



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 |
|-----------------------|------------|

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 |
| Arm title | 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.

| | |
|------------------|-------------------------------------|
| Arm title | Elderly (lead in from study 14571A) |
|------------------|-------------------------------------|

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.

| Number of subjects in period 1 | 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

| Arm title | 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.

| Number of subjects in period 2 | 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 ^[1] |
| 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 |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | Total |
|-----------------------|-------|

Reporting group description: -

| Serious adverse events | 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 %

| Non-serious adverse events | 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

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 |
|---|

Notes: