Clinical trial results:
Interventional, open-label, flexible-dose, long-term study to evaluate the safety and tolerability of brexpiprazole as adjunctive treatment in elderly patients with major depressive disorder with an inadequate response to antidepressant treatment

Summary

EudraCT number	2014-003547-35
Trial protocol	EE DE FI PL
Global end of trial date	01 June 2016

Results information

Result version number	v1 (current)
This version publication date	18 June 2017
First version publication date	18 June 2017

Trial information

Trial identification

Sponsor protocol code	16160A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02400346
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark, 2500
Public contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@lundbeck.com
Scientific contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, +45 36301311, 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	01 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2016
Global end of trial reached?	Yes
Global end of trial date	01 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of brexpiprazole (1 to 3 mg/day) as adjunct treatment to antidepressant treatment (ADT) in elderly patients with MDD and inadequate response to ADT.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013) and ICH Good Clinical Practice (1996)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 March 2015
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	United States: 52
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Estonia: 21
Country: Number of subjects enrolled	Finland: 27
Country: Number of subjects enrolled	Germany: 15
Worldwide total number of subjects	132
EEA total number of subjects	80

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)	0
From 65 to 84 years	130

85 years and over	2

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 trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Adjunct brexpiprazole

Arm description:

Weeks 1-4 titration from 0.5 up to 2 mg once daily, in weekly steps. For the rest of the 26 treatment weeks, maintenance with 1-3 mg once daily. Tablets for oral use once daily during 26 weeks. Tablet strengths: 0.5 mg, 1 mg, 2 mg and 3 mg.

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:

Once daily dosing during 26 weeks. Weeks 1-4 titration from 0.5 up to 2 mg once daily, in weekly steps. For the rest of the 26 treatment weeks, maintenance with 1-3 mg once daily.Tablet strengths: 0.5 mg, 1 mg, 2 mg and 3 mg.

Number of subjects in period 1	Adjunct brexpiprazole
Started	132
Completed	88
Not completed	44
Consent withdrawn by subject	7
Non-complianc with IMP	1
Adverse event, non-fatal	24
Lost to follow-up	1
Lack of efficacy	9
Administrative reason	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	132	132	
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)	0	0	
From 65-84 years	130	130	
85 years and over	2	2	
Age continuous Units: years			
arithmetic mean	71		
standard deviation	± 5.3	-	
Gender categorical Units: Subjects			
Female	107	107	
Male	25	25	
Race Units: Subjects			
White	130	130	
Black or African American	2	2	

End points

End points reporting groups

Reporting group title	Adjunct brexpiprazole

Reporting group description:

Weeks 1-4 titration from 0.5 up to 2 mg once daily, in weekly steps. For the rest of the 26 treatment weeks, maintenance with 1-3 mg once daily. Tablets for oral use once daily during 26 weeks. Tablet strengths: 0.5 mg, 1 mg, 2 mg and 3 mg.

Primary: Number of Patients With Treatment-Emergent Adverse Events [Time Frame: 30 weeks]

End point title	Number of Patients With Treatment-Emergent Adverse Events [Time Frame: 30 weeks][1]

End point description:

End point type	Primary

End point timeframe:

Baseline to 30 weeks

Notes:

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

End point values	Adjunct brexpiprazole			
Subject group type	Reporting group			
Number of subjects analysed	132			
Units: Count of participants	102			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to 30 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Adjunct brexpiprazole

Reporting group description:

Weeks 1-4 titration from 0.5 up to 2 mg once daily, in weekly steps. For the rest of the 26 treatment weeks, maintenance with 1-3 mg once daily. Tablets for oral use once daily during 26 weeks. Tablet strengths: 0.5 mg, 1 mg, 2 mg and 3 mg.

Serious adverse events	Adjunct brexpiprazole		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 132 (4.55%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Eye contusion			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Facial bones fracture			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			

subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Myocardial rupture			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Major depression			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Panic attack			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Postoperative wound infection			

subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Adjunct brexpiprazole		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 132 (59.85%)		
Investigations			
Weight increased			
subjects affected / exposed	11 / 132 (8.33%)		
occurrences (all)	12		
Nervous system disorders			
Akathisia			
subjects affected / exposed	11 / 132 (8.33%)		
occurrences (all)	13		
Dizziness			
subjects affected / exposed	10 / 132 (7.58%)		
occurrences (all)	10		
Headache			
subjects affected / exposed	7 / 132 (5.30%)		
occurrences (all)	7		
Tremor			
subjects affected / exposed	9 / 132 (6.82%)		
occurrences (all)	11		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	20 / 132 (15.15%)		
occurrences (all)	20		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 132 (6.06%)		
occurrences (all)	8		
Anxiety			

subjects affected / exposed occurrences (all) Restlessness subjects affected / exposed occurrences (all)	10 / 132 (7.58%) 10 17 / 132 (12.88%) 18		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 7 / 132 (5.30%) 7		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 8 / 132 (6.06%) 8		
Metabolism and nutrition disorders Increased appetite subjects affected / exposed occurrences (all)	 13 / 132 (9.85%) 13		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 March 2015	The main reason for this amendment was to follow a request from Competent Authorities to include the MMSE scale at the Completion/Withdrawal Visit in addition to the Baseline Visit to assess the cognitive aspects as part of long-term safety assessment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported