UCB reference No.: RXCE06E1670

Approved by UCB 18-Mar-2008

Clinical Study Summary (CSS)

DEV/SGE/00372.2008

CT Registry ID#: NCT00160511
Study No.: N01087

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: RRCE06A1601

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

Name of Sponsor/Company: UCB Pharma Inc

Title of Study:
A double-blind, randomized, placebo-controlled, parallel-group, 16 week, multicenter trial evaluating the efficacy and safety of levetiracetam 500 mg tablets in bid administration (daily dose ranging from 1000 mg to 3000 mg), in adults (≥ 18 years of age) suffering from postherpetic neuralgia.

Study Center(s) (number only): 28

Length of Study:
Date first patient enrolled: 30-Apr-2004
Date last patient completed: 23-Sep-2005

Phase of Development: II (Therapeutic exploratory)

Abstract:
The objective of this trial was to assess the efficacy, safety, and tolerability of levetiracetam (LEV) compared to placebo (PBO) in the treatment of postherpetic neuralgia. The primary efficacy variable was the absolute change in the average weekly Pain Intensity Scale (PIS) from the baseline period to the last 7 days of the evaluation period. Safety assessments included monitoring of adverse events (AEs), safety laboratory tests, vital signs, and LEV plasma levels. Subjects were to be at least 18 years old, suffering from neuralgia which lasted at least 3 months since the healing of acute herpes zoster skin rash, with postherpetic neuralgia pain meeting the criteria of a Visual Analog Scale ≥ 40 mm at baseline and an average daily PIS score of ≥ 4 during the baseline period, had an estimated creatinine clearance ≥ 50 mL/min, had no professional psychological support within 2 weeks prior to screening, had no previous neurolytic or neurosurgical therapy for post-herpetic neuralgia, had no treatment with a transcutaneous electrical nerve stimulator within the 2 weeks prior to screening, and had no treatment with a spinal cord stimulator at screening. The trial consisted of a 1-week baseline period, a 12-week evaluation period (4-week titration period up to 3000 mg LEV daily dose or PBO and a 8-week stable dose period), a taper blinded period followed by a 1-week drug-free period. The treatment groups (Intent-to-Treat population) were compared using a mixed model for repeated measures. The model included the variables of Pooled Center, baseline period mean PIS, and time by treatment interaction.

Number of Subjects:	**PBO**	**LEV**
Planned, N:	85	85
Enrolled, N:	86	84
Intent-To-Treat population, n (%):	85 (98.8)	82 (97.6)
Completed, n (%):	66 (76.7)	54 (64.3)
Number of Subjects Withdrawn, n (%):	19 (22.1)	28 (33.3)
Withdrawn due to Adverse Events, n (%):	2 (2.3)	13 (15.5)
Withdrawn due to lack of efficacy, n (%):	5 (5.8)	8 (9.5)
Withdrawn for other reasons, n (%):	12 (14.1)	7 (8.5)
Demography:	**PBO (N=85)**	**LEV (N=82)**
Gender (Females/Males):	40/45	37/45
Age (years), mean (SD):	71.13 (12.24)	69.08 (12.31)

CT Registry ID#: NCT00160511
Study No.: N01087

Race, n (%):		
Caucasian:	76 (89.4)	73 (89.0)
African/American:	5 (5.9)	3 (3.7)
Asian/Pacific Islander:	0	2 (2.4)
Hispanic:	3 (3.5)	3 (3.7)
American Indian/Alaskan native:	0	1 (1.2)
Other/mixed race:	1 (1.2)	0

Safety Outcomes:

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

Overall, 77.1% and 61.6% of the subjects in the LEV and PBO groups, respectively, reported treatment-emergent (TE) AEs. The most commonly reported TEAEs in the LEV and PBO groups were nervous system disorders (44.6% and 12.8% of subjects, respectively), general disorders and administration site conditions (28.9% and 17.4%, respectively), gastrointestinal disorders (18.1% and 15.1%, respectively), and infections and infestations (15.7% and 17.4%, respectively). TEAEs considered to be related to the study drug by the Investigator were reported for 50.6% and 27.9% of the subjects in the LEV and PBO groups, respectively. There were no deaths during this trial. Serious AEs (SAEs) were reported by 2 subjects in each treatment group. None were considered to be related to the study drug. TEAEs leading to permanent study drug discontinuation were reported for 14.5% of the subjects in the PBO group.

No analysis of vital signs and laboratory data was performed.

Treatment Emergent AEs (TEAE):	**PBO (N=86)**	**LEV (N=83)[a]**
Subjects with at least one TEAE, n (%):	53 (61.6)	64 (77.1)
MedDRA Primary System Organ Class with an incidence of > 10%	*n (%) [n considered drug-related by the Investigator]*	
Nervous system disorders	11 (12.8) [6]	37 (44.6) [34]
General disorders and administration site conditions	15 (17.4) [10]	24 (28.9) [15]
Gastrointestinal disorders	13 (15.1) [7]	15 (18.1) [10]
Infections and infestations	15 (17.4) [0]	13(15.7) [0]
Musculoskeletal and connective tissue disorders	10 (11.6) [0]	12 (14.5) [2]
Psychiatric disorders	4 (4.7) [4]	9 (10.8) [7]

[a]One subject did not take any study medication and was therefore excluded from the safety population.

SAEs:	**PBO (N=86)**	**LEV (N=83)**
Subjects with SAEs, n (%):	2 (2.3)	2 (2.4)
MedDRA Primary System Organ Class	*n (%) [n considered drug-related by the Investigator]*	
General disorders and administration site conditions	2 (2.3) [0]	0
Infections and infestations	0	1 (1.2) [0]
Respiratory, thoracic and mediastinal disorders	0	1 (1.2) [0]

Primary Outcomes:

The Least Squares (LS) Means for the absolute PIS changes from baseline are -1.50 in subjects who received PBO and -1.84 in subjects who received LEV. The estimate [2-sided 95% CI] of the difference between these LS Means was 0.34 [-0.47, 1.15]. The difference did not reach the statistical threshold of significance (p=0.41).

Publication Reference(s) based on the study: None

Date of report: 18-Mar-2008