UCB reference No.: RXCE06E1674

Approved by UCB 20-Dec-2007

Clinical Study Summary (CSS)

DEV/SGE/04569.2007

CT Registry ID#: NCT00160576
Study No.: N01105

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: RRCE04H0403

Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
Keppra® Tablet	Levetiracetam	Parkinson's disease

Name of Sponsor/Company: UCB Pharma SA

Title of Study:
A therapeutic exploratory, single arm, multicenter trial to evaluate the efficacy and safety of levetiracetam up to 4000 mg/day (500 mg oral tablets) on levodopa induced dyskinesias in adults with idiopathic Parkinson's disease

Investigator(s) (number only): 8

Study Center(s) (number only): 8

Length of Study:
Date first patient enrolled: 03-Jul-2003
Date last patient completed: 08-Nov-2004

Phase of Development: Phase II (therapeutic exploratory trial)

Abstract:
The primary objective of this trial was to evaluate the efficacy of levetiracetam (LEV) b.i.d. during the first 10-week treatment Period in controlling Levodopa induced dyskinesias in adults with idiopathic Parkinson's disease, without negative impact on the benefit on motor function of the antiparkisonian treatment. The primary efficacy variable was the reduction (hour) from Baseline in mean duration of dyskinesias (troublesome or not) per day during "On" Periods, as measured at the last Evaluation Visit of Part A. Safety assessments included monitoring of adverse events (AE), clinical laboratory tests, physical and neurological examinations, vital signs, body weight, and electrocardiogram (ECG). Subjects were to be male or female, ≥ 30 years old; suffering from idiopathic Parkinson's disease for ≥ 3 years (diagnosed according to UK Brain Bank Criteria), stabilized with regard to the motor function; treated with Levodopa whether or not combined with other antiparkinsonian drugs for ≥ 1 year; experienced persistent troublesome dyskinesias during "On" periods, and reported between Screening and Baseline ≥ 1 hour with troublesome dyskinesias per day and ≥ 9 hours over the 3 evaluation days. The study consisted of two consecutive parts (Part A and optional Part B). Part A consisted of a 1-2 weeks single blind placebo Baseline period, ≤ 8 weeks open label LEV up-titration, ≥ 2 weeks stable dose and a maximum of 2 weeks down-titration including ≥ 3 drug-free days. The optional Part B consisted of 24 weeks treatment period and ≤ 3 weeks down-titration including ≥ 1 drug-free week. Descriptive statistics and 2-sided 95% confidence interval (CI) of the reduction in mean duration of dyskinesias per day was used to evaluate the effect of LEV.

Number of Subjects:	**LEV**	
	Part A	**Part B**
Planned, N:	30	
Enrolled, N:	31	10
Completed, n (%):	22 (71.0)	9 (90.0)
Number of Subjects Withdrawn, n (%):	9 (29.0)	1 (10.0)
Withdrawn due to Adverse Events, n (%):	5 (16.1)	0
Withdrawn for Other Reasons, n (%):	4 (12.9)	1 (10.0)

CT Registry ID#: NCT00160576
Study No.: N01105

Demography:	**LEV (N=31)**
Gender (Females/Males):	16/15
Age (years), mean (SD):	62.1 (10.2)
Race, n (%):	
Caucasian	31 (100)

Safety Outcomes:

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

Overall, 87.1% of the subjects in Part A and 60.0% of the subjects in Part B reported treatment-emergent (TE) AEs. The most common reported TEAEs during the treatment period were nervous system disorders (71.0% and 20.0% of the subjects in Part A and Part B, respectively), psychiatric disorders (25.8% and 20.0% of the subjects in Part A and Part B, respectively), and gastrointestinal disorders (19.4% and 10.0% of the subjects in Part A and Part B, respectively).

Serious AEs (SAEs) were reported in Part A of the study for 3 (9.7%) subjects. No deaths were reported. Two subjects (6.5%) reported at least 1 drug-related SAE. TEAEs leading to permanent study drug discontinuation occurred in 7 (22.6%) subjects in Part A.

Two subjects had abnormal blood chemistry levels reported as TEAE in Part B. No clinically significant abnormalities were observed for hematology values, vital signs, body weight, and ECG.

Treatment Emergent AEs (TEAE):	**LEV**	
	Part A (N=31)	**Part B (N=10)**
Subjects with at least one TEAE, n (%):	27 (87.1)	6 (60.0)
Primary System Organ Class with an incidence of ≥ 15%	*n (%) [n considered drug-related by the Investigator]*	
Nervous system disorders	22 (71.0) [22]	2 (20.0) [2]
Psychiatric disorders	8 (25.8) [5]	2 (20.0) [2]
Gastrointestinal disorders	6 (19.4) [3]	1 (10.0) [1]
Metabolism and nutrition disorders	0	2 (20.0) [1]
SAEs:	**LEV**	
	Part A (N=31)	**Part B (N=10)**
Subjects with SAEs, n (%):	3 (9.7)	0
Primary System Organ Class	*n (%) [n considered drug-related by the Investigator]*	
Gastrointestinal disorders	1 (3.2) [0]	0
Injury, poisoning and procedural complications	1 (3.2) [1]	0
Nervous system disorders	2 (6.5) [2]	0
Vascular disorders	1 (3.2) [0]	0

Primary Outcomes:

The mean (SD) change from Baseline in the duration of dyskinesias (troublesome or not) per day during the "On" period at Week 10 or early discontinuation was -1.54 hours (4.18) with a 2-sided 95% CI [-3.19, 0.12]. Out of the 27 evaluable subjects, 13 (48.1%) subjects had a reduction from baseline of more than 2 hours.

Publication Reference(s) based on the study: None

Date of report: 20-Dec-2007