Clinical trial results:
Interventional, Randomised, Double-blind, Parallel-group, Placebo-controlled, Active-reference, Flexible-dose Study of Brexpiprazole in Patients With Acute Schizophrenia

Summary

EudraCT number	2012-002252-17
Trial protocol	CZ DE EE SK PL RO
Global end of trial date	17 December 2014

Results information

Result version number	v1 (current)
This version publication date	14 July 2016
First version publication date	14 July 2016

Trial information

Trial identification

Sponsor protocol code	14644A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01810380
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark, 2500
Public contact	Email contact via, H. Lundbeck A/S, LundbeckClinicalTrials@Lundbeck.com
Scientific contact	Email contact via, H. Lundbeck A/S, LundbeckClinicalTrials@Lundbeck.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 December 2014
Global end of trial reached?	Yes
Global end of trial date	17 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy and safety of brexpiprazole for the treatment of adults experiencing an acute episode of schizophrenia

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2008) and ICH Good Clinical Practice (1996)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 March 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Estonia: 11
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Poland: 15
Country: Number of subjects enrolled	Romania: 38
Country: Number of subjects enrolled	Russian Federation: 116
Country: Number of subjects enrolled	Serbia: 35
Country: Number of subjects enrolled	Slovakia: 3
Country: Number of subjects enrolled	Ukraine: 88
Country: Number of subjects enrolled	United States: 160
Worldwide total number of subjects	468
EEA total number of subjects	69

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	466
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects who met each of the inclusion and none of the exclusion criteria were eligible to participate in the study

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

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

Dosage and administration details:

Once daily as tablets and capsules, orally

Arm title	Brexpiprazole

Arm description: -

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

Dosage and administration details:

Brexpiprazole: 2-4 mg/day, once daily, tablets, orally

Arm title	Quetiapine extended release

Arm description: -

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

Dosage and administration details:

Quetiapine extended release: 400-800 mg/day, once daily, encapsulated tablets, orally

Number of subjects in period 1	Placebo	Brexpiprazole	Quetiapine extended release
Started	163	151	154
Treated	161	150	153
Completed	108	113	122
Not completed	55	38	32
Consent withdrawn by subject	6	-	6
Randomised not treated	2	1	1
Administrative or other reasons	11	13	9
Adverse event, non-fatal	11	14	4
Lack of efficacy	24	10	11
Protocol deviation	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Brexpiprazole
Reporting group description: -	
Reporting group title	Quetiapine extended release
Reporting group description: -	

Reporting group values	Placebo	Brexpiprazole	Quetiapine extended release
Number of subjects	163	151	154
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	163	150	153
From 65-84 years	0	1	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	40.59	39.81	41.07
standard deviation	± 10.75	± 10.96	± 10.89
Gender, Male/Female Units: participants			
Female	70	67	64
Male	93	84	90
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	2	1	0
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	37	33	38
White	123	114	114
More than one race	0	0	0
Unknown or Not Reported	0	2	1

Reporting group values	Total		
Number of subjects	468		
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)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	466		
From 65-84 years	2		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female			
Units: participants			
Female	201		
Male	267		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1		
Asian	3		
Native Hawaiian or Other Pacific Islander	2		
Black or African American	108		
White	351		
More than one race	0		
Unknown or Not Reported	3		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Brexpiprazole
Reporting group description: -	
Reporting group title	Quetiapine extended release
Reporting group description: -	

Primary: Change from baseline to Week 6 in PANSS total score

End point title	Change from baseline to Week 6 in PANSS total score

End point description:

The Positive and Negative Syndrome Scale (PANSS) is a 30-item scale for assessing the symptoms of schizophrenia. For each PANSS item, symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. The PANSS total score (30 items) ranged from 30 to 210 with a higher score indicating greater severity of symptoms.

