

**Clinical trial results:**

**Interventional, open-label, long-term extension study to evaluate the safety and tolerability of brexpiprazole as adjunctive treatment in patients with major depressive disorder.**

**THE STUDY WAS PREMATURELY TERMINATED AND NO FIRM CONCLUSIONS CAN BE DRAWN REGARDING SAFETY AND EFFICACY**

**Summary**

EudraCT number	2012-004169-42
Trial protocol	SE LT DE GB IT FI SK PL BG LV EE
Global end of trial date	13 May 2014

**Results information**

Result version number	v1 (current)
This version publication date	06 July 2016
First version publication date	22 July 2015

**Trial information****Trial identification**

Sponsor protocol code	000014767B
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01944969
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	13 May 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 May 2014
Global end of trial reached?	Yes
Global end of trial date	13 May 2014
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of brexpiprazole as adjunct treatment to antidepressant (ADT)

Protection of trial subjects:

Safety data were reviewed regularly by the Lundbeck brexpiprazole Safety Committee to ensure that prompt action was taken, if needed, to maximise patient safety.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 October 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	Slovakia: 2
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Estonia: 3
Country: Number of subjects enrolled	Finland: 2
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	United States: 14
Worldwide total number of subjects	26
EEA total number of subjects	12

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)	3
From 65 to 84 years	23
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients who had completed a randomised, double-blind study with adjunctive brexpiprazole treatment of MDD (lead-in studies 14570A or 14571A) were eligible to enter this extension study.

### Pre-assignment

Screening details:

Patients who had completed a randomised, double-blind study with adjunctive brexpiprazole treatment of MDD (lead-in studies 14570A or 14571A) were eligible to enter this extension study.

### Period 1

Period 1 title	Baseline (week 0-4)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Adult (lead in from study 14570A)

Arm description:

Baseline visit in this study was the same as completion visit in the lead in study 14570A (adults).

Arm type	Experimental
Investigational medicinal product name	Brexpiprazole
Investigational medicinal product code	Lu AF41156
Other name	OPC-34712
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The patients received brexpiprazole 1 mg/day for the first week, and during the next 3 weeks were up-titrated in weekly steps to maximally 3 mg/day. In addition they received the same ADT as used in the lead in study.

<b>Arm title</b>	Elderly (lead in from study 14571A)
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Arm description:

Baseline visit was the same as the completion visit in the lead in study 14571A (elderly).

Arm type	Experimental
Investigational medicinal product name	Brexpiprazole
Investigational medicinal product code	Lu AF41156
Other name	OPC-34712
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The patients received brexpiprazole 0.5 mg/day for the first week, and during the next 3 weeks were up-titrated in weekly steps to maximally 3 mg/day. In addition they received the same ADT as used in the lead in study.

<b>Number of subjects in period 1</b>	Adult (lead in from study 14570A)	Elderly (lead in from study 14571A)
Started	3	23
Completed	3	23

## Period 2

Period 2 title	Maintenance treatment (week 4 onwards)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

## Arms

<b>Arm title</b>	Total
Arm description:	
Up to 3 mg brexpiprazole per day plus continuation of adjunctive treatment to antidepressant treatment (ADT) received in lead in study	
Arm type	Experimental
Investigational medicinal product name	Brexpiprazole
Investigational medicinal product code	Lu AF41156
Other name	OPC-34712
Pharmaceutical forms	Tablet
Routes of administration	Oral use

### Dosage and administration details:

The dose of brexpiprazole could be increased or decreased during the study within the range of 1 to 3 mg/day. The dose of ADT should remain stable as much as possible, but could be changed from Week 14 onwards, if considered necessary by the investigator. Treatment with brexpiprazole was to be continued up to 52 weeks. However, the study was prematurely terminated.

<b>Number of subjects in period 2</b>	Total
Started	26
Completed	0
Not completed	26
Adverse event, non-fatal	1
Non-compliance with IMP	1
Early termination of the study	23
Lack of efficacy	1



## Baseline characteristics

### Reporting groups

Reporting group title	Adult (lead in from study 14570A)
Reporting group description:	
Baseline visit in this study was the same as completion visit in the lead in study 14570A (adults).	
Reporting group title	Elderly (lead in from study 14571A)
Reporting group description:	
Baseline visit was the same as the completion visit in the lead in study 14571A (elderly).	

Reporting group values	Adult (lead in from study 14570A)	Elderly (lead in from study 14571A)	Total
Number of subjects	3	23	26
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)	3	0	3
From 65-84 years	0	23	23
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	44	69	
standard deviation	± 16.52	± 3.74	-
Gender categorical			
Units: Subjects			
Female	3	18	21
Male	0	5	5

## End points

### End points reporting groups

Reporting group title	Adult (lead in from study 14570A)
Reporting group description:	
Baseline visit in this study was the same as completion visit in the lead in study 14570A (adults).	
Reporting group title	Elderly (lead in from study 14571A)
Reporting group description:	
Baseline visit was the same as the completion visit in the lead in study 14571A (elderly).	
Reporting group title	Total
Reporting group description:	
Up to 3 mg brexpiprazole per day plus continuation of adjunctive treatment to antidepressant treatment (ADT) received in lead in study	

### Primary: Total number of treatment-emergent adverse events

End point title	Total number of treatment-emergent adverse events <sup>[1]</sup>
End point description:	
Please see Adverse events section for full adverse event report	
End point type	Primary
End point timeframe:	
baseline to end of study (prematurely terminated)	
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 comparison between parameters were performed. Only number of adverse event are reported	

End point values	Total	Adult (lead in from study 14570A)	Elderly (lead in from study 14571A)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	3	23	
Units: number	28	2	26	

### 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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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### Reporting groups

Reporting group title	Total
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Reporting group description: -

<b>Serious adverse events</b>	Total		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

<b>Non-serious adverse events</b>	Total		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 26 (19.23%)		
Injury, poisoning and procedural complications			
Accidental overdose			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 26 (11.54%)		
occurrences (all)	3		
Nervous system disorders			
Lethargy			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 26 (7.69%)		
occurrences (all)	2		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 April 2014	Early termination	-

Notes:

### Limitations and caveats

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

Early termination leading to a small number analysed; only AEs reported
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Notes: