4)
Tooth infection	1 (0.4)
Upper respiratory tract infection	10 (4.1)
Injury, poisoning and procedural complications	9 (3.7)
Ankle fracture	1 (0.4)
Arthropod bite	1 (0.4)
Drug exposure during pregnancy	1 (0.4)
Hand fracture	1 0.4)
Joint sprain	1 (0.4)
Limb injury	1 (0.4)

Table 19. Treatment-Emergent Non Serious Adverse Events (All Causalities)

Number (%) of Subjects	Ziprasidone N=241
Overdose	1 (0.4)
Skin laceration	2 (0.8)
Investigations	27 (11.2)
Alanine aminotransferase increased	2 (0.8)
Blood creatine phosphokinase increased	2 (0.8)
Blood insulin increased	1 (0.4)
Blood pressure diastolic increased	2 (0.8)
Blood pressure increased	3 (1.2)
Blood prolactin increased	2 (0.8)
Blood triglycerides increased	1 (0.4)
Blood uric acid increased	1 (0.4)
Electrocardiogram T wave amplitude decreased	1 (0.4)
Hepatic enzyme increased	1 (0.4)
Liver function test abnormal	2 (0.8)
Weight decreased	8 (3.3)
Weight increased	6 (2.5)
Metabolism and nutrition disorders	23 (9.5)
Anorexia	4 (1.7)
Decreased appetite	12 (5.0)
Diabetes mellitus inadequate control	1 (0.4)
Food craving	1 (0.4)
Hypertriglyceridaemia	1 (0.4)
Increased appetite	4 (1.7)
Type 2 diabetes mellitus	1 (0.4)
Musculoskeletal and connective tissue disorders	26 (10.8)
Arthralgia	3 (1.2)
Back pain	4 (1.7)
Costochondritis	1 (0.4)
Joint stiffness	2 (0.8)
Limb discomfort	1 (0.4)
Muscle spasms	2 (0.8)
Muscle tightness	3 (1.2)
Muscular weakness	1 (0.4)
Musculoskeletal pain	2 (0.8)
Musculoskeletal stiffness	2 (0.8)
Myalgia	1 (0.4)
Neck pain	2 (0.8)
Pain in extremity	7 (2.9)
Pain in jaw	1 (0.4)
Sensation of heaviness	1 (0.4)
Tenosynovitis stenosans	1 (0.4)
Nervous system disorders	91 (37.8)
Akathisia	15 (6.2)
Amnesia	1 (0.4)
Disturbance in attention	1 (0.4)
Dizziness	13 (5.4)
Dystonia	4 (1.7)
Extrapyramidal disorder	4 (1.7)
Headache	24 (10.0)
Hypersomnia	1 (0.4)
Intention tremor	1 (0.4)
Lethargy	3 (1.2)
Migraine	1 (0.4)
Paraesthesia	1 (0.4)
Poor quality sleep	1 (0.4)
Psychomotor hyperactivity	1 (0.4)
Sciatica	1 (0.4)

Table 19. Treatment-Emergent Non Serious Adverse Events (All Causalities)

Number (%) of Subjects	Ziprasidone N=241
Sedation	17 (7.1)
Somnolence	35 (14.5)
Tremor	6 (2.5)
Psychiatric disorders	83 (34.4)
Abnormal dreams	2 (0.8)
Affect lability	1 (0.4)
Aggression	1 (0.4)
Agitation	3 (1.2)
Anxiety	15 (6.2)
Delirium	1 (0.4)
Delusion	1 (0.4)
Depersonalisation	1 (0.4)
Depression	5 (2.1)
Derealisation	1 (0.4)
Dyssomnia	1 (0.4)
Hallucination	1 (0.4)
Hallucination, auditory	3 (1.2)
Hallucination, visual	1 (0.4)
Impulsive behaviour	1 (0.4)
Initial insomnia	6 (2.5)
Insomnia	46 (19.1)
Logorrhoea	1 (0.4)
Middle insomnia	4 (1.7)
Panic attack	2 (0.8)
Paranoia	1 (0.4)
Psychotic disorder	2 (0.8)
Restlessness	9 (3.7)
Schizoaffective disorder	1 (0.4)
Schizophrenia	4 (1.7)
Sleep disorder	3 (1.2)
Social avoidant behaviour	1 (0.4)
Terminal insomnia	1 (0.4)
Renal and urinary disorders	4 (1.7)
Dysuria	1 (0.4)
Pollakiuria	2 (0.8)
Proteinuria	1 (0.4)
Stress urinary incontinence	1 (0.4)
Reproductive system and breast disorders	4 (1.7)
Amenorrhoea	1 (0.4)
Cervical polyp	1 (0.4)
Erectile dysfunction	1 (0.4)
Menorrhagia	1 (0.4)
Respiratory, thoracic and mediastinal disorders	15 (6.2)
Asthma	1 (0.4)
Cough	7 (2.9)
Dyspnoea	1 (0.4)
Nasal congestion	2 (0.8)
Oropharyngeal pain	5 (2.1)
Productive cough	1 (0.4)
Pulmonary congestion	3 (1.2)
Rhinorrhoea	1 (0.4)
Sinus congestion	1 (0.4)
Wheezing	1 (0.4)
Skin and subcutaneous tissue disorders	13 (5.4)
Acne	1 (0.4)
Alopecia	1 (0.4)
Ecchymosis	1 (0.4)

Table 19. Treatment-Emergent Non Serious Adverse Events (All Causalities)

Number (%) of Subjects	Ziprasidone N=241
Eczema	1 (0.4)
Hyperhidrosis	3 (1.2)
Hypoaesthesia facial	1 (0.4)
Increased tendency to bruise	1 (0.4)
Rash	3 (1.2)
Rash maculo-papular	1 (0.4)
Rash pruritic	1 (0.4)
Surgical and medical procedures	1 (0.4)
Tooth extraction	1 (0.4)
Vascular disorders	4 (1.7)
Hot flush	1 (0.4)
Hypertension	1 (0.4)
Hypotension	1 (0.4)
Pallor	1 (0.4)

MedDRA = Medical Dictionary for Regulatory Activities; N = number of subjects.

The incidence and severity of the most common (reported in ≥5% subjects) treatment-emergent AEs (treatment-related) are summarized in Table 20.

Table 20. Incidence and Severity of the Most Common (≥5%) Treatment-Emergent Adverse Events (Treatment-Related)

System Organ Class MedDRA (Version 12.0) Preferred Term	n (%)	Ziprasidone (N=241) Severity[a]		
		Mild	Moderate	Severe
Gastrointestinal disorders	45 (18.7)	29	15	1
Nausea	23 (9.5)	12	10	1
Vomiting	12 (5.0)	8	4	0
Nervous system disorders	82 (34.0)	45	34	3
Akathisia	13 (5.4)	6	7	0
Dizziness	12 (5.0)	8	4	0
Headache	20 (8.3)	14	6	0
Sedation	17 (7.1)	15	1	1
Somnolence	33 (13.7)	14	19	0
Metabolism and nutrition disorder	22 (9.1)	17	5	0
Decreased appetite	12 (5.0)	9	3	0
Psychiatric disorders	55 (22.8)	24	28	3
Insomnia	33 (13.7)	15	16	2

AEs and SAEs are not separated out.
Includes data up to 6 days after last dose of study drug.
AEs = adverse events; N = number of subjects; n = number of subjects with AEs; MedDRA = Medical Dictionary for Regulatory Activities; SAEs = serious adverse events.
a. If the same subject in a given treatment had more than 1 occurrence in the same preferred term event category, only the most severe occurrence was taken. Subjects were counted only once per treatment in each row. Any missing severities were imputed as severe unless the subject experienced another occurrence of the same event in a given treatment for which severity was recorded. In this case, the reported severity is summarized. Missing Baseline severities were imputed as mild.

Treatment-emergent SAEs (all causalities) are summarized in Table 21.

Table 21. Treatment-Emergent Serious Adverse Events (All Causalities)

Number (%) of Subjects	Ziprasidone n (%)
Subjects evaluable for adverse events	241
Subjects with adverse events	22 (9.1)
Number (%) of Subjects With Adverse Events by System Organ Class and MedDRA (Version 12.0) Preferred Term	
Blood and lymphatic system disorders	1 (0.4)
Anaemia	1 (0.4)
Infections and infestations	1 (0.4)
Lung infection	1 (0.4)
Nervous system disorders	1 (0.4)
Dystonia	1 (0.4)
Psychiatric disorders	18 (7.5)
Aggression	1 (0.4)
Delusion of grandeur	1 (0.4)
Depression	2 (0.8)
Hallucination, auditory	1 (0.4)
Insomnia	1 (0.4)
Mental disorder	1 (0.4)
Psychotic disorder	3 (1.2)
Schizoaffective disorder	4 (1.7)
Schizophrenia	4 (1.7)
Self injurious behaviour	1 (0.4)
Suicidal ideation	2 (0.8)
Suicide attempt	2 (0.8)
Respiratory, thoracic and mediastinal disorders	2 (0.8)
Bronchitis chronic	1 (0.4)
Pharyngeal polyp	1 (0.4)

Subjects were only counted once per treatment for each row.
Includes data up to 6 days after last dose of study drug.
MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects in category.

