Clinical Study Summary (CSS)

DEV/SGE/00568.2008

CT Registry ID#: NCT00630968
Study No.: N01031

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: RRCE04G2602

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

Name of Sponsor/Company: UCB Pharma SA

Title of Study:
A phase IV, open-label, multi-center, community-based trial studying the safety and efficacy of Keppra® as adjunctive therapy in adult patients with uncontrolled partial epilepsy.
Short title: S.K.A.T.E.: **S**afety of **K**eppra® as **A**djunctive **T**herapy in **E**pilepsy.

Investigator(s) (number only): 240

Study Center(s) (number only): 240

Length of Study:
Date first patient enrolled: 18-Aug-2000
Date last patient completed: 23-Feb-2004

Phase of Development: IV (Therapeutic use)

Abstract:
The objectives of the study were to obtain further information about the optimal dose and the efficacy of levetiracetam (LEV) in daily clinical practice and to confirm the favorable safety and tolerability profiles of the drug observed during clinical development. The primary efficacy parameters were the percentage reduction from historical baseline in seizure frequency per week for partial and total seizures over the 16-week treatment period and the retention rate at week 16, defined as the number of subjects continuing to take LEV at the end of 16-week treatment period divided by the number of subjects who took at least one dose of study medication. Safety assessments included the monitoring of adverse events (AEs) and optimal dosage. Subjects were to be male or female, ≥ 16 years old with epilepsy experiencing partial seizure, whether or not secondarily generalized (classifiable according to the International classification of Epileptic Seizure), had at least 1 and no more than 14 partial seizures per month as averaged over a 3-month historical baseline, and were taking at least 1 but no more than 2 concomitant marketed antiepileptic drugs at stable dose. The study lasted between 16 and 22 weeks for every subject. At week 16, every subject was given the opportunity to continue with LEV on Investigator's prescription or to enter a 2 to 4 weeks down-titration period followed by a safety visit. Efficacy variables were analyzed descriptively using summary statistics.

Number of Subjects:	**LEV**
Planned, N:	3000-5000
Intent-to-Treat population, N	1541
Completed, n (%):	1346 (87.3)
Number of Subjects Withdrawn, n (%):	195 (12.7)
Withdrawn due to Adverse Events, n (%):	116 (7.5)
Withdrawn due to Lack of Efficacy, n (%)	37 (2.4)
Withdrawn for Other Reasons, n (%):	42 (3.6)

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Demography:	**LEV (N=1541)**
Gender (Females/Males):	773/768
Age (years), mean (SD):	38.49 (13.77)
Race, n (%):	
Asian/Pacific Islander	14 (0.9)
Black	8 (0.5)
Caucasian	1408 (91.4)
Hispanic	91 (5.9)
Indian/Pakistani	6 (0.4)
Other	9 (0.6)
Unknown	5 (0.3)
Safety Outcomes: **- Summary of treatment emergent adverse events, deaths, other serious adverse events and certain other significant adverse events:** Overall, 60.7% of the subjects reported treatment-emergent (TE) AEs during the trial. The most common TEAEs reported during the trial were nervous system disorders (37.8% of the subjects), general disorders and administration site conditions (18.9% of the subjects), psychiatric disorders (14.3% of the subjects) and gastrointestinal disorders (11.8% of the subjects). Drug-related TEAEs were reported for 778 subjects (50.5%). Serious AEs (SAEs) were reported for 52 subjects (3.4%) of which 1 subject had an SAE with fatal outcome. The Investigator considered this SAE leading to death as not related to the study medication. For 1% of the subjects, these SAEs were reported to be drug-related. TEAEs leading to permanent study drug discontinuation occurred in 141 subjects (9.1%). The optimal dosage, i.e., the mean daily dose (SD) of exposure over the last 8 weeks of individual titration period for subjects completing the study was 2001 (805) mg.	
Treatment Emergent AEs (TEAE):	**LEV (N=1541)**
Subjects with at least one TEAE, n (%):	936 (60.7)
MedDRA Primary System Organ Class with an incidence of ≥ 10%	*n (%) [n considered drug-related by the Investigator]*
Nervous system disorders	582 (37.8) [494]
General disorders and administration site conditions	291 (18.9) [260]
Psychiatric disorders	220 (14.3) [189]
Gastrointestinal disorders	182 (11.8) [109]
Death and Other SAEs:	**LEV (N=1541)**
Death, n (%):	1 (0.1)
Subjects with SAEs, n (%):	52 (3.4)
MedDRA Primary System Organ Class with an incidence of ≥ 0.5%	*n (%) [n considered drug-related by the Investigator]*
Nervous system disorders	19 (1.2) [4]
Psychiatric disorders	11 (0.7) [9]
Gastrointestinal disorders	10 (0.6) [1]

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Primary Outcomes:
The median (Q1-Q3) percentage reduction from historical baseline in partial (Type I) and total (Type I + II + III) seizure frequency per week over the 16-week treatment period was 51.35% (0.89 - 84.45) and 50.16% (0.00 – 84.14), respectively. At the end of the 16-week treatment period, 1187 (77.0%) subjects were continuing LEV treatment.

Percentage reduction from historical Baseline	**LEV (N=1541)**
Partial seizure frequency	
N	1513
Mean (SD)	19.09 (130.85)
Median (Q1-Q3)	51.35 (0.89 - 84.45)
Total weekly seizure frequency	
N	1528
Mean (SD)	18.61 (131.08)
Median (Q1-Q3)	50.16 (0.00 - 84.14)

Publication Reference(s) based on the study: Steinhoff et al. – Epilepsy Res. 2007; 76: 6-14

Date of report: 06-Mar-2008