



Clinical trial results:

A Multicenter, Open-label, Follow-up Trial Evaluating the Long-term Safety of Levetiracetam, for Patients Suffering From Epilepsy and Coming From the Study N01175 (NCT00175903)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2006-000173-29 |
| Trial protocol | FI BE |
| Global end of trial date | 29 April 2008 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 30 June 2016 |
| First version publication date | 10 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | N01237 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00291655 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | UCB S.A. |
| Sponsor organisation address | Allée de la Recherche, 60, Brussels, Belgium, B – 1070 |
| Public contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 15 15, clinicaltrials@ucb.com |
| Scientific contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 15 15, clinicaltrials@ucb.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 June 2008 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|---------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 29 April 2008 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

For ethical reasons to give opportunity for adult subjects (≥ 16 or 18 years) suffering from newly diagnosed epilepsy who completed the therapeutic confirmatory, open-label trial N01175 conducted with levetiracetam in monotherapy and who benefited from the treatment, to receive treatment with levetiracetam until the monotherapy indication for levetiracetam is granted in Europe.

Protection of trial subjects:

Adequate information was provided to the subject in both oral and written form and consent was obtained in writing prior to performance of any study specific procedure. The content and process of obtaining informed consent was in accordance with all applicable regulatory and IEC/IRB requirements.

If the subject was unable to provide informed consent, the subject's legally acceptable representative was informed of all pertinent aspects of the trial including the written information which had been previously submitted to the IEC/IRB.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

| | |
|---|--------------|
| Actual start date of recruitment | 26 June 2006 |
| 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 | Finland: 9 |
| Country: Number of subjects enrolled | France: 18 |
| Country: Number of subjects enrolled | Poland: 32 |
| Country: Number of subjects enrolled | Belgium: 25 |
| Country: Number of subjects enrolled | Bulgaria: 31 |
| Country: Number of subjects enrolled | Switzerland: 15 |
| Worldwide total number of subjects | 130 |
| EEA total number of subjects | 115 |

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) | 111 |
| From 65 to 84 years | 16 |
| 85 years and over | 3 |

Subject disposition

Recruitment

Recruitment details:

This study began recruiting in June 2006 and concluded in April 2008.

Pre-assignment

Screening details:

Baseline demographics consists of the Intent-to-Treat (ITT) population, which is defined as all subjects who took at least one dose of study medication in N01237 trial.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------|------------------------------------|
| Arm title | Levetiracetam Open-label Treatment |
|------------------|------------------------------------|

Arm description:

Open-label treatment with Levetiracetam 500 mg oral tablets in monotherapy, 1000 - 3000 mg/day bid over up to 18 months.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Levetiracetam |
| Investigational medicinal product code | LEV |
| Other name | Keppra |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

500 mg oral tablets, 1000 - 3000 mg/day, twice a day (bid), duration of the study.

| Number of subjects in period 1 | Levetiracetam Open-label Treatment |
|--------------------------------|------------------------------------|
| Started | 130 |
| Completed | 115 |
| Not completed | 15 |
| Consent withdrawn by subject | 7 |
| AE, non-serious non-fatal | 1 |
| Other Reason | 2 |
| Lost to follow-up | 2 |
| Lack of efficacy | 3 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------------------------|
| Reporting group title | Levetiracetam Open-label Treatment |
|-----------------------|------------------------------------|

Reporting group description:

Open-label treatment with Levetiracetam 500 mg oral tablets in monotherapy, 1000 - 3000 mg/day bid over up to 18 months.

| Reporting group values | Levetiracetam Open-label Treatment | Total | |
|------------------------------------|------------------------------------|-------|--|
| Number of subjects | 130 | 130 | |
| Age categorical Units: Subjects | | | |

| | | | |
|---|------------------|----|--|
| Age Continuous Units: years arithmetic mean standard deviation | 40.68 ± 18.35 | - | |
| Gender Categorical Units: Subjects | | | |
| Female | 58 | 58 | |
| Male | 72 | 72 | |
| Region of Enrollment Units: Subjects | | | |
| France | 18 | 18 | |
| Finland | 9 | 9 | |
| Poland | 32 | 32 | |
| Belgium | 25 | 25 | |
| Bulgaria | 31 | 31 | |
| Switzerland | 15 | 15 | |

End points

End points reporting groups

| | |
|--|------------------------------------|
| Reporting group title | Levetiracetam Open-label Treatment |
| Reporting group description: Open-label treatment with Levetiracetam 500 mg oral tablets in monotherapy, 1000 - 3000 mg/day bid over up to 18 months. | |

Primary: Assessment of safety of levetiracetam as per adverse event (AE) reporting in open-label therapy phase

| | |
|---|--|
| End point title | Assessment of safety of levetiracetam as per adverse event (AE) reporting in open-label therapy phase ^[1] |
| End point description: Summarization for occurrence of adverse events like number of subjects with any adverse events or drug related adverse events is provided (see categories). | |
| End point type | Primary |
| End point timeframe: During open-label therapy phase of 18 months | |

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: The primary objective was to give opportunity for adult subjects suffering from newly diagnosed epilepsy, who completed study N01175 conducted with levetiracetam (LEV) in monotherapy and who benefited from the treatment, to receive treatment with LEV until the monotherapy indication for LEV has been granted in Europe. The safety profile of LEV was summarized descriptively across several safety variables. Therefore, no inferential statistics were performed in this safety study.

| End point values | Levetiracetam Open-label Treatment | | | |
|--|------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 130 | | | |
| Units: participants | | | | |
| Subjects with at least one AE | 40 | | | |
| Subjects with AEs leading to dose change | 8 | | | |
| Subjects with AEs leading to trial discontinuation | 1 | | | |
| Subjects with drug-related AEs | 16 | | | |
| Subjects with AEs of severe intensity | 4 | | | |
| Subjects with serious AEs | 6 | | | |
| Subjects with study drug-related serious AEs | 0 | | | |
| Number of deaths | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in body weight to withdrawal or end of study after

18 months

| | |
|-----------------|---|
| End point title | Change from baseline in body weight to withdrawal or end of study after 18 months |
|-----------------|---|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Start of open-label therapy (Baseline) to withdrawal or end of study after 18 months

| End point values | Levetiracetam Open-label Treatment | | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 79 | | | |
| Units: kg | | | | |
| arithmetic mean (standard deviation) | | | | |
| mean (standard deviation) | 0.71 (± 3.16) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Open-label treatment over 18 months.

Adverse event reporting additional description:

Treatment-emergent Adverse Events consist of the Safety Set, which is all subjects who took at least one dose of study medication in N01237 trial.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|-----|
| Dictionary version | 9.0 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Levetiracetam Open- Label Treatment |
|-----------------------|-------------------------------------|

Reporting group description:

Open-label treatment with Levetiracetam 500 mg oral tablets in monotherapy, 1000 - 3000 mg/day bid over up to 18 months

| Serious adverse events | Levetiracetam Open- Label Treatment | | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 130 (4.62%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Skin laceration | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Foot fracture | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |

| | | | |
|---|-----------------|--|--|
| Grand mal convulsion | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Alcoholism | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | | |
| 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 | Levetiracetam Open-Label Treatment | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 130 (5.38%) | | |
| Investigations | | | |
| Weight increased | | | |
| subjects affected / exposed | 7 / 130 (5.38%) | | |
| occurrences (all) | 7 | | |

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