Population Description: Full Analysis Set (FAS)

End point type	Primary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: units on a scale				
arithmetic mean (standard error)	-15.9 (± 1.5)	-20 (± 1.5)	-24 (± 1.5)	

Statistical analyses

Statistical analysis title	Placebo vs. Brexpiprazole

Statistical analysis description:

The overall significance level was 0.05. The primary and the key secondary endpoints were tested hierarchically. Only if the primary endpoint was statistically significant would confirmatory testing continue with the key secondary endpoint.

Comparison groups	Placebo v Brexpiprazole

Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.056 [1]
Method	Mixed models analysis
Parameter estimate	Least square mean difference
Point estimate	-4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.2
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	2.1

Notes:

[1] - For all efficacy analyses the primary comparison is the difference between brexpiprazole 2 to 4 mg/day and placebo at Week 6.

Statistical analysis title	Placebo vs. Quetiapine Extended Release
Comparison groups	Placebo v Quetiapine extended release
Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0002
Method	Mixed models analysis
Parameter estimate	Least square mean difference
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.2
upper limit	-3.9
Variability estimate	Standard error of the mean
Dispersion value	2.1

Secondary: Change from baseline to Week 6 in CGI-S score

End point title	Change from baseline to Week 6 in CGI-S score

End point description:

The Clinical Global Impression – Severity of Illness (CGI-S) provides the clinician’s impression of the patient’s current state of mental illness. The clinician uses his or her clinical experience of this patient population to rate the severity of the patient's current mental illness on a 7-point scale ranging from 1 (normal - not at all ill) to 7 (among the most extremely ill patients).

Population Description: FAS

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: units on a scale				
arithmetic mean (standard error)	-0.9 (± 0.1)	-1.2 (± 0.1)	-1.4 (± 0.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: CGI-I score at Week 6

End point title	CGI-I score at Week 6

End point description:

The Clinical Global Impression – Global Improvement (CGI-I) provides the clinician's impression of the patient's improvement (or worsening). The clinician assesses the patient's condition relative to a baseline on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse). In all cases, the assessment should be made independent of whether the rater believes the improvement is drug-related or not.

Population Description: FAS

End point type	Secondary

End point timeframe:

Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: units on a scale				
arithmetic mean (standard error)	3 (± 0.1)	2.7 (± 0.1)	2.5 (± 0.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 6 in PANSS Positive Subscale score

End point title	Change from baseline to Week 6 in PANSS Positive Subscale score

End point description:

The Positive and Negative Syndrome Scale (PANSS) is a clinician rated scale designed to measure severity of psychopathology in adult patients with schizophrenia, schizoaffective disorders and other psychotic disorders. It emphasizes positive and negative symptoms. The PANSS Positive Subscale score is calculated from 7 items (for example: delusions, conceptual disorganization and hallucinatory behaviour). Symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. Higher score indicating greater severity of symptoms

Population Description: FAS

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: units on a scale				
arithmetic mean (standard error)	-5.4 (± 0.5)	-7 (± 0.5)	-8.1 (± 0.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 6 in PANSS Negative Subscale score

End point title	Change from baseline to Week 6 in PANSS Negative Subscale score

End point description:

The Positive and Negative Syndrome Scale (PANSS) is a clinician rated scale designed to measure severity of psychopathology in adult patients with schizophrenia, schizoaffective disorders and other psychotic disorders. It emphasizes positive and negative symptoms. The PANSS Negative Subscale score is calculated from 7 items (for example: blunted affect, emotional withdrawal and poor rapport). Symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. Higher score indicating greater severity of symptoms

Population Description: FAS

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: units on a scale				
arithmetic mean (standard error)	-3.1 (± 0.4)	-3.7 (± 0.4)	-4.5 (± 0.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 6 in PANSS General Psychopathology Subscale score

End point title	Change from baseline to Week 6 in PANSS General Psychopathology Subscale score

End point description:

