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Approved by UCB 06-Mar-2008

Clinical Study Summary (CSS)

DEV/SGE/03905.2007

CT Registry ID#: NCT00175955
Study No.: N01142

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: RRCE06E0804

Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
Keppra® tablets	Levetiracetam	Neuroleptic-induced tardive dyskinesia

Name of Sponsor/Company: UCB Pharma SA

Title of Study:
An 8-week exploratory, double-blind, placebo controlled randomized trial: evaluation of the efficacy and safety of levetiracetam up to 3000 mg/day (250-500 mg oral tablets in *b.i.d.* administration) on neuroleptic-induced tardive dyskinesia in subjects with stable axis I psychiatric disorder, aged from at least 18 years to 80 years.

Investigator(s) (number only): 15

Study Center(s) (number only): 15

Length of Study:
Date first patient enrolled: 12-May-2005
Date last patient completed: 29-Dec-2005

Phase of Development: Phase II (Therapeutic exploratory trial)

Abstract:
The primary objective of the study was to compare the efficacy of levetiracetam (LEV) to placebo (PBO) on neuroleptic-induced tardive dyskinesia. The primary efficacy parameter was the change from baseline on the total mean score of hyperkinesia (using the scores of the hyperkinesia subscale of the St Hans rating scale [SHRS]) estimated at the evaluation visit (V6) as evaluated by an independent blinded central reviewer. Safety assessments included adverse event (AE) monitoring, clinical laboratory assessments, physical and neurological examinations, vital signs, body weight and electrocardiogram (ECG). Subjects were to be 18 to 80 years old, met the DSM IV criteria for stable Axis I psychiatric disorder since ≥ 6 months and neuroleptic-induced tardive dyskinesia since ≥ 1 month prior to screening, did not suffer from any Axis II condition since the last 6 months prior to screening, had a total mean hyperkinesia score of ≥ 5 on the SHRS at screening and baseline, were on antipsychotic treatment for ≥ 6 months prior to screening and were on a stable dose of antipsychotic treatment for ≥ 1 month at screening (if applicable). The trial consisted of a 1-week baseline period, a 8-week treatment period with LEV (250 mg to 1500 mg *b.i.d.*) or PBO, and a 2-week down-titration period. The treatment period consisted of a 4-week up-titration period, including 1 week each at doses 250 mg, 500 mg, 1000 mg, and 1500 mg b.i.d., followed by a 4-week stable dose period at 1500 mg b.i.d. All data are presented on the intent-to-Treat population (all randomized subjects who took at least one dose of study medication. The primary efficacy analysis was performed by a linear mixed model for longitudinal data with the change from baseline in total mean score of hyperkinesia as dependent variable and visit by treatment interaction, baseline total mean score of hyperkinesia, gender and age as independent variables.

Number of Subjects:	**PBO**	**LEV**
Planned, N:	35	35
Randomized, N:	36[(a)]	34
Completed, n (%):	30 (85.7)	33 (97.1)
Number of Subjects Withdrawn, n (%):	5 (14.3)	1 (2.9)
Withdrawn due to Adverse Events, n (%):	5 (14.3)	1 (2.9)

[(a)] One subject withdrew consent prior to taking study drug and was not part of the Intent-to-Treat population.

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Demography:	**PBO (N=35)**	**LEV (N=34)**
Gender (Females/Males):	18/17	17/17
Age (years), mean (SD):	57.21 (13.40)	53.92 (10.83)
Race, n (%):		
Caucasian	35 (100)	34 (100)

Safety Outcomes:

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

During the treatment period, 23.5% and 45.7% of the subjects treated with LEV and PBO, respectively reported treatment-emergent (TE) AEs. The most common TEAEs in the LEV and PBO treatment groups were nervous system disorders (17.6% and 20.0%, respectively). TEAE considered to be related to the study drug by the Investigator during the treatment period were reported for 14.7% and 25.7% of the subjects in the LEV and PBO groups, respectively.

No deaths were reported during this trial. One subject receiving PBO reported a drug-related serious AE (SAE) during the treatment period. One subject (2.9%) receiving LEV and 4 subjects (11.4%) receiving PBO discontinued the trial due to an AE occurring during the treatment period. One additional subject discontinued study medication intake following an AE during the stable dose period while on PBO. Since the subject had a final visit, the AE was allocated to the down-titration period.

No clinically relevant changes were observed for laboratory parameters, vital signs and body weight monitoring, physical and neurological follow up and ECG monitoring.

Treatment Emergent AEs (TEAE):	**Treatment period**	
	PBO (N=35)	**LEV (N=34)**
Subjects with at least one TEAE, n (%):	16 (45.7)	8 (23.5)
Primary System Organ Class with an incidence of ≥ 5%	*n (%) [n considered drug-related by the Investigator]*	
Nervous system disorders	7 (20.0) [5]	6 (17.6) [5]
Gastrointestinal disorders	5 (14.3) [2]	1 (2.9) [1]
Psychiatric disorders	3 (8.6) [2]	2 (5.9) [1]
General disorders and administration site conditions	2 (5.7) [1]	2 (5.9) [1]
Infections and infestations	2 (5.7) [0]	2 (5.9) [0]
Investigations	2 (5.7) [1]	0
Respiratory, thoracic and mediastinal disorders	2 (5.7) [1]	0

Death and Other SAEs:	**Treatment period**	
	PBO (N=35)	**LEV (N=34)**
Deaths, n (%):	0	0
Subjects with SAEs, n (%):	1 (2.9)	0
Primary System Organ Class	*n (%) [n considered drug-related by the Investigator]*	
Psychiatric disorders	1 (2.9) [1]	0

Primary Outcomes:

The change from Baseline on the total mean (SD) score of hyperkinesia did not statistically significantly differ between PBO (-0.34 [1.87]) and LEV (-0.21 [1.79]) treatment groups (p=0.655).

Publication Reference(s) based on the study: None

Date of report: 06-Mar-2008