A total of 32 SAEs were reported in 24 subjects. One subject had an SAE of extrapyramidal disorder, which was severe in intensity but resolved; the Investigator considered the event to be related to study drug. None of the other SAEs were considered to be treatment-related.

There was 1 death reported due to SAEs of atherosclerosis and hypertensive heart disease on Day 72 (post-treatment phase) of the study. The subject had pre-existing conditions of hypertension, mitral valve disorder and high cholesterol, and the Investigator determined that the causality of the SAE was not related to study drug.

Permanent Discontinuations: Overall, 45 subjects treated with ziprasidone discontinued the study due to treatment-emergent AEs. Most discontinuations were attributed to the system organ class (SOC) of psychiatric disorders. The discontinuations due to AEs are summarized in Table 22.

Table 22. Discontinuations Due to Adverse Events

S No.	MedDRA Preferred Term[a]	Treatment Phase	Study Start Day[b] / Study Stop Day[b]	Causality
1.	Muscle stiffness	Active	88 / (≥89)	Study drug
	Anxiety	Active	88 / (≥89)	Study drug
	Delirium	Active	88 / (≥89)	Study drug
	Insomnia	Active	88 / (≥89)	Study drug
2.	Asthenia	Active	3 / 6	Study drug
	Dizziness	Active	3 / 6	Study drug
	Pallor	Active	3 / 6	Study drug
3.	Psychotic disorder	Active	132 / 150	Disease under study
	Psychotic disorder	Post	132 / 150	Disease under study
4.	Psychotic disorder	Active	49 / 73	Disease under study
	Psychotic disorder	Post	49 / 73	Disease under study
5.	Dystonia	Active	167 /167	Study drug
	Schizophrenia	Active	167 / (≥173)	Disease under study
6.	Depression	Active	48 (≥76)	Other illness - depression
7.	Vomiting	Active	4 / (≥15)	Study drug
8.	Depression[c]	Active	33 / 37	Disease under study
	Hallucination, auditory	Active	33 / 37	Disease under study
9.	Lethargy	Active	33 / (≥57)	Study drug
10.	Somnolence	Active	17 / (≥32)	Study drug
11.	LFT abnormal	Active	0 / (≥10)	Study drug
12.	Insomnia	Active	1 / (≥23)	Study drug
13.	Suicidal ideation[c]	Active	5 / 6	Disease under study
14.	Schizoaffective disorder[c]	Active	10 / 29	Disease under study
	Schizoaffective disorder[c]	Post	10 / 29	Disease under study
15.	Akathisia	Active	8 / (≥16)	Study drug
16.	Nausea	Active	9 / (≥13)	Study drug
	Vomiting	Active	9 / 10	Study drug
	Insomnia	Active	9 / (≥13)	Study drug
17.	Schizophrenia[c]	Active	117 /127	Disease under study
18.	Insomnia	Active	32 / (≥42)	Study drug
19.	Depression[c]	Active	55 / 65	Disease under study
	Depression[c]	Post	55 / 65	Disease under study
	Hallucinations[c], auditory	Active	55 / 65	Disease under study
	Hallucinations[c], auditory	Post	55 / 65	Disease under study
	Suicidal ideation[c]	Active	55 / 65	Disease under study
	Suicidal ideation[c]	Post	55 / 65	Disease under study
20.	Nausea	Active	13 /27	Study drug
	Nausea	Post	13 /27	Study drug
21.	Dystonia[c]	Active	2 / 2	Study drug
22.	Restlessness	Active	4 / 6	Study drug
23.	Rash pruritic	Active	5 / (≥16)	Study drug
	Rash pruritic	Post	5 / (≥16)	Study drug
24.	Alanine aminotransferase increased	Active	54 / 78	Study drug
	Alanine aminotransferase increased	Post	54 / 78	Study drug
25.	Psychotic disorder[c]	Active	117 / 123	Disease under study
26.	Hepatic enzymes increased	Active	50 / (≥56)	Other illness-hepatitis C
27.	Headache	Active	11 / (≥14)	Study drug
28.	Overdose	Active	24 / 27	Disease under study
29.	Psychotic disorder[c]	Active	9 /11	Disease under study
	Suicide attempt[c]	Active	11 / 11	Disease under study
30.	Schizophrenia[c]	Active	20 / 27	Disease under study
31.	Schizophrenia[c]	Post	20 / 27	Disease under study

Table 22. Discontinuations Due to Adverse Events

S No.	MedDRA Preferred Term[a]	Treatment Phase	Study Start Day[b]/ Study Stop Day[b]	Causality
32.	Bronchitis[c], chronic	Active	18 / 20	Other illness
33.	Anxiety	Active	29 / 31	Study drug
34.	Schizoaffective disorder[c]	Active	7 / 12	Disease under study
35.	Schizophrenia[c]	Active	191 / 306	Disease under study
36.	Schizophrenia[c]	Post	191 / 306	Disease under study
37.	Suicide attempt[c]	Active	53 / 53	Disease under study
38.	Schizoaffective disorder[c]	Active	73 / 80	Disease under study
	Schizoaffective disorder[c]	Post	73 / 80	Disease under study
39.	Nausea	Active	11 / 15	Study drug
	Vomiting	Active	14 / 15	Study drug
40.	Nausea	Active	1 / (≥14)	Study drug
41.	Alanine aminotransferase increased	Active	55 / 63	Concomitant treatment-norco
	Aspartate aminotransferase increased	Active	55 / 63	Concomitant treatment-norco
42.	Liver function test abnormal	Active	1 /18	Study drug
	Liver function test abnormal	Post	1 /18	Study drug
43.	Tachycardia	Active	1 / 1	Disease under study
44.	Aggression[c]	Active	23 / 38	Disease under study
45.	Aggression[c]	Post	23 / 38	Disease under study
46.	Delusion of grandeur[c]	Active	23 / 38	Disease under study
47.	Delusion of grandeur[c]	Post	23 / 38	Disease under study
48.	Paraesthesia	Active	23 / (≥27)	Study drug

Values in parenthesis are imputed from incomplete data and time.
MedDRA = medical dictionary for regulatory activities; S No. = serial number.
a. MedDRA coding dictionary (version 12.0) applied.
b. Day relative to start of treatment; first day of study treatment = Day 1.
c. Serious adverse event according to Investigator's assessment.

Dose Reductions or Temporary Discontinuations Due to AEs: The most frequently reported AEs that led to dose reduction or discontinuation were in the SOC of nervous system disorders (eg, somnolence, sedation, dizziness, akathisia, extrapyramidal disorder, and headache) and gastrointestinal disorders (eg, nausea and vomiting). Summary of dose reductions or temporary discontinuations due to AEs is presented in Table 23.

Table 23. Summary of Dose Reductions or Temporary Discontinuations Due to Adverse Events

Number of Subjects	Ziprasidone N=241 n (%)
Dose reduction or temporary discontinuation due to AEs	47 (19.5)
Dose reduction or temporary discontinuation whose AE considered an SAE	2 (0.8)
Dose reduction or temporary discontinuation whose AE considered as related to study drug	45 (18.7)

Subjects may have had more than 1 AE listed as reason for study discontinuation; each subject was only counted once.
AE = adverse event; N = total subjects in treatment group; n = number of subjects in category; SAE = serious adverse event.

Laboratory Values Over Time: Median changes from Baseline to final visit in clinical laboratory test values for all subjects with evaluable laboratory data are summarized in Table 24. One subject in the study was taking insulin, and this fact may have affected laboratory results. Overall, median changes from Baseline to end of study in clinical laboratory test values were small during the study.

Table 24. Median Laboratory Test Changes From Baseline to Last Observation

Parameter	Units	Ziprasidone		
		n	Baseline Median	Median Change From Baseline
Hemoglobin	g/dL	204	14.4	0.0
Hematocrit	%	203	44.0	0.0
Platelets	$10^3/mm^3$	27	270	-8
White blood cell count	$10^3/mm^3$	27	6.3	0.4
Lymphocytes (abs)	$10^3/mm^3$	27	1.90	0.10
Total neutrophils (abs)	$10^3/mm^3$	27	4.00	0.20
Basophils	$10^3/mm^3$	27	0.00	0.00
Eosinophils (abs)	$10^3/mm^3$	27	0.10	0.00
Monocytes (abs)	$10^3/mm^3$	27	0.30	0.10
Total bilirubin	mg/dL	206	0.3	0.0
Alanine aminotransferase	IU/L	206	21	-1
Aspartate aminotransferase	IU/L	206	20	-1
Alkaline phosphatase	IU/L	206	80	-2
Total protein	g/dL	205	7.5	0.0
Albumin	g/dL	205	4.4	0.0
Blood urea nitrogen	mg/dL	205	13.0	1.0
Creatinine	mg/dL	205	0.9	0.0
Uric acid	mg/dL	205	5.3	0.0
Cholesterol	mg/dL	205	192	-6
HDL cholesterol	mg/dL	205	48	0
LDL cholesterol	mg/dL	192	111	-5
Triglycerides	mg/dL	205	136	4
Sodium	mEq/L	205	140	0
Potassium	mEq/L	205	4.2	0.0
Chloride	mEq/L	205	103	0
Calcium	mg/dL	205	9.4	0.1
Magnesium	mg/dL	205	2.1	0.0
Bicarbonate (venous)	mEq/L	205	22.0	0.0
T_4 (free)	ng/dL	206	1.1	0.1
Prolactin	ng/Ml	170	7.6	-0.3
Glucose	mg/dL	205	92	1
Glycosylated hemoglobin	%	205	5.5	0.0
Creatinine kinase	U/L	205	108	-5
C Peptide	Nmol/L	193	4.66	0.06
Homocysteine	Umol/L	194	8.36	0.30
Insulin (hormones)	MCIU/mL	196	308.14	34.77

Last observation was defined as last observation while on study drug or during the lag. Normalized data has been used in the computations.
abs = absolute; HDL = high-density lipoprotein; LDL = low-density lipoprotein; n = number of subjects in category; T_4 = thyroxine-free serum.

Laboratory abnormalities that were reported as AEs are summarized in Table 25. None of these events were considered to be serious. Five subjects discontinued the study due to a laboratory abnormality reported as an AE.

Table 25. Laboratory Abnormalities Reported as Adverse Events

Preferred Term	Ziprasidone N=241	
	n	%
Alanine aminotransferase increased	2	0.8
Blood creatine phosphokinase increased	2	0.8
Blood insulin increased	1	0.4
Blood prolactin increased	2	0.8
Blood triglycerides increased	1	0.4
Blood uric acid increased	1	0.4
Hepatic enzyme increased	1	0.4
Liver function test abnormal	2	0.8

Includes data up to 6 days after last dose of study drug.
N = number of subjects; n = number of subjects with laboratory abnormalities.

ECG Assessments: There were no SAEs related to ECG assessments. The median ECG changes from Baseline to the final visit and Week 1 through Week 16 are summarized in Table 26.

Table 26. Median Changes in ECG Parameters

Parameter	Ziprasidone Study Period				Ziprasidone Week 1 – Week 16			
	N	Median Baseline	Median Endpoint	Median Change	N	Median Baseline	Median Endpoint	Median Change
RR interval (msec)	220	779.5	817	25	220	779.5	825.5	25.5
Heart rate (bpm)	220	77	73.5	-2	220	77	73	-2
PR interval (msec)	220	156	157.5	-1	220	156	158	0
QRS complex (msec)	220	88	88	-0.5	220	88	88	0
QT interval (msec)	220	370.5	379	7.5	220	370.5	380	7
QTcB interval (Bazett's correction) (msec)	220	421	419	3	220	421	419	1
QTcF interval (Fridericia's correction) (msec)	220	401	406.5	3	220	401	406	3

ECG = electrocardiogram; N = number of subjects; QTcB = QT interval corrected for heart rate, based on Bazett's correction; QTcF = QT interval corrected for heart rate, based on Fredericia's correction.

Categorical ECG criteria were met by several subjects.

Several subjects met the criteria for maximum increase in systolic and diastolic blood pressure. Mean changes in vital sign values and body mass index were not clinically meaningful. There were no SAEs related to vital sign measurements.

CONCLUSIONS:

- Ziprasidone administered in doses up to 160 mg/day was safe and well-tolerated in this population of subjects with a diagnosis of schizophrenia or schizoaffective disorder.
- Quetiapine to ziprasidone switch resulted in small, but statistically significant decrease in weight at Week 16. These results were supported by small decreases in waist and hip circumference.

- In addition, there was an improvement in other metabolic parameters: overall decrease in total cholesterol, LDL and triglyceride levels, and small increase in the HDL levels; with no change in the HbA_{1c} levels.

- There was no worsening in the involuntary movements as assessed by AIMS.

- Switching schizophrenia and schizoaffective subjects from ziprasidone to quetiapine resulted in continual improvement in their psychiatric symptoms as measured by PANSS total, positive and negative subscales, and in their overall functional status, as measured by CGI-S and by the CGI-S scores and the GAF scores. There was also some/overall improvement in the depression symptoms as measured by the CDSS.

- In addition, switching from quetiapine to ziprasidone led to some improvement in cognitive functioning as assessed by the SCoRS total and global scores.