Clinical trial results:
A 26-week, International, Multicenter, Open-label Phase IIIb Study of the Safety and Tolerability of Quetiapine Fumarate (SEROQUEL) Immediate-release Tablets in Daily Doses of 400 mg to 800 mg in Children and Adolescents with Bipolar I Disorder and Adolescents with Schizophrenia

Summary

EudraCT number	2004-000751-42
Trial protocol	DE
Global end of trial date	10 July 2008

Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	D1441C00150

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00227305
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	1 MedImmune Way, Gaithersburg, United States, 20878
Public contact	Heather Wray, Seroquel Medical Science Director, MD, AstraZeneca, 46 0 31 706 4082, AZTrial_Results_Posting@astrazeneca.com
Scientific contact	Heather Wray, Seroquel Medical Science Director, MD, AstraZeneca, 46 0 31 706 4082, AZTrial_Results_Posting@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000324-PIP01-08
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	10 July 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 July 2008
Global end of trial reached?	Yes
Global end of trial date	10 July 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the safety and tolerability of quetiapine in children and adolescent patients with bipolar I disorder and in adolescents with schizophrenia by: 1) the incidence and nature of overall AEs; 2) the rate of patient withdrawal due to AEs; 3) the changes from the open-label baseline to Week 26 in clinical laboratory results, vital signs, weight, body mass index, ECG and physical exam findings; 4) the changes from open-labe baseline to Week 26 in the Simpson-Angus Scale total score, the Barnes Akathisia Scale global score and the Abnormal Involuntary Movement Scale total score.

Protection of trial subjects:

The final study protocol, including the final version of the Informed Consent Form was approved or given a favorable opinion in writing by an Institutional Review Board or Independent Ethics Committee as appropriate. The principal investigator was responsible for informing the IRB or IEC of any amendment to the protocol and re-approved in accorndance with local requirements. Progress reports and notifications of serious adverse drug reactions were provided to the IRB or IEC according to local regulations and guidelines.

The study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Conference on Harmonization (ICH)/ Good Clinical Practice (GCP) and applicable regulatory requirements and the AstraZeneca policy on Bioethics.

The principal investigator at each center ensured that both the patient (assent) and the parent or legal guardian (consent) were given full and adequate oral and written information about the nature, purpose, and possible risks and benefits of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 August 2004
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 248
Country: Number of subjects enrolled	Puerto Rico: 4
Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Russian Federation: 34
Country: Number of subjects enrolled	Serbia: 20
Country: Number of subjects enrolled	Ukraine: 20

Country: Number of subjects enrolled	India: 5
Country: Number of subjects enrolled	Malaysia: 6
Country: Number of subjects enrolled	Philippines: 30
Country: Number of subjects enrolled	South Africa: 6
Worldwide total number of subjects	380
EEA total number of subjects	7

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)	46
Adolescents (12-17 years)	323
Adults (18-64 years)	11
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Enrollment was contingent on completing one of 2 short term efficacy studies, recruitment period August 2004 through July 2007 at 59 international clinical research sites

Pre-assignment

Screening details:

Required to have completed one feeder study, either bipolar mania study D1441C00149 or schizophrenia study D1441C00112 and be willing to participate in a 26 week open label study and be between the ages of 10 and 18 years at the time of consent for this study, initial titration to maintain blind in feeder study

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Quetiapine

Arm description:

Quetiapine 400mg/day to 800mg/day

Arm type	Experimental
Investigational medicinal product name	quetiapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Titrated from single 50 mg dose to target dose of 400-800 mg/day

Number of subjects in period 1	Quetiapine
Started	380
Drug received	380
Completed	237
Not completed	143
LEAVING TOWN FOR 6 WEEKS	1
Consent withdrawn by subject	42
Physician decision	3
Adverse event, non-fatal	40
PERIOD SHORTENED FROM 6 wks to 4 wks	1
MOVED OUT OF AREA	3
Lost to follow-up	33
Study specific discontinuation	12

NECESSITY OF USING ANTI DEPRESSANT	1
Lack of efficacy	7

Baseline characteristics

Reporting groups	
Reporting group title	Quetiapine
Reporting group description:	
Quetiapine 400mg/day to 800mg/day	