The Positive and Negative Syndrome Scale (PANSS) is a clinician rated scale designed to measure severity of psychopathology in adult patients with schizophrenia, schizoaffective disorders and other psychotic disorders. It emphasizes positive and negative symptoms. The PANSS General Psychopathology Subscale score is calculated from 16 items (for example: somatic concern, anxiety and guilt feelings). Symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. Higher score indicating greater severity of symptoms

Population Description: FAS

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: units on a scale				
arithmetic mean (standard error)	-8.2 (± 0.7)	-9.9 (± 0.7)	-11.6 (± 0.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 6 in PANSS Excited Component score

End point title	Change from baseline to Week 6 in PANSS Excited Component score

End point description:

The Positive and Negative Syndrome Scale (PANSS) is a clinician rated scale designed to measure severity of psychopathology in adult patients with schizophrenia, schizoaffective disorders and other psychotic disorders. It emphasizes positive and negative symptoms. The PANSS Excited Component score is calculated from 5 items (for example: poor impulse control, tension and hostility). Symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. Higher score indicating greater severity of symptoms

Population Description: FAS

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: units on a scale				
arithmetic mean (standard error)	-2.5 (± 0.3)	-3.3 (± 0.3)	-3.9 (± 0.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 6 in PANSS Marder Factor scores: negative symptoms

End point title	Change from baseline to Week 6 in PANSS Marder Factor scores: negative symptoms

End point description:

The Positive and Negative Syndrome Scale (PANSS) is a clinician rated scale designed to measure severity of psychopathology in adult patients with schizophrenia, schizoaffective disorders and other psychotic disorders. It emphasizes positive and negative symptoms. The PANSS Marder Factor scores: negative symptoms is calculated from 7 items (for example: blunted affect, emotional withdrawal and motor retardation). Symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. Higher score indicating greater severity of symptoms

Population Description: FAS

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: units on a scale				
arithmetic mean (standard error)	-3.6 (± 0.4)	-4.3 (± 0.4)	-4.8 (± 0.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 6 in PANSS Marder Factor scores: positive symptoms

End point title	Change from baseline to Week 6 in PANSS Marder Factor scores: positive symptoms

End point description:

The Positive and Negative Syndrome Scale (PANSS) is a clinician rated scale designed to measure severity of psychopathology in adult patients with schizophrenia, schizoaffective disorders and other

psychotic disorders. It emphasizes positive and negative symptoms. The PANSS Marder Factor scores: positive symptoms is calculated from 8 items (for example: delusions, conceptual disorganization and stereotype thinking). Symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. Higher score indicating greater severity of symptoms

Population Description: FAS

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: units on a scale				
arithmetic mean (standard error)	-5.7 (± 0.5)	-7.1 (± 0.5)	-8.4 (± 0.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 6 in PANSS Marder Factor scores: disorganized thoughts

End point title	Change from baseline to Week 6 in PANSS Marder Factor scores: disorganized thoughts

End point description:

The Positive and Negative Syndrome Scale (PANSS) is a clinician rated scale designed to measure severity of psychopathology in adult patients with schizophrenia, schizoaffective disorders and other psychotic disorders. It emphasizes positive and negative symptoms. The PANSS Marder Factor scores: disorganized thoughts is calculated from 7 items (for example: conceptual disorganization, difficulty in abstract thinking and mannerisms and posturing). Symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. Higher score indicating greater severity of symptoms

Population Description: FAS

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: units on a scale				
arithmetic mean (standard error)	-3.2 (± 0.4)	-4 (± 0.4)	-4.8 (± 0.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 6 in PANSS Marder Factor scores: uncontrolled hostility/excitement

End point title	Change from baseline to Week 6 in PANSS Marder Factor scores: uncontrolled hostility/excitement

End point description:

The Positive and Negative Syndrome Scale (PANSS) is a clinician rated scale designed to measure severity of psychopathology in adult patients with schizophrenia, schizoaffective disorders and other psychotic disorders. It emphasizes positive and negative symptoms. The PANSS Marder Factor scores: uncontrolled hostility/excitement is calculated from 4 items (for example: excitement, hostility, and uncooperativeness).Symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. Higher score indicating greater severity of symptoms

