Clinical trial results:
The switch study - efficacy of early antipsychotic switch versus maintenance in patients with schizophrenia poorly responding to two weeks of antipsychotic treatment

Summary

EudraCT number	2009-012031-15
Trial protocol	DE RO
Global end of trial date	06 February 2014

Results information

Result version number	v1 (current)
This version publication date	12 June 2021
First version publication date	12 June 2021

Trial information

Trial identification

Sponsor protocol code	01KG0910

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01029769
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Technische Universität München, Fakultät für Medizin
Sponsor organisation address	Ismaninger Str. 22, München, Germany, 81675
Public contact	Prof. Dr. Stefan Leucht, Klinikum rechts der Isar der TU München, Klinik für Psychiatrie, 49 4140 4249, stefan.leucht@tum.de
Scientific contact	Prof. Dr. Stefan Leucht, Klinikum rechts der Isar der TU München, Klinik für Psychiatrie, 49 4140 4249, stefan.leucht@tum.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 February 2014
Global end of trial reached?	Yes
Global end of trial date	06 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the current trial is to examine the superior effectiveness of an early switch of antipsychotic treatment in patients poorly responding to two weeks of randomized treatment with either olanzapine or amisulpride. The primary endpoint is the number of patients in remission after another six weeks of treatment after either continuing on the initially started antipsychotic or having been switched to the alternative study drug.

Protection of trial subjects:

The conduct of this clinical study met the local legal and regulatory requirements. The study was conducted in accordance the ethical principles of Good Clinical Practice (GCP).
Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision.
The study was regularly monitored by the Sponsor and all investigators connected to the study were GCP trained.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 February 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 150
Country: Number of subjects enrolled	Romania: 177
Worldwide total number of subjects	327
EEA total number of subjects	327

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)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	325
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Pre-screening processes were in place. Between 08.02.2010 and 06.02.2014 all patients were randomised.

Pre-assignment

Screening details:

Adult patients diagnosed with schizophrenia or schizoaffective disorder or a schizophrenic disorder examined with regard to ther suitability. This was followed by the 1st double-blind randomization (olanzapine- or amisulpride-arm).

Period 1

Period 1 title	Phase I
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Blinding implementation details:

Medication was encapsulated in capsules identical in shape, colour and taste

Arms

Arm title	Phase I amisulpride or olanzapine

Arm description:

Amisulpride 200-800 mg/day or olanzapine 5-20mg/day.
In phase I participants were randomised to either amisulpride (164 participants) or olanzapine (163 participants). The reason was that we wanted to rule out by the study design that any differences between switching and staying in phase II were related to the drug the participants were originally designed to in phase I. However, differences between amisulpride and olanzapine in phase I were not analysed.

Arm type	Treatment before phase of interest (phase II)
Investigational medicinal product name	Amisulpride
Investigational medicinal product code	ATC Code N05AH03
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

200-800mg/day

Investigational medicinal product name	Olanzapine
Investigational medicinal product code	ATC Code 37872.00.00
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

5-20mg/day

Number of subjects in period 1	Phase I amisulpride or olanzapine
Started	327
Completed	285
Not completed	42
Consent withdrawn by subject	18
Physician decision	2
Adverse event, non-fatal	8
Lost to follow-up	3
Lack of efficacy	4
Involuntary admission	1
Protocol deviation	6

Period 2

Period 2 title	Phase II
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Blinding implementation details:

Capsules of identical shape, colour and size

Arms

Are arms mutually exclusive?	Yes
Arm title	Switch

Arm description:

Non-improvers in phase I switch to the drug they were not assigned to in phase I

Arm type	Experimental
Investigational medicinal product name	Amisulpride
Investigational medicinal product code	ATC Code 37872.00.00
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Per Day: 200-800 milligram(s)

Investigational medicinal product name	Olanzapine
Investigational medicinal product code	ATC Code N05AH03
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

per day: 5-20mg milligram(s)

Arm title	Stay
Arm description:	
Non-improvers in phase I stay on the drug they were assigned to in phase I	
Arm type	Active comparator
Investigational medicinal product name	Amisulpride
Investigational medicinal product code	ATC Code 37872.00.00
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
Daily dose: 200-800 milligram(s)	
Investigational medicinal product name	Olanzapine
Investigational medicinal product code	ATC code N05AH03
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
Daily dose: 5-20 milligram(s)	
Arm title	Early improvers
Arm description:	
Early improvers in phase I continued to receive the same drug in phase II. Differences between early improvers and stayers/switchers were not analysed.	
Arm type	Follow-up of early improvers
Investigational medicinal product name	Amisulpride
Investigational medicinal product code	ATC Code 37872.00.00
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
Daily dose: 200-800 milligram(s)	
Investigational medicinal product name	Olanzapine
Investigational medicinal product code	ATC code N05AH03
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
Daily dose: 5-20 milligram(s)	

Number of subjects in period 2[1]	Switch	Stay	Early improvers
Started	70	72	140
Completed	60	55	104
Not completed	10	17	36
Consent withdrawn by subject	3	4	12
Physician decision	-	2	-
Administrative	-	-	2
Adverse event, non-fatal	2	1	3

suicide attempt	1	-	-
Lost to follow-up	-	1	7
Lack of efficacy	2	6	5
Protocol deviation	2	3	6
Randomisation error	-	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 3 participants were not re-randomised in phase II

Baseline characteristics

Reporting groups	
Reporting group title	Phase I

Reporting group description:

The patients were randomised to amisulpride group or olanzapine. We present the results of both drugs combined. Differences between drugs were not analysed.

Reporting group values	Phase I	Total	
Number of subjects	327	327	
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)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	325	325	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	39.5		
standard deviation	± 11.5	-	
Gender categorical Units: Subjects			
Female	154	154	
Male	173	173	

End points

End points reporting groups

Reporting group title	Phase I amisulpride or olanzapine

Reporting group description:

Amisulpride 200-800 mg/day or olanzapine 5-20mg/day.
In phase I participants were randomised to either amisulpride (164 participants) or olanzapine (163 participants). The reason was that we wanted to rule out by the study design that any differences between switching and staying in phase II were related to the drug the participants were originally designed to in phase I. However, differences between amisulpride and olanzapine in phase I were not analysed.

Reporting group title	Switch

Reporting group description:

Non-improvers in phase I switch to the drug they were not assigned to in phase I

Reporting group title	Stay

Reporting group description:

Non-improvers in phase I stay on the drug they were assigned to in phase I

Reporting group title	Early improvers

Reporting group description:

Early improvers in phase I continued to receive the same drug in phase II. Differences between early improvers and stayers/switchers were not analysed.

Primary: Symptomatic remission

End point title	Symptomatic remission

End point description:

Remission according to Andreasen et al. 2005
Reference:
Andreasen NC, Carpenter WT Jr, Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in schizophrenia: proposed criteria and rationale for consensus. Am J Psychiatry. 2005 Mar;162(3):441-9

End point type	Primary

End point timeframe:

End of phase II

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[1]	55[2]		
Units: Participants	41	25		

Notes:

[1] - The numbers presented are the phase 2 completers

[2] - The numbers presented are the phase II completers

Statistical analyses

Statistical analysis title	Logistic regression symptomatic remission

Statistical analysis description:

Logistic regression model with "remission" as the dependent variable and "switch" of treatment (yes/no) and PANSS-total score at visit 3 as independent variables was used. Multiple imputation (based upon 20 imputations).

Comparison groups	Switch v Stay

Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 [3]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.35
upper limit	6.72

Notes:

[3] - the result was 0.007

Secondary: PANSS Total Score change from Switch Randomization

End point title	PANSS Total Score change from Switch Randomization

End point description:

End point type	Secondary

End point timeframe:

Change from Switch Randomization to endpoint

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[4]	55[5]		
Units: PANSS units				
arithmetic mean (standard deviation)	-22.8 (± 19.9)	-17.3 (± 15.1)		

Notes:

[4] - Completers

[5] - Completers

Statistical analyses

Statistical analysis title	Mixed-model of repeated measurements
Comparison groups	Switch v Stay
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	-4.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.58
upper limit	0.51

Secondary: Positive PANSS, Change from Switch Randomization	
End point title	Positive PANSS, Change from Switch Randomization
End point description:	
End point type	Secondary
End point timeframe:	
Change from Switch Randomization to endpoint	

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[6]	55[7]		
Units: PANSS points				
arithmetic mean (standard deviation)	-6.25 (± 5.22)	-5.96 (± 5.89)		

Notes:

[6] - Completers

[7] - Completers

Statistical analyses

Statistical analysis title	MMRM
Comparison groups	Switch v Stay
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.32
upper limit	0.59

Secondary: Negative PANSS, Change from Switch Randomization	
End point title	Negative PANSS, Change from Switch Randomization
End point description:	
End point type	Secondary
End point timeframe:	
Change from Switch Randomization to endpoint	

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[8]	55[9]		
Units: PANSS points				
arithmetic mean (standard deviation)	-6 (± 7.15)	-3.64 (± 4.7)		

Notes:

[8] - Completers

[9] - Completers

Statistical analyses

No statistical analyses for this end point

Secondary: General PANSS, change from Switch Randomization

End point title	General PANSS, change from Switch Randomization

End point description:

End point type	Secondary

End point timeframe:

Change from Switch Randomization to endpoint

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[10]	55[11]		
Units: PANSS points				
arithmetic mean (standard deviation)	-10.5 (± 9.8)	-7.75 (± 6.81)		

Notes:

[10] - Completers

[11] - Completers

Statistical analyses

Statistical analysis title	Mixed-model of repeated measurement
Comparison groups	Switch v Stay
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.43

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.64
upper limit	0.77

Secondary: CGI Severity, Change from Switch Randomization

End point title	CGI Severity, Change from Switch Randomization

End point description:

End point type	Secondary

End point timeframe:

Change from Switch Randomization to endpoint

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[12]	55[13]		
Units: CGI points				
arithmetic mean (standard deviation)	-1.42 (± 0.944)	-1.11 (± 0.956)		

Notes:

[12] - Completers

[13] - Completers

Statistical analyses

Statistical analysis title	MMRM
Comparison groups	Stay v Switch
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	-0.05

Secondary: CGI Global Improvement, Change from Switch Randomization

End point title	CGI Global Improvement, Change from Switch Randomization

End point description:

End point type	Secondary

End point timeframe:
Change from Switch Randomization to endpoint

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	55[14]		
Units: CGI points				
arithmetic mean (standard deviation)	-1.03 (± 0.843)	-0.709 (± 1.01)		

Notes:
[14] - Completers

Statistical analyses

Statistical analysis title	Continuous outcomes switchers versus stayers
Comparison groups	Switch v Stay
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	-0.05

Secondary: Subjective Well-Being under Neuroleptics Scale (SWN), Change from Switch Randomization

End point title	Subjective Well-Being under Neuroleptics Scale (SWN), Change from Switch Randomization

End point description:

End point type	Secondary

End point timeframe:
Change from Switch Randomization to endpoint

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59[15]	55[16]		
Units: SWN points				
arithmetic mean (standard deviation)	8.37 (± 15.3)	5.85 (± 10.9)		

Notes:
[15] - Completers
[16] - Completers

Statistical analyses

Statistical analysis title	MMRM
Comparison groups	Switch v Stay
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.52
upper limit	4.93

Secondary: Psychosocial Performance Scale (PSP), Change from Switch Randomization

End point title	Psychosocial Performance Scale (PSP), Change from Switch Randomization

End point description:

End point type	Secondary

End point timeframe:
Change from Switch Randomization to endpoint

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[17]	54[18]		
Units: PSP points				
arithmetic mean (standard deviation)	11.8 (± 13.6)	10.4 (± 10.2)		

Notes:
[17] - Completers
[18] - Completers

Statistical analyses

Statistical analysis title	MMRM
Comparison groups	Switch v Stay

Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.98
upper limit	8.45

Secondary: Drug Attitude Inventory (DAI), Change from Switch Randomisation

End point title	Drug Attitude Inventory (DAI), Change from Switch Randomisation

End point description:

End point type	Secondary

End point timeframe:

Change from Switch Randomization to endpoint

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58[19]	54[20]		
Units: DAI points				
arithmetic mean (standard deviation)	1.21 (± 3.98)	1.04 (± 3.35)		

Notes:

[19] - Completers

[20] - Completers

Statistical analyses

Statistical analysis title	MMRM
Comparison groups	Switch v Stay
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.14
upper limit	1.27

Secondary: Riedel-Spellmann-Musil Scale Patient (RSMP), Change from Switch Randomisation

End point title	Riedel-Spellmann-Musil Scale Patient (RSMP), Change from Switch Randomisation

End point description:

End point type	Secondary

End point timeframe:

Change from Switch Randomization to endpoint

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59[21]	54[22]		
Units: RSMP points				
arithmetic mean (standard deviation)	-0.0847 (± 8.56)	2.11 (± 9.5)		

Notes:

[21] - Completers

[22] - Completers

Statistical analyses

Statistical analysis title	MMRM
Comparison groups	Switch v Stay
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.16
upper limit	2.04

Secondary: Riedel-Spellmann-Musil Scale Observer (RSMO), Riedel-Spellmann-Musil Scale Patient (RSMP), Change from Switch Randomisation

End point title	Riedel-Spellmann-Musil Scale Observer (RSMO), Riedel-Spellmann-Musil Scale Patient (RSMP), Change from Switch Randomisation

End point description:

End point type	Secondary

End point timeframe:

Change from Switch Randomization to endpoint

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58[23]	55[24]		
Units: RSMO points				
arithmetic mean (standard deviation)	0.931 (± 4.82)	0.509 (± 5.6)		

Notes:

[23] - Completers

[24] - Completers

Statistical analyses

Statistical analysis title	MMRM
Comparison groups	Switch v Stay
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	3.08

Secondary: Barnes Akathisia Scale, change from switch randomisation

End point title	Barnes Akathisia Scale, change from switch randomisation

End point description:

End point type	Secondary

End point timeframe:

Change from Switch Randomization to endpoint

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[25]	55[26]		
Units: Barnes Akathisia Scale points				
arithmetic mean (standard deviation)	-0.25 (± 1.79)	-0.49 (± 1.91)		

Notes:

[25] - Completers

[26] - Completers

Statistical analyses

Statistical analysis title	Mixed-model of repeated measurements
Comparison groups	Switch v Stay
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39
upper limit	0.69

Secondary: Simpson Angus Scale, change from Switch Randomization

End point title	Simpson Angus Scale, change from Switch Randomization

End point description:

End point type	Secondary

End point timeframe:

Change from Switch Randomization to endpoint

End point values	Switch	Stay		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60[27]	54[28]		
Units: Simpson Angus Scale points				
arithmetic mean (standard deviation)	-0.13 (± 2.53)	0.11 (± 3.35)		

Notes:

[27] - Completers

[28] - Completers

Statistical analyses

Statistical analysis title	Mixed-model of repeated measurement
Comparison groups	Switch v Stay
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	1

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For the groups "switchers phase II", "stayers phase II", "early improvers phase II": from randomization for phase II to endpoint
For the group "Adverse events in phase I amisulpride and olanzapine combined": from randomization for phase I to end phase I

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Switchers phase II

Reporting group description:

Randomised to switch in phase II and received at least one dose of study drug

Reporting group title	Stayers phase II

Reporting group description:

Randomised to staying on the same drug in phase II and received at least one dose of study drug

Reporting group title	Early improvers phase II

Reporting group description:

Improved in phase I, remained on the same study drug, and received at least one dose of study drug

Reporting group title	Phase I amisulpride and olanzapine combined

Reporting group description:

As the comparison of amisulpride and olanzapine is not the aim of the study, we present the adverse events that occured in phase I for both groups combined

Serious adverse events	Switchers phase II	Stayers phase II	Early improvers phase II
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 70 (4.29%)	4 / 72 (5.56%)	9 / 140 (6.43%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Lithium intoxication			
subjects affected / exposed	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Pulmonary thrombosis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Worsening of psychosis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 72 (0.00%)	5 / 140 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Affective worsening			
subjects affected / exposed	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 70 (1.43%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	1 / 70 (1.43%)	1 / 72 (1.39%)	0 / 140 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic relapse			
subjects affected / exposed	0 / 70 (0.00%)	3 / 72 (4.17%)	1 / 140 (0.71%)
occurrences causally related to treatment / all	0 / 0	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase I amisulpride and olanzapine combined		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 327 (1.53%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 327 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Lithium intoxication			
subjects affected / exposed	1 / 327 (0.31%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary thrombosis			
subjects affected / exposed	0 / 327 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Worsening of psychosis			
subjects affected / exposed	2 / 327 (0.61%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Affective worsening			
subjects affected / exposed	0 / 327 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	0 / 327 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Agitation			
subjects affected / exposed	0 / 327 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychotic relapse			
subjects affected / exposed	1 / 327 (0.31%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Switchers phase II	Stayers phase II	Early improvers phase II
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 70 (44.29%)	28 / 72 (38.89%)	63 / 140 (45.00%)
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed[1]	0 / 70 (0.00%)	1 / 72 (1.39%)	0 / 140 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed[2]	1 / 70 (1.43%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed[3]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			
subjects affected / exposed[4]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed[5]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed[6]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Galactorrhoea			
subjects affected / exposed[7]	1 / 70 (1.43%)	0 / 72 (0.00%)	2 / 140 (1.43%)
occurrences (all)	1	0	2
Menstruation delayed			
subjects affected / exposed[8]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1

Sexual dysfunction			
subjects affected / exposed[9]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Dysmenorrhoea			
subjects affected / exposed[10]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Gynaecomastia			
subjects affected / exposed[11]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Pharyngeal dyskinesia			
subjects affected / exposed[12]	1 / 70 (1.43%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed[13]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed[14]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed[15]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed[16]	2 / 70 (2.86%)	0 / 72 (0.00%)	4 / 140 (2.86%)
occurrences (all)	2	0	4
Anxiety			
subjects affected / exposed[17]	3 / 70 (4.29%)	1 / 72 (1.39%)	2 / 140 (1.43%)
occurrences (all)	3	1	2
Insomnia			
subjects affected / exposed[18]	9 / 70 (12.86%)	2 / 72 (2.78%)	7 / 140 (5.00%)
occurrences (all)	9	2	7
Irritability			
subjects affected / exposed[19]	1 / 70 (1.43%)	1 / 72 (1.39%)	0 / 140 (0.00%)
occurrences (all)	1	1	0
Psychotic disorder			

subjects affected / exposed[20]	0 / 70 (0.00%)	2 / 72 (2.78%)	5 / 140 (3.57%)
occurrences (all)	0	2	5
Restlessness			
subjects affected / exposed[21]	1 / 70 (1.43%)	3 / 72 (4.17%)	3 / 140 (2.14%)
occurrences (all)	1	3	3
Tension			
subjects affected / exposed[22]	1 / 70 (1.43%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed[23]	0 / 70 (0.00%)	0 / 72 (0.00%)	5 / 140 (3.57%)
occurrences (all)	0	0	5
Nervousness			
subjects affected / exposed[24]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed[25]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Apathy			
subjects affected / exposed[26]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Catatonia			
subjects affected / exposed[27]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed[28]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Disorientation			
subjects affected / exposed[29]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Drug use disorder			
subjects affected / exposed[30]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Libido increased			
subjects affected / exposed[31]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Panic attack			

subjects affected / exposed[32]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Investigations			
Electrocardiogram repolarisation abnormality	Additional description: QT prolonged		
subjects affected / exposed[33]	0 / 70 (0.00%)	1 / 72 (1.39%)	0 / 140 (0.00%)
occurrences (all)	0	1	0
Hepatic enzyme increased			
subjects affected / exposed[34]	1 / 70 (1.43%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	1	0	1
Transaminases increased			
subjects affected / exposed[35]	1 / 70 (1.43%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed[36]	0 / 70 (0.00%)	1 / 72 (1.39%)	0 / 140 (0.00%)
occurrences (all)	0	1	0
Weight increased			
subjects affected / exposed[37]	1 / 70 (1.43%)	1 / 72 (1.39%)	4 / 140 (2.86%)
occurrences (all)	1	1	4
C-reactive protein increased			
subjects affected / exposed[38]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed[39]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Toxicity to various agents			
subjects affected / exposed[40]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Hypotension			
subjects affected / exposed[41]	0 / 70 (0.00%)	1 / 72 (1.39%)	0 / 140 (0.00%)
occurrences (all)	0	1	0
Myocardial infarction			
subjects affected / exposed[42]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Myocardial ischaemia			

subjects affected / exposed[43]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed[44]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed[45]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dysaesthesia			
subjects affected / exposed[46]	0 / 70 (0.00%)	1 / 72 (1.39%)	0 / 140 (0.00%)
occurrences (all)	0	1	0
Extrapyramidal disorder			
subjects affected / exposed[47]	2 / 70 (2.86%)	2 / 72 (2.78%)	0 / 140 (0.00%)
occurrences (all)	2	2	0
Headache			
subjects affected / exposed[48]	4 / 70 (5.71%)	1 / 72 (1.39%)	6 / 140 (4.29%)
occurrences (all)	4	1	6
Oromandibular dystonia			
subjects affected / exposed[49]	0 / 70 (0.00%)	1 / 72 (1.39%)	0 / 140 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed[50]	1 / 70 (1.43%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	1	0	0
Parkinson gait			
subjects affected / exposed[51]	1 / 70 (1.43%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	1	0	0
Psychomotor hyperactivity			
subjects affected / exposed[52]	1 / 70 (1.43%)	0 / 72 (0.00%)	2 / 140 (1.43%)
occurrences (all)	1	0	2
Sedation			
subjects affected / exposed[53]	3 / 70 (4.29%)	2 / 72 (2.78%)	6 / 140 (4.29%)
occurrences (all)	3	2	6
Somnolence			
subjects affected / exposed[54]	0 / 70 (0.00%)	1 / 72 (1.39%)	1 / 140 (0.71%)
occurrences (all)	0	1	1

Tremor			
subjects affected / exposed[55]	4 / 70 (5.71%)	2 / 72 (2.78%)	8 / 140 (5.71%)
occurrences (all)	4	2	8
Akathisia			
subjects affected / exposed[56]	0 / 70 (0.00%)	0 / 72 (0.00%)	7 / 140 (5.00%)
occurrences (all)	0	0	7
Dizziness			
subjects affected / exposed[57]	0 / 70 (0.00%)	0 / 72 (0.00%)	2 / 140 (1.43%)
occurrences (all)	0	0	2
Dystonia			
subjects affected / exposed[58]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Hypokinesia			
subjects affected / exposed[59]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Dyskinesia			
subjects affected / exposed[60]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed[61]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed[62]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed[63]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed[64]	1 / 70 (1.43%)	2 / 72 (2.78%)	2 / 140 (1.43%)
occurrences (all)	1	2	2
accomodation disorder			
subjects affected / exposed[65]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Dry eye			

subjects affected / exposed[66]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed[67]	2 / 70 (2.86%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	2	0	0
Dry mouth			
subjects affected / exposed[68]	1 / 70 (1.43%)	2 / 72 (2.78%)	4 / 140 (2.86%)
occurrences (all)	1	2	4
Nausea			
subjects affected / exposed[69]	0 / 70 (0.00%)	1 / 72 (1.39%)	0 / 140 (0.00%)
occurrences (all)	0	1	0
Salivary hypersecretion			
subjects affected / exposed[70]	1 / 70 (1.43%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed[71]	1 / 70 (1.43%)	1 / 72 (1.39%)	2 / 140 (1.43%)
occurrences (all)	1	1	2
Abdominal discomfort			
subjects affected / exposed[72]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed[73]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed[74]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed[75]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed[76]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed[77]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed[78]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed[79]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed[80]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Dermal cyst			
subjects affected / exposed[81]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed[82]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed[83]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperprolactinaemia			
subjects affected / exposed[84]	0 / 70 (0.00%)	1 / 72 (1.39%)	0 / 140 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed[85]	0 / 70 (0.00%)	1 / 72 (1.39%)	0 / 140 (0.00%)
occurrences (all)	0	1	0
Muscle rigidity			
subjects affected / exposed[86]	2 / 70 (2.86%)	2 / 72 (2.78%)	4 / 140 (2.86%)
occurrences (all)	2	2	4
Arthralgia			
subjects affected / exposed[87]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed[88]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0

Limb discomfort			
subjects affected / exposed[89]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Torticollis			
subjects affected / exposed[90]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Tooth infection			
subjects affected / exposed[91]	0 / 70 (0.00%)	1 / 72 (1.39%)	0 / 140 (0.00%)
occurrences (all)	0	1	0
Febrile infection			
subjects affected / exposed[92]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Furuncle			
subjects affected / exposed[93]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Vaginal infection			
subjects affected / exposed[94]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed[95]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed[96]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed[97]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed[98]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Viral rhinitis			
subjects affected / exposed[99]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			

Increased appetite			
subjects affected / exposed[100]	0 / 70 (0.00%)	0 / 72 (0.00%)	1 / 140 (0.71%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed[101]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed[102]	0 / 70 (0.00%)	0 / 72 (0.00%)	0 / 140 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase I amisulpride and olanzapine combined		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 327 (30.58%)		
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed[1]	0 / 325 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed[2]	0 / 325 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed[3]	1 / 325 (0.31%)		
occurrences (all)	1		
General physical health deterioration			
subjects affected / exposed[4]	1 / 325 (0.31%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed[5]	1 / 325 (0.31%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed[6]	2 / 325 (0.62%)		
occurrences (all)	2		
Reproductive system and breast disorders			

Galactorrhoea subjects affected / exposed[7] occurrences (all)	0 / 325 (0.00%) 0		
Menstruation delayed subjects affected / exposed[8] occurrences (all)	0 / 325 (0.00%) 0		
Sexual dysfunction subjects affected / exposed[9] occurrences (all)	0 / 325 (0.00%) 0		
Dysmenorrhoea subjects affected / exposed[10] occurrences (all)	1 / 325 (0.31%) 1		
Gynaecomastia subjects affected / exposed[11] occurrences (all)	1 / 325 (0.31%) 1		
Respiratory, thoracic and mediastinal disorders			
Pharyngeal dyskinesia subjects affected / exposed[12] occurrences (all)	0 / 325 (0.00%) 0		
Nasal congestion subjects affected / exposed[13] occurrences (all)	1 / 325 (0.31%) 1		
Rhinorrhoea subjects affected / exposed[14] occurrences (all)	0 / 325 (0.00%) 0		
Oropharyngeal pain subjects affected / exposed[15] occurrences (all)	1 / 325 (0.31%) 1		
Psychiatric disorders			
Agitation subjects affected / exposed[16] occurrences (all)	8 / 325 (2.46%) 8		
Anxiety subjects affected / exposed[17] occurrences (all)	5 / 325 (1.54%) 5		
Insomnia			

subjects affected / exposed[18]	14 / 325 (4.31%)			
occurrences (all)	14			
Irritability				
subjects affected / exposed[19]	0 / 325 (0.00%)			
occurrences (all)	0			
Psychotic disorder				
subjects affected / exposed[20]	6 / 325 (1.85%)			
occurrences (all)	6			
Restlessness				
subjects affected / exposed[21]	4 / 325 (1.23%)			
occurrences (all)	4			
Tension				
subjects affected / exposed[22]	3 / 325 (0.92%)			
occurrences (all)	3			
Depression				
subjects affected / exposed[23]	1 / 325 (0.31%)			
occurrences (all)	2			
Nervousness				
subjects affected / exposed[24]	0 / 325 (0.00%)			
occurrences (all)	0			
Sleep disorder				
subjects affected / exposed[25]	5 / 325 (1.54%)			
occurrences (all)	5			
Apathy				
subjects affected / exposed[26]	1 / 325 (0.31%)			
occurrences (all)	1			
Catatonia				
subjects affected / exposed[27]	1 / 325 (0.31%)			
occurrences (all)	1			
Confusional state				
subjects affected / exposed[28]	1 / 325 (0.31%)			
occurrences (all)	1			
Disorientation				
subjects affected / exposed[29]	1 / 325 (0.31%)			
occurrences (all)	1			
Drug use disorder				

subjects affected / exposed[30]	1 / 325 (0.31%)		
occurrences (all)	1		
Libido increased			
subjects affected / exposed[31]	1 / 325 (0.31%)		
occurrences (all)	1		
Panic attack			
subjects affected / exposed[32]	1 / 325 (0.31%)		
occurrences (all)	1		
Investigations			
Electrocardiogram repolarisation abnormality	Additional description: QT prolonged		
subjects affected / exposed[33]	0 / 325 (0.00%)		
occurrences (all)	0		
Hepatic enzyme increased			
subjects affected / exposed[34]	0 / 325 (0.00%)		
occurrences (all)	0		
Transaminases increased			
subjects affected / exposed[35]	2 / 325 (0.62%)		
occurrences (all)	2		
Weight decreased			
subjects affected / exposed[36]	3 / 325 (0.92%)		
occurrences (all)	3		
Weight increased			
subjects affected / exposed[37]	19 / 325 (5.85%)		
occurrences (all)	19		
C-reactive protein increased			
subjects affected / exposed[38]	0 / 325 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed[39]	0 / 325 (0.00%)		
occurrences (all)	0		
Toxicity to various agents			
subjects affected / exposed[40]	1 / 325 (0.31%)		
occurrences (all)	1		
Cardiac disorders			

Hypotension				
subjects affected / exposed[41]	3 / 325 (0.92%)			
occurrences (all)	3			
Myocardial infarction				
subjects affected / exposed[42]	1 / 325 (0.31%)			
occurrences (all)	1			
Myocardial ischaemia				
subjects affected / exposed[43]	1 / 325 (0.31%)			
occurrences (all)	1			
Pericardial effusion				
subjects affected / exposed[44]	1 / 325 (0.31%)			
occurrences (all)	1			
Tachycardia				
subjects affected / exposed[45]	2 / 325 (0.62%)			
occurrences (all)	2			
Nervous system disorders				
Dysaesthesia				
subjects affected / exposed[46]	0 / 325 (0.00%)			
occurrences (all)	0			
Extrapyramidal disorder				
subjects affected / exposed[47]	8 / 325 (2.46%)			
occurrences (all)	8			
Headache				
subjects affected / exposed[48]	7 / 325 (2.15%)			
occurrences (all)	7			
Oromandibular dystonia				
subjects affected / exposed[49]	2 / 325 (0.62%)			
occurrences (all)	2			
Paraesthesia				
subjects affected / exposed[50]	0 / 325 (0.00%)			
occurrences (all)	0			
Parkinson gait				
subjects affected / exposed[51]	0 / 325 (0.00%)			
occurrences (all)	0			
Psychomotor hyperactivity				

subjects affected / exposed[52] occurrences (all)	1 / 325 (0.31%) 1		
Sedation subjects affected / exposed[53] occurrences (all)	15 / 325 (4.62%) 15		
Somnolence subjects affected / exposed[54] occurrences (all)	3 / 325 (0.92%) 3		
Tremor subjects affected / exposed[55] occurrences (all)	17 / 325 (5.23%) 17		
Akathisia subjects affected / exposed[56] occurrences (all)	13 / 325 (4.00%) 13		
Dizziness subjects affected / exposed[57] occurrences (all)	2 / 325 (0.62%) 2		
Dystonia subjects affected / exposed[58] occurrences (all)	2 / 325 (0.62%) 2		
Hypokinesia subjects affected / exposed[59] occurrences (all)	3 / 325 (0.92%) 3		
Dyskinesia subjects affected / exposed[60] occurrences (all)	2 / 325 (0.62%) 2		
Syncope subjects affected / exposed[61] occurrences (all)	1 / 325 (0.31%) 1		
Blood and lymphatic system disorders Leukocytosis subjects affected / exposed[62] occurrences (all)	1 / 325 (0.31%) 1		
Ear and labyrinth disorders Ear pain			

subjects affected / exposed[63]	1 / 325 (0.31%)		
occurrences (all)	1		
Eye disorders			
Vision blurred			
subjects affected / exposed[64]	1 / 325 (0.31%)		
occurrences (all)	1		
accomodation disorder			
subjects affected / exposed[65]	2 / 325 (0.62%)		
occurrences (all)	2		
Dry eye			
subjects affected / exposed[66]	1 / 325 (0.31%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed[67]	6 / 325 (1.85%)		
occurrences (all)	6		
Dry mouth			
subjects affected / exposed[68]	5 / 325 (1.54%)		
occurrences (all)	5		
Nausea			
subjects affected / exposed[69]	4 / 325 (1.23%)		
occurrences (all)	4		
Salivary hypersecretion			
subjects affected / exposed[70]	3 / 325 (0.92%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed[71]	1 / 325 (0.31%)		
occurrences (all)	1		
Abdominal discomfort			
subjects affected / exposed[72]	1 / 325 (0.31%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed[73]	2 / 325 (0.62%)		
occurrences (all)	2		
Dyspepsia			

subjects affected / exposed[74] occurrences (all)	1 / 325 (0.31%) 1		
Dysphagia subjects affected / exposed[75] occurrences (all)	2 / 325 (0.62%) 2		
Gastritis subjects affected / exposed[76] occurrences (all)	1 / 325 (0.31%) 1		
Toothache subjects affected / exposed[77] occurrences (all)	3 / 325 (0.92%) 3		
Skin and subcutaneous tissue disorders			
Acne subjects affected / exposed[78] occurrences (all)	0 / 325 (0.00%) 0		
Alopecia subjects affected / exposed[79] occurrences (all)	0 / 325 (0.00%) 0		
Rash subjects affected / exposed[80] occurrences (all)	0 / 325 (0.00%) 0		
Dermal cyst subjects affected / exposed[81] occurrences (all)	1 / 325 (0.31%) 1		
Eczema subjects affected / exposed[82] occurrences (all)	2 / 325 (0.62%) 2		
Hyperhidrosis subjects affected / exposed[83] occurrences (all)	2 / 325 (0.62%) 2		
Endocrine disorders			
Hyperprolactinaemia subjects affected / exposed[84] occurrences (all)	0 / 325 (0.00%) 0		
Musculoskeletal and connective tissue disorders			

Back pain				
subjects affected / exposed[85]	1 / 325 (0.31%)			
occurrences (all)	1			
Muscle rigidity				
subjects affected / exposed[86]	10 / 325 (3.08%)			
occurrences (all)	10			
Arthralgia				
subjects affected / exposed[87]	1 / 325 (0.31%)			
occurrences (all)	1			
Bursitis				
subjects affected / exposed[88]	1 / 325 (0.31%)			
occurrences (all)	1			
Limb discomfort				
subjects affected / exposed[89]	1 / 325 (0.31%)			
occurrences (all)	1			
Torticollis				
subjects affected / exposed[90]	1 / 325 (0.31%)			
occurrences (all)	1			
Infections and infestations				
Tooth infection				
subjects affected / exposed[91]	1 / 325 (0.31%)			
occurrences (all)	1			
Febrile infection				
subjects affected / exposed[92]	0 / 325 (0.00%)			
occurrences (all)	0			
Furuncle				
subjects affected / exposed[93]	0 / 325 (0.00%)			
occurrences (all)	0			
Vaginal infection				
subjects affected / exposed[94]	3 / 325 (0.92%)			
occurrences (all)	3			
Nasopharyngitis				
subjects affected / exposed[95]	4 / 325 (1.23%)			
occurrences (all)	4			
Pharyngitis				

subjects affected / exposed[96]	1 / 325 (0.31%)		
occurrences (all)	1		
Respiratory tract infection viral			
subjects affected / exposed[97]	1 / 325 (0.31%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed[98]	2 / 325 (0.62%)		
occurrences (all)	2		
Viral rhinitis			
subjects affected / exposed[99]	1 / 325 (0.31%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Increased appetite			
subjects affected / exposed[100]	1 / 325 (0.31%)		
occurrences (all)	1		
Decreased appetite			
subjects affected / exposed[101]	1 / 325 (0.31%)		
occurrences (all)	0		
Hypercholesterolaemia			
subjects affected / exposed[102]	1 / 325 (0.31%)		
occurrences (all)	1		

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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 March 2010	supply of olanzapine medication by EliLilly, specification of inclusion criteria, qualification and training of study personal concerning examination with the Positive and Negative Syndrome Scale, specification of date for blood measurement, specification of randomisation and treatment allocation, specification in terms of prolactin levels, deletion of AIMS scale, amendment and specification of rescue medication
07 October 2010	dosing of olanzapine and amisulpride in the first 3 days, amendment of the exclusion criterion patients under guardianship, specification of the relevance of the pregnancy test at screening, specification about laboratory values as adverse events, specification of drug accountability, specification about destruction of study medication, prolongation of follow-up period, specification about inclusion criterion increase in level of care, specification of pre-study treatment, correction of writing error in protocol
14 September 2011	inclusion of patients with legal guardianship, specification of exclusion criterion sufficient dose of study drugs before the study, definition of a time window for visits, end of electronic documentation of study data with electronic CRF, formal changes
09 November 2012	expansion of the study to Romania, specification of pseudonymisation of Romanian participants, registration of the study in Romania, participant insurance for Romania, procedure in the case of protocol changes, change of the run time of the study, number of centers in Germany, amendment of measurement of body size in the protocol, exclusion of participants with legal guardianship in Romania

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.

The data of one site which violated good clinical practice in other trials were excluded.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26227799