UCB reference No.: RXCE06H1602

Approved by UCB 21-July-2006

Clinical Study Summary

CT Registry ID#: NCT00150774
Study No.: N166

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: RRCE04F1404

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

Name of Sponsor/Company: UCB

Title of Study: A double-blind, multicenter, randomized, placebo-controlled study to evaluate the efficacy and safety of levetiracetam (LEV) (oral tablets of 500 mg b.i.d.), at a dose of 3000 mg/day as adjunctive treatment in adolescents (≥ 12 years) and adults (≤ 65 years) suffering from idiopathic generalized epilepsy with myoclonic seizures.

Investigator(s) (number only): 53

Study Center(s) (number only): 53

Length of Study:
Date first patient enrolled: 03-Sep-2001
Date last patient completed: 13-Dec-2004

Phase of Development: Phase III (therapeutic confirmatory)

Abstract:
The study objectives were to assess the efficacy of adjunctive treatment with levetiracetam (LEV) 3000 mg/day in reducing myoclonic seizures in adolescents (≥ 12 years of age) and adults (≤ 65 years of age) suffering from idiopathic generalized epilepsy, and to evaluate the safety and tolerability of LEV in the same population. The study consisted of four phases with a maximum duration of 30 weeks: baseline period (single-blind placebo), 8 weeks; up-titration period, 4 weeks; evaluation period, 12 weeks; and conversion/down-titration period, 6 weeks (switch to open-label follow-up study or down-titration including a 2-week drug-free period). The primary efficacy endpoint was the proportion of subjects with at least a 50% reduction in the number of myoclonic seizure days per week during the treatment period (up-titration and evaluation periods) as compared to baseline. Safety was assessed by the occurrence of adverse events (AEs), laboratory test results, electrocardiograms, physical and neurological examinations, and vital signs. The treatment groups were compared with respect to the primary efficacy variable using logistic regression analysis. The model included treatment group as factors, and the baseline myoclonic seizure days per week as covariate. The analysis was based on the ITT population, i.e., all randomized subjects who took at least one dose of randomized study medication. An estimate and 95% confidence interval (CI) for the treatment odds ratio was presented.

Publication Reference(s) based on the study:
None

Number of Patients:	**PBO**	**LEV**
Planned, N:	58	58
Enrolled, N:	60	62
Completed, n (%):	51 (85.0)	53 (86.9)
Number of Patients Withdrawn, n (%):	9 (15.0)	8 (13.1)
Withdrawn due to Adverse Events, n (%):	1 (1.7)	3 (4.9)
Withdrawn for Other Reasons, n (%):	8 (13.3)	5 (8.2)

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Demography:	**PBO (N=60)**	**LEV (N=61)**
Gender (Females/Males):	38/22	39/22
Age (years), mean(SD):	26.84 (9.48)	25.01 (7.44)
Race, n (%):	Caucasian, 47 (78.3)	Caucasian, 46 (75.4)

Safety Outcomes:
- Summary of treatment emergent adverse events, deaths, other serious adverse events and certain other significant adverse events:
Overall, during the up-titration and evaluation periods, 66.7% of the subjects in the PBO group and 75.0% of the subjects in the LEV group experienced at least 1 treatment-emergent adverse event (TEAE). The most frequently reported TEAEs, with a higher incidence in the LEV group than in the PBO group, were vertigo, influenza, pharyngitis, neck pain, somnolence, and depression. Six treatment-emergent SAEs were reported in 5 subjects (1 in the PBO group and 4 in the LEV group). They were considered not related to the study drug and none of them led to study drug discontinuation. None of the changes in hematology or biochemistry laboratory parameters were considered clinically significant. No clinically relevant changes in vital signs or electrocardiograms were noted.

Treatment Emergent AEs (Treatment Period, ITT Population):	**PBO (N=60)**	**LEV (N=60)**
Patients with at least one TEAE, n (%):	40 (66.7)	45 (75.0)
Patients with TEAEs (by Primary System Organ Class)	*n (%) [n considered drug-related by the Investigator]*	
Blood and Lymphatic System Disorders	1 (1.7) [1]	0
Cardiac Disorders	0	1 (1.7) [0]
Ear and Labyrinth Disorders	3 (5.0) [2]	3 (5.0) [2]
Eye Disorders	1 (1.7) [0]	2 (3.3) [2]
Gastrointestinal Disorders	10 (16.7) [2]	12 (20.0) [4]
General Disorders and Administration Site Conditions	7 (11.7) [5]	3 (5.0) [3]
Hepatobiliary Disorders	1 (1.7) [0]	2 (3.3) [0]
Immune System Disorders	1 (1.7) [0]	1 (1.7) [0]
Infections and Infestations	11 (18.3) [1]	16 (26.7) [3]
Injury, Poisoning, and Procedural Complications	1 (1.7) [0]	2 (3.3) [0]
Investigations	1 (1.7) [1]	0
Metabolism and Nutrition Disorders	3 (5.0) [1]	4 (6.7) [1]
Musculoskeletal and Connective Tissue Disorders	5 (8.3) [0]	5 (8.3) [0]
Nervous System Disorders	21 (35.0) [8]	22 (36.7) [10]
Psychiatric Disorders	11 (18.3) [5]	12 (20.0) [6]
Renal and Urinary Disorders	1 (1.7) [0]	0
Reproductive System and Breast Disorders	0	1 (1.7) [0]
Respiratory, Thoracic, and Mediastinal Disorders	1 (1.7) [0]	5 (8.3) [2]
Skin and Subcutaneous Tissue Disorders	3 (5.0) [0]	4 (6.7) [3]
Vascular Disorders	1 (1.7) [0]	0
Death, SAEs, and Other SAEs: (Entire Study, ITT Population)		
Death, n (%):	0	0
Patients with SAEs, n (%):	1 (1.7) [0]	4 (6.7) [0]

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Primary Outcome:

The 50% responder rate in myoclonic seizure days per week was 35/60 (58.3%) for the subjects in the LEV group compared to 14/60 (23.3%) for the subjects in the PBO group. The odds to respond to treatment were 4.77 times higher on LEV than on PBO. This difference was statistically significant (p=0.0002).

50% Responder Rate in Myoclonic Seizure Days per Week over the Treatment Period (ITT Population)	**PBO (N=60)**	**LEV (N=60)**
Responders, n (%)	14 (23.3)	35 (58.3)
Non-responders, n (%)	46 (76.7)	25 (41.7)
Odds ratio (LEV vs PBO)	4.77	
95% CI	(2.12, 10.77)	
p-value	0.0002	