Population Description: FAS

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: units on a scale				
arithmetic mean (standard error)	-1.8 (± 0.3)	-2.5 (± 0.3)	-2.8 (± 0.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 6 in PANSS Marder Factor scores: anxiety/depression

End point title	Change from baseline to Week 6 in PANSS Marder Factor scores: anxiety/depression

End point description:

The Positive and Negative Syndrome Scale (PANSS) is a clinician rated scale designed to measure severity of psychopathology in adult patients with schizophrenia, schizoaffective disorders and other psychotic disorders. It emphasizes positive and negative symptoms. The PANSS Marder Factor scores: anxiety/depression is calculated from 4 items (for example: anxiety, guilt feelings, and tension). Symptom severity was rated on a 7-point scale, from 1=absent to 7=extreme. Higher score indicating greater severity of symptoms

Population Description: FAS

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: units on a scale				
arithmetic mean (standard error)	-2.9 (± 0.2)	-3.2 (± 0.2)	-3.6 (± 0.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Discontinuation due to lack of efficacy during the study

End point title	Discontinuation due to lack of efficacy during the study

End point description:

Discontinuation due to lack of efficacy was based on the primary reason for withdrawal, based on all patients treated set (APTS)

End point type	Secondary

End point timeframe:

Baseline to Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	161	150	153	
Units: percentage of patients				
number (not applicable)	14.91	6.67	7.19	

Statistical analyses

No statistical analyses for this end point

Secondary: Response rate at Week 6

End point title	Response rate at Week 6

End point description:

The response rate was defined as a reduction of ≥30% from baseline in PANSS total score OR a CGI-I score of 1 or 2

Population Description: FAS (last assessment)

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	150	150	
Units: percentage of responders				
number (not applicable)	32.1	48.7	62.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 6 in PSP total score

End point title	Change from baseline to Week 6 in PSP total score

End point description:

The Personal and Social Performance Scale (PSP) is a clinician-rated scale designed and validated to measure a patient's current level of social functioning. The PSP scale consists of a 100-point single-item rating scale, subdivided into 10 equal intervals. Scores of 1 to 10 indicate lack of autonomy in basic functioning, whereas scores of 91 to 100 reflect excellent functioning. The total score is and is based on 4 primary domains of PSP (socially useful activities (including work and study), personal and social relationships, self-care, and disturbing and aggressive behaviours). The 4 domains are assessed on a 6-point scale, from absent to very severe. A higher score indicates a better performance.
Population Description: only patients with PSP assessments between Days 15 to 27 and after Day 35 were included in this analysis; the number of participants analysed is therefore smaller than the defined FAS and also smaller than other PSP analyses using LOCF

End point type	Secondary

End point timeframe:

Baseline and Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	139	133	138	
Units: units on a scale				
arithmetic mean (standard error)	9.4 (± 1)	13 (± 1)	15.3 (± 1)	

Statistical analyses

No statistical analyses for this end point

Secondary: PSP functional remission rate at Week 6

End point title	PSP functional remission rate at Week 6

End point description:

The PSP functional remission rate was defined as a PSP total score ≥71

FAS (last assessment). Patients who have no post-baseline PSP values available were not included as response is defined based on change from baseline and no baseline carried forward analysis was planned; the number of participants analyzed is therefore smaller than the defined FAS.

End point type	Secondary

End point timeframe:

Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	157	146	146	
Units: percentage of remitters				
number (not applicable)	5.7	9.6	14.4	

Statistical analyses

No statistical analyses for this end point

Secondary: PSP functional response rate at Week 6

End point title	PSP functional response rate at Week 6

End point description:

The PSP functional response rate was defined as ≥10 point improvement from Baseline on the PSP total score

Population Description : Patients who have no post-baseline PSP values available were not included as response is defined based on change from baseline and no baseline carried forward analysis was planned; the number of participants analyzed is therefore smaller than the defined FAS.

End point type	Secondary

End point timeframe:

Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	157	146	146	
Units: percentage of responders				
number (not applicable)	36.3	53.4	64.4	

Statistical analyses

No statistical analyses for this end point

Secondary: PSP domain D: disturbing and aggressive behaviours at Week 6

End point title	PSP domain D: disturbing and aggressive behaviours at Week 6

End point description:

PSP domain D: disturbing and aggressive behaviours were categorised as "aggressive" (corresponding to mild, manifest, marked, severe, or very severe) or "nonaggressive" (corresponding to absent)

Population Description: only patients who have PSP assessment at Week 6 were included in this analysis; the number of participants analysed is therefore smaller than the defined FAS and also smaller than other PSP analyses where last assessment carried forward was used

End point type	Secondary

End point timeframe:

Week 6

End point values	Placebo	Brexpiprazole	Quetiapine extended release	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	112	114	126	
Units: percentage of aggressive patients				
number (not applicable)	30.4	27.2	22.2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First dose to follow-up	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Quetiapine Extended Release
Reporting group description: -	
Reporting group title	Brexpiprazole
Reporting group description: -	

Serious adverse events	Placebo	Quetiapine Extended Release	Brexpiprazole
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 161 (3.73%)	2 / 153 (1.31%)	7 / 150 (4.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Grand mal convulsion			
subjects affected / exposed	0 / 161 (0.00%)	0 / 153 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 161 (0.00%)	0 / 153 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 161 (0.62%)	0 / 153 (0.00%)	0 / 150 (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
Psychotic disorder			

subjects affected / exposed	1 / 161 (0.62%)	1 / 153 (0.65%)	0 / 150 (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
Schizophrenia			
subjects affected / exposed	4 / 161 (2.48%)	1 / 153 (0.65%)	3 / 150 (2.00%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia, paranoid type			
subjects affected / exposed	1 / 161 (0.62%)	0 / 153 (0.00%)	0 / 150 (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
Suicide attempt			
subjects affected / exposed	0 / 161 (0.00%)	0 / 153 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 161 (0.00%)	0 / 153 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	Quetiapine Extended Release	Brexpiprazole
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 161 (27.33%)	73 / 153 (47.71%)	48 / 150 (32.00%)
Investigations			
Weight increased			
subjects affected / exposed	6 / 161 (3.73%)	20 / 153 (13.07%)	8 / 150 (5.33%)
occurrences (all)	6	21	8
Nervous system disorders			
Akathisia			
subjects affected / exposed	4 / 161 (2.48%)	6 / 153 (3.92%)	9 / 150 (6.00%)
occurrences (all)	5	8	9
Dizziness			

subjects affected / exposed	1 / 161 (0.62%)	18 / 153 (11.76%)	4 / 150 (2.67%)
occurrences (all)	1	21	4
Headache			
subjects affected / exposed	11 / 161 (6.83%)	9 / 153 (5.88%)	8 / 150 (5.33%)
occurrences (all)	12	9	10
Sedation			
subjects affected / exposed	5 / 161 (3.11%)	8 / 153 (5.23%)	4 / 150 (2.67%)
occurrences (all)	5	8	4
Somnolence			
subjects affected / exposed	8 / 161 (4.97%)	34 / 153 (22.22%)	7 / 150 (4.67%)
occurrences (all)	8	45	8
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	2 / 161 (1.24%)	13 / 153 (8.50%)	2 / 150 (1.33%)
occurrences (all)	2	14	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	10 / 161 (6.21%)	4 / 153 (2.61%)	13 / 150 (8.67%)
occurrences (all)	11	5	18
Schizophrenia			
subjects affected / exposed	11 / 161 (6.83%)	4 / 153 (2.61%)	6 / 150 (4.00%)
occurrences (all)	11	6	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported