UCB reference No.: RXCE06E1668

Approved by UCB 18-Mar-2008

Clinical Study Summary (CSS)

DEV/SGE/00364.2008

CT Registry ID#: NCT00245713
Study No.: N01085

These results are supplied for informational purposes only. Prescribing decisions should be made based on the approved package insert.

Based on Clinical Study Report document reference code: RRCE06B0711

Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
Keppra® Tablets	Levetiracetam	Epilepsy

Name of Sponsor/Company: UCB Pharma SA

Title of Study:
A 9–11 week multicenter, randomized, double-blind, placebo-controlled, parallel group study to determine the effects of adjunctive levetiracetam on the sleep architecture of adult subjects (18 - 45 years of age) with partial onset epilepsy receiving a first generation anti-epileptic drug.

Investigator(s) (number only): 7

Study Center(s) (number only): 7

Length of Study:
Date first patient enrolled: 17-Feb-2003
Date last patient completed: 19-Nov-2004

Phase of Development: Phase IV

Abstract:
The primary objective of the trial was to assess the effects of levetiracetam (LEV) during a 6-week treatment period on the sleep architecture of partial onset epilepsy subjects taking a first generation antiepileptic drug (AED) (either phenytoin or carbamazepine). The primary efficacy endpoints were the changes from Baseline to Visit 7 in percent Rapid Eye Movement (REM), percent slow wave sleep (SWS), and sleep efficiency (SE) (total sleep time divided by the time in bed), with particular focus on the SE. Data were collected by means of polysomnography. Safety assessments included monitoring of adverse events (AEs), laboratory test results and vital signs. Subjects were to be 18 to 45 years old, have had at least 1 partial onset seizure during the preceding 6 months but no more than an average of 1 seizure per 2 weeks during the last 3 months, received treatment with either carbamazepine or phenytoin at a stable dose for a period of 4 weeks, and had no specific nor non-specific sleep disorders. The evaluation period consisted of 42 days including an increase from 1000 mg/day to 2000 mg/day LEV or placebo (PBO) after 14 days and an increase to 3000 mg/day LEV or PBO after 28 days. The study was stopped due to poor accrual rate. The primary efficacy endpoints were therefore analyzed using descriptive statistics.

Number of Subjects:	**PBO**	**LEV**
Planned, N:	20	20
Enrolled, N:	11	6
Completed, n (%):	9 (81.8)	5 (83.3)
Number of Subjects Withdrawn, n (%):	2 (18.2)	1 (16.7)
Withdrawn due to Adverse Events, n (%):	1 (0.9)	0
Withdrawn for Other Reasons, n (%):	1 (0.9)	1 (16.7)
Demography:	**PBO (N=11)**	**LEV (N=6)**
Gender (Females/Males):	7/4	3/3
Age (years), mean (SD):	35.12 (10.67)	35.00 (9.06)
Race, n (%):		
Caucasian	11 (100)	4 (66.7)
African/American	0	2 (33.3)

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Safety Outcomes:

- Summary of treatment emergent adverse events, deaths, other serious adverse events and certain other significant adverse events:

Overall, 50.0% and 63.6% of subjects in the LEV and PBO group, respectively, reported treatment-emergent (TE) AEs during the trial. The most commonly reported TEAEs in the LEV and PBO groups were infections and infestations (0% and 45.5% of subjects, respectively), nervous system disorders (33.3% and 9.1% of subjects, respectively), and psychiatric disorders (16.7% and 18.2% of subjects, respectively). Fifty and 18.2% of subjects in the LEV and PBO groups, respectively, reported TEAEs during the trial considered to be drug-related by the Investigator.

No deaths of other serious AEs occurred during the trial. One subject in the PBO group experienced a TEAE leading to permanent drug discontinuation.

Treatment Emergent AEs (TEAE):	**PBO (N=11)**	**LEV (N=6)**
Subjects with at least one TEAE, n (%):	7 (63.6)	3 (50.0)
Primary System Organ Class with an incidence of ≥ 10%	*n (%) [n considered drug-related by the Investigator]*	
Infections and infestations	5 (45.5) [0]	0
Nervous system disorders	1 (9.1) [1]	2 (33.3) [2]
Psychiatric disorders	2 (18.2) [0]	1 (16.7) [1]
General disorders and administration site conditions	2 (18.2) [0]	0
Injury, poisoning and procedural complications	2 (18.2) [0]	0
Musculoskeletal/connective tissue disorders	1 (9.1) 0]	1 (16.7) [0]
Skin and subcutaneous tissue disorders	2 (18.2) [1]	0
Blood and lymphatic system disorders	0	1 (16.7) [1]

Primary Outcomes:

The mean (SD) change from Baseline at Visit 7 for SE was -0.207 (0.291) and -0.022 (0.094) for LEV and PBO treatment groups, respectively. Changes from Baseline at Visit 7 in mean (SD) percent REM and SWS were -0.17 (5.88) and -6.23 (7.33), respectively for the LEV treatment group, and -1.61 (3.06) and 0.53 (6.97), respectively for PBO treatment.

Publication Reference(s) based on the study: None

Date of report: 18-Mar-2008