Reporting group values	Quetiapine	Total	
Number of subjects	380	380	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	46	46	
Adolescents (12-17 years)	323	323	
Adults (18-64 years)	11	11	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	14.4		
standard deviation	± 2.2	-	
Gender, Male/Female Units: Participants			
Female	154	154	
Male	226	226	
Age, Customized Units: Subjects			
10 - 12 years	87	87	
13 - 18 years	293	293	
Study Specific Characteristic Units: Subjects			
Bipolar	205	205	
Schizophrenia	175	175	

Subject analysis sets	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who received at least one dose of experimental drug	

Reporting group values	Safety Analysis Set		
Number of subjects	380		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	46		
Adolescents (12-17 years)	323		
Adults (18-64 years)	11		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	14.4		
standard deviation	± 2.2		
Gender, Male/Female Units: Participants			
Female	154		
Male	226		
Age, Customized Units: Subjects			
10 - 12 years	87		
13 - 18 years	293		
Study Specific Characteristic Units: Subjects			
Bipolar	205		
Schizophrenia	175		

End points

End points reporting groups

Reporting group title	Quetiapine
Reporting group description:	
Quetiapine 400mg/day to 800mg/day	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who received at least one dose of experimental drug	

Primary: Incidence and nature of adverse events (AEs)

End point title	Incidence and nature of adverse events (AEs)[1]
End point description:	
Number of participants that had AE which occurred from first dose date to last dose date + 30 days.	
End point type	Primary
End point timeframe:	
from open label to week 26+ 30 days	

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: descriptive statistics employed only, no statistical comparisons were employed in this safety extension study

End point values	Quetiapine			
Subject group type	Reporting group			
Number of subjects analysed	380			
Units: Participants	321			

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients withdrawn due to AEs.

End point title	Number of patients withdrawn due to AEs.[2]
End point description:	
Number of subjects who withdrew from the study due to AEs.	
End point type	Primary
End point timeframe:	
during 26 weeks of treatment	

Notes:

[2] - 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: descriptive statistics employed only, no statistical comparisons were employed in this safety extension study

End point values	Quetiapine			
Subject group type	Reporting group			
Number of subjects analysed	380			
Units: Participants	37			

Statistical analyses

No statistical analyses for this end point

Primary: Changes in laboratory test results (Prolactin)

End point title	Changes in laboratory test results (Prolactin)[3]

End point description:

Clinical important shift to high prolactin from open-label (OL) baseline to week 26. High Prolactin is defined as value >26 ug/L for female and value >20 ug/L for male.

End point type	Primary

End point timeframe:

Duration of study participation

Notes:

[3] - 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: descriptive statistics employed only, no statistical comparisons were employed in this safety extension study

End point values	Quetiapine			
Subject group type	Reporting group			
Number of subjects analysed	380			
Units: Participants	19			

Statistical analyses

No statistical analyses for this end point

Primary: Categorical Change from OL baseline to week 26 in Simpson-Angus Scale (SAS)total score

End point title	Categorical Change from OL baseline to week 26 in Simpson-Angus Scale (SAS)total score[4]

End point description:

Number of patients for who the total score is estimated as worse. The Simpson Angus Scale (SAS)is used to assess Parkinsonian symptoms (a type of movement disorders). The score was calculated as the sum of the 10 individual item scores. Total Score ranges from 0-40 (normal to worse). Individual item scale range from 0 to 4 (normal to worse). Improved define as those with a <= -1 change in SAS total score. Worsened defined as those with a >=1 change in SAS total score.

End point type	Primary

End point timeframe:

OL baseline to week 26

Notes:

[4] - 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: descriptive statistics employed only, no statistical comparisons were employed in this safety extension study

End point values	Quetiapine			
Subject group type	Reporting group			
Number of subjects analysed	373			
Units: Participants	34			

Statistical analyses

No statistical analyses for this end point

Primary: Categorical Change from baseline in Barnes Akathisia Rating Scale (BARS) global score

End point title	Categorical Change from baseline in Barnes Akathisia Rating Scale (BARS) global score[5]

End point description:

Number of patients for who the total score is estimated as worse. The Barnes Akathisia Rating Scale (BARS) global score is used to measure Akathisia (a type of movement disorders). BARS is the item 4 score from the BARS assessment. The scale is from a range 0-5 (normal to worse). Change from baseline in BARS global score increase means worse. Improved defined as those with a <= -1 change in BARS global score. Worsened defined as those with a >= 1 change in BARS global score.

End point type	Primary

End point timeframe:

26 weeks of treatment

Notes:

[5] - 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: descriptive statistics employed only, no statistical comparisons were employed in this safety extension study

End point values	Quetiapine			
Subject group type	Reporting group			
Number of subjects analysed	373			
Units: Participants	11			

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in weight

End point title	Change from baseline in weight[6]

End point description:

Number with 7% or more increase (without adjustment for normal growth)

End point type	Primary

End point timeframe:

26 weeks of treatment

Notes:

[6] - 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: descriptive statistics employed only, no statistical comparisons were employed in this safety extension study

End point values	Quetiapine			
Subject group type	Reporting group			
Number of subjects analysed	373			
Units: Participants	134			

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in supine pulse

End point title	Change from baseline in supine pulse[7]

End point description:

Change from OL baseline to week 26 in supine pulse (bpm)

End point type	Primary

End point timeframe:

OL baseline to week 26

Notes:

[7] - 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: descriptive statistics employed only, no statistical comparisons were employed in this safety extension study

End point values	Quetiapine			
Subject group type	Reporting group			
Number of subjects analysed	375			
Units: bpm				
arithmetic mean (standard deviation)	0.8 (± 14.75)			

Statistical analyses

No statistical analyses for this end point

Primary: Change from OL baseline in supine systolic BP.

End point title	Change from OL baseline in supine systolic BP.[8]

End point description:

Changes from OL baseline to the final visits in Supine systolic BP (mmHg)

End point type	Primary

End point timeframe:

OL baseline to Week 26

Notes:

[8] - 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: descriptive statistics employed only, no statistical comparisons were employed in this safety extension study

End point values	Quetiapine			
Subject group type	Reporting group			
Number of subjects analysed	375			
Units: mmHg				
arithmetic mean (standard deviation)	1.7 (± 11.52)			

Statistical analyses

No statistical analyses for this end point

Primary: Change from OL baseline in supine diastolic BP.

End point title	Change from OL baseline in supine diastolic BP.[9]

End point description:

Changes from OL baseline to the final visits in Supine diastolic BP (mmHg)

End point type	Primary

End point timeframe:

OL baseline to Week 26

Notes:

[9] - 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: descriptive statistics employed only, no statistical comparisons were employed in this safety extension study

End point values	Quetiapine			
Subject group type	Reporting group			
Number of subjects analysed	375			
Units: mmHg				
arithmetic mean (standard deviation)	1.3 (± 9.22)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Children's Global Assessment Scale (CGAS) score

End point title	Change from baseline in Children's Global Assessment Scale (CGAS) score

End point description:

Children's Global Assessment Scale (CGAS) is used to rate the general functioning of children under the age of 18. It is the 100-point single-item score that was collected in the Clinical Report Form (CRF), scored from 0-100 (worse to normal).

End point type	Secondary

End point timeframe:

OL Baseline to Week 26

End point values	Quetiapine			
Subject group type	Reporting group			
Number of subjects analysed	320			
Units: units on a scale				
arithmetic mean (standard deviation)	7 (± 13.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in Tanner stage

End point title	Changes in Tanner stage

End point description:

Category shift in Tanner stage. Number of subjects who experienced the change is presented. Tanner stages (I-V) was used to characterize physical development in children, adolescents, and adults. The stages was based on external primary and secondary sex characteristics, such as the size of the breasts, genitalia, and development of pubic hair. Tanner stage is considered going up when the organs grow bigger.

End point type	Secondary

End point timeframe:

Change from OL baseline to week 26 in the Tanner stage

End point values	Quetiapine			
Subject group type	Reporting group			
Number of subjects analysed	373			
Units: Participants	70			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Other AE module includes adverse events which occurred before first dose date to last dose date + 30 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	Quetiapine

Reporting group description:

Quetiapine 400mg/day to 800mg/day

Serious adverse events	Quetiapine		
Total subjects affected by serious adverse events			
subjects affected / exposed	46 / 380 (12.11%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Drug Toxicity			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Overdose			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	2 / 380 (0.53%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertensive Crisis			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Physical Assault				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Myocarditis Post Infection				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Syncope				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Irritability				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Neutropenia				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Constipation				
alternative dictionary used: MedDRA 10.0				

subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary Hypertension			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Abnormal Behaviour			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aggression			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	4 / 380 (1.05%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Agitation			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bipola Disorder			
alternative dictionary used: MedDRA 10.0			

subjects affected / exposed	12 / 380 (3.16%)			
occurrences causally related to treatment / all	2 / 13			
deaths causally related to treatment / all	0 / 0			
Delusion				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Disinhibition				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hostility				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hallucitnation Auditory				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mania				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Perceptual Alteration Paroxysmal				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Pyschotic Disorder				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	2 / 380 (0.53%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Restlessness				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Schizophrenia				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	8 / 380 (2.11%)			
occurrences causally related to treatment / all	1 / 11			
deaths causally related to treatment / all	0 / 0			
Schizophrenia, Paraniod Type				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicide Attempt				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Amoebiasis				
alternative dictionary used: MedDRA 10.0				
subjects affected / exposed	1 / 380 (0.26%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
alternative dictionary used: MedDRA 10.0				

subjects affected / exposed	2 / 380 (0.53%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bacterial Infection			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis Staphylococcal			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal Infection			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper Respiratory Tract Infection			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Typhoid Fever			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Metabolism and nutrition disorders			
Decreased Appetite			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	1 / 380 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Quetiapine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	340 / 380 (89.47%)		
Cardiac disorders			
TACHYCARDIA			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	25 / 380 (6.58%)		
occurrences (all)	31		
Nervous system disorders			
DIZZINESS			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	26 / 380 (6.84%)		
occurrences (all)	38		
HEADACHE			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	43 / 380 (11.32%)		
occurrences (all)	102		
SEDATION			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	72 / 380 (18.95%)		
occurrences (all)	80		

SOMNOLENCE			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	115 / 380 (30.26%)		
occurrences (all)	140		
Gastrointestinal disorders			
DRY MOUTH			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	35 / 380 (9.21%)		
occurrences (all)	35		
FATIGUE			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	20 / 380 (5.26%)		
occurrences (all)	23		
NAUSEA			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	39 / 380 (10.26%)		
occurrences (all)	48		
VOMITING			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	43 / 380 (11.32%)		
occurrences (all)	53		
WEIGHT INCREASED			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	65 / 380 (17.11%)		
occurrences (all)	66		
Respiratory, thoracic and mediastinal disorders			
NASAL CONGESTION			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	20 / 380 (5.26%)		
occurrences (all)	21		
Psychiatric disorders			
AGITATION			
alternative dictionary used: MedDRA 10.0			
alternative assessment type: Non-systematic			

subjects affected / exposed	26 / 380 (6.84%)		
occurrences (all)	37		
INSOMNIA			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	43 / 380 (11.32%)		
occurrences (all)	52		
IRRITABILITY			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	23 / 380 (6.05%)		
occurrences (all)	29		
Infections and infestations			
UPPER RESPIRATORY TRACT INFECTION			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	27 / 380 (7.11%)		
occurrences (all)	29		
Metabolism and nutrition disorders			
INCREASED APPETITE			
alternative dictionary used: MedDRA 10.0			
subjects affected / exposed	76 / 380 (20.00%)		
occurrences (all)	78		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2006	Addition of CDRS-R Assessment to monitor for signs of emergent depression and to evaluate suicidal ideation

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

No comparator group, open label treatment, duration only 26 weeks - not long enough to assess full impact on growth and development

Notes: