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Clinical Study Summary

DEV/CCM/03157.2007

CT Registry ID#: NCT00521131
Study No.: A00333

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: RRCE04C2301

Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
Xyzal® Tablets	Levocetirizine dihydrochloride	Perennial allergic rhinitis to house dust mites

Name of Sponsor/Company: UCB Pharma SA

Title of Study:
A double-blind, placebo-controlled, randomized, multicenter phase IV trial: evaluation of the efficacy, using the number of comfortable days, and of the safety of levocetirizine dihydrochloride 5 mg oral tablets, administered once daily in the evening, for 30 days, to subjects suffering from perennial allergic rhinitis to house dust mites.

Study Center(s) (number only): 74

Length of Study:
Date first patient enrolled: 09-Sep-2002
Date last patient completed: 20-May-2003

Phase of Development: IV (therapeutic use)

Abstract:
The primary objective of the study was to evaluate the efficacy of levocetirizine 5 mg (LCTZ 5 mg) in increasing the number of comfortable days over a 30-day treatment period (CD30) in subjects with perennial allergic rhinitis, to prospectively confirm the effect of LCTZ 5 mg on this new criterion. Subjects were male or female (except if pregnant, potentially pregnant or breast feeding), ≥ 12 years of age with perennial allergic rhinitis to house dust mites for > 2 years, a positive skin test or positive Radio-Allergo-Sorbent-Test for house dust mites, and having a mean Total 4 Symptoms Score ≥ 5 (T4SS; sum of the scores of the severity of sneezing, rhinorrhea, nasal pruritis and ocular prurtis) over the selection period and a T4SS ≥ 5 on the day before randomization. The primary analysis was carried out on both the intention-to-treat (ITT) and per-protocol (PP) populations. The primary efficacy variable was analyzed using an ANCOVA on the ranks model, including the ranks of the baseline CD30 as covariate and treatment as factor. Baseline CD30 was the number of comfortable days over the baseline week, adjusted for 30 days. The treatment effect was described using a 2-sided 95% confidence interval (95% CI) for the difference in the adjusted means between placebo (PBO) and LCTZ 5 mg, obtained from an ANCOVA on the original data. Safety assessments included collection of adverse events (AEs), physical examinations and vital signs.

Number of Subjects:	**PBO**	**LCTZ 5 mg**
Planned, N:	245	245
Enrolled, N:	227	226
Completed, n (%):	175 (77.1)	193 (85.4)
Number of Subjects Withdrawn, n (%):	52 (22.9)	33 (14.6)
Withdrawn due to Adverse Events, n (%):	6 (2.6)	10 (4.4)
Withdrawn for Other Reasons, n (%):	46 (20.3)	23 (10.2)
Demography:	**PBO (N=227)**	**LCTZ 5 mg (N=226)**
Gender (Females/Males):	136/91	150/76
Age (years), mean (SD):	30.63 (11.61)	31.32 (11.95)
Race, n (%):		
Caucasian	217 (95.6)	211 (93.4)
Asian/Pacific Islander	5 (2.2)	2 (0.9)
Black	4 (1.8)	13 (5.8)

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Other	1 (0.4)	0

Safety Outcomes:
- Summary of treatment-emergent adverse events (TEAEs), deaths, other serious adverse events and certain other significant adverse events:
Overall, 85 subjects (37.4%) in the PBO group and 94 subjects (41.6%) in the LCTZ 5 mg group experienced at least 1 TEAE. The most frequently reported TEAEs by SOC were nervous system disorders, experienced by 23 subjects (10.1%) in the PBO group and 41 subjects (18.1%) in the LCTZ 5 mg group. There were no deaths during the study.
Serious (S)AEs were experienced by 2 subjects, with 1 subject in the PBO group experiencing an SAE in the general disorders and administration site conditions SOC and 1 subject in the LCTZ 5 mg group experiencing an SAE in the injury, poisoning and procedural complications SOC. Neither SAE was considered related to the study drug. In the PBO group, 6 subjects (2.6%) permanently discontinued the study medication due to an AE, as did 10 subjects (4.4%) in the LCTZ 5 mg group. No clinically relevant changes in vital signs or electrocardiograms were noted.

Treatment-Emergent AEs:	**PBO (N=227)**	**LCTZ (N=226)**
Subjects with at least 1 TEAE, n (%):	85 (37.4)	94 (41.6)
Subjects with TEAEs (by System Organ Class)	*n (%) [n considered drug-related by the Investigator]*	
Ear and labyrinth disorders	1 (0.4) [0]	1 (0.4) [0]
Eye disorders	2 (0.9) [0]	1 (0.4) [0]
Gastrointestinal disorders	17 (7.5) [2]	18 (8.0) [10]
General disorders and administration site conditions	6 (2.6) [2]	15 (6.6) [8]
Infections and infestations	31 (13.7) [1]	29 (12.8) [0]
Injury, poisoning and procedural complications	0	5 (2.2) [1]
Metabolism and nutrition disorders	0	2 (0.9) [2]
Musculoskeletal and connective tissue disorders	6 (2.6) [1]	6 (2.7) [0]
Nervous system disorders	23 (10.1) [6]	41 (18.1) [23]
Psychiatric disorders	4 (1.8) [1]	1 (0.4) [0]
Renal and urinary disorders	0	1 (0.4) [1]
Reproductive system and breast disorders	4 (1.8) [0]	1 (0.4) [0]
Respiratory, thoracic and mediastinal disorders	19 (8.4) [4]	21 (9.3) [7]
Skin and subcutaneous tissue disorders	5 (2.2) [2]	4 (1.8)[3]
Vascular disorders	0	1 (0.4) [0]
Death and other significant SAEs:	**PBO (N=227)**	**LCTZ (N=226)**
Death, n (%):	0	0
Subjects with SAEs, n (%):	1 (0.44)	1 (0.44)
Subjects with SAEs (by Primary System Organ Class)	*n (%) [n considered drug-related by the Investigator]*	
Injury, poisoning and procedural complications	0	1 (0.46) [0]
General disorders and administration site conditions	1 (0.45) [0]	0

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Primary Outcomes:
On the ITT population, during treatment with LCTZ 5 mg, 3.40 comfortable days (Adjusted Means 95% CI: 1.48, 5.32) were gained compared to PBO. The difference between the 2 treatment groups was highly significant (p=0.002; ANCOVA on the ranks). On the PP population, the difference of the adjusted means between LCTZ 5 mg and PBO was slightly higher: 3.81 days in favor of LCTZ 5 mg (95% CI: 1.41, 6.20). The difference was also statistically significant (p=0.005; ANCOVA on the ranks). These results showed that LCTZ 5 mg, once daily, was statistically superior to the PBO in increasing the number of comfortable days for subjects suffering from perennial allergic rhinitis**.**

Comparison of the CD30, ITT population	**PBO (N=224)**	**LCTZ 5 mg (N=219)**
Total treatment period mean (SD)	9.36 (9.86)	12.81 (11.08)
Adjusted mean (SE)	9.38 (0.69)	12.78 (0.70)
Difference in adjusted mean (95% Cl), LCTZ 5 mg minus PBO	3.40 (1.48, 5.32)	
p-value (ANCOVA on the ranks)	0.002	

Publication Reference(s) based on the study: none

Date of report: 20-Jul-2007