Clinical Study Summary

DEV/CCM/03161.2007

CT Registry ID#: NCT00544388
Study No.: A00379

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Based on Clinical Study Report document reference code: RRCE05A0403

Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
Xyzal® Tablets	Levocetirizine dihydrochloride	Seasonal allergic rhinitis in ragweed-sensitive subjects

Name of Sponsor/Company: UCB Pharma SA

Title of Study:
Double-blind, double dummy, parallel groups, randomized, placebo-controlled exploratory clinical trial to compare the efficacy of a single dose of levocetirizine 5 mg tablets and cetirizine 10 mg tablets in reducing symptoms of seasonal allergic rhinitis in ragweed sensitive subjects exposed to pollen challenge in an environmental exposure unit (EEU)

Investigator(s) (number only): 1

Study Center(s) (number only): 1

Length of Study:
Date first patient enrolled: 20-Apr-2004
Date last patient completed: 11-Jul-2004

Phase of Development: Phase IIIb (therapeutic exploratory)

Abstract:
The primary objective of this study was to compare the efficacy of levocetirizine 5 mg (LCTZ) versus cetirizine 10 mg (CTZ) as measured by the mean change from baseline in Major Symptoms Complex (MSC) score over Period 2. The study consisted of 3 phases: Phase I (screening visit), Phase II (priming exposure) and Phase III (double-blind treatment and pollen challenge). Phase III was divided into 2 study periods: Period 1 on day 1 (5 hours after the drug intake; 11:00 to 16:00) and Period 2 on day 2 (from 21 hours after the drug intake; 8:00 to 16:00). Study medication was taken at 11:00 am on day 1 of Phase III. Subjects were male or female aged > 16 years with seasonal allergic rhinitis requiring pharmacologic therapy for the last 2 consecutive years (i.e., the last 2 ragweed pollen seasons), a documented seasonal allergy to ragweed pollen (positive skin prick test performed at screening or within 12 months prior to screening), and a Total Symptom Complex (TSC) score of ≥ 18 points over the combined 3 half-hourly post-pollen evaluations during priming exposure and over the 3 half-hourly pre-treatment evaluations during the pollen challenge. Subjects were excluded if they had a nasal obstruction > 50%, acute sinusitis within 30 days prior to study Phase II, impaired function or disease including asthma requiring > 3 uses per week of short-acting β_2-agonist, a history of malignancy or intolerance to antihistamines, or were receiving immunotherapy. Subjects were given either LCTZ, CTZ, placebo (PBO) matching LCTZ, or PBO matching CTZ as a single oral dose on Day 1 of study phase III. The primary efficacy variable was the mean change from baseline of the MSC score for Period 2 (the 16 half-hourly post-dose measurements on Day 2 from 08:30 to 16:00). The primary efficacy analysis compared LCTZ and CTZ using analysis of covariance (ANCOVA) including treatment as a factor and the baseline score as covariate. The difference between the treatment groups was estimated by the difference in least square (LS) means together with their 2-sided 95% confidence intervals (CI). Safety assessments included adverse events (AEs), vital signs and physical examinations.

Number of Subjects:	**PBO**	**CTZ**	**LCTZ**
Planned, N:	90	225	225
Enrolled, N:	95	235	240
Completed, n (%):	94 (98.9)	233 (99.1)	236 (98.3)
Number of Subjects Withdrawn, n (%):	1 (1.1)	2 (0.9)	4 (1.7)
Withdrawn due to Adverse Events, n (%):	1 (1.1)	2 (0.9)	2 (0.8)
Withdrawn for Other Reasons, n (%):	0	0	2 (0.8)

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Demography:	**PBO (N=95)**	**CTZ (N=235)**	**LCTZ (N=240)**
Gender (Females/Males):	57/38	138/97	142/98
Age (years), mean (SD):	31.22 (11.04)	33.65 (12.82)	32.33 (11.09)
Race, n (%):			
Caucasian	87 (91.6)	221 (94.0)	235 (97.9)
African	3 (3.2)	5 (2.1)	1 (0.4)
Asian/Pacific	4 (4.2)	7 (3.0)	3 (1.3)
Other/mixed	1 (1.1)	2 (0.9)	1 (0.4)

Safety Outcomes:

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

Overall, 35 subjects (14.6%) in the LCTZ group, 43 subjects (18.3%) in the CTZ group, and 15 subjects (15.8%) in the PBO group experienced ≥ 1 treatment emergent (TE) AE. The most frequently reported TEAEs were nervous system disorders (6.7% of LCTZ subjects, 8.9% of CTZ subjects, and 7.4% of PBO subjects), general disorders and administration site conditions (2.1% of LCTZ subjects, 2.6% of CTZ subjects, and 3.2% of PBO subjects), and gastrointestinal disorders (1.3% of LCTZ subjects, 3.4% of CTZ subjects, and 2.1% of PBO subjects). Two subjects (0.8%) in the LCTZ group discontinued the study because of AEs, as did 2 subjects (0.9%) in the CTZ group and 1 subject (1.1%) in the PBO group. There were no deaths or serious (S)AEs during the study.

Mean heart rate and mean blood pressure were similar at screening and at the final evaluation, as well as across the 3 treatment groups, and did not show any clinically relevant differences.

Treatment-Emergent AEs:	**PBO (N=95)**	**CTZ (N=235)**	**LCTZ (N=240)**
Subjects with at least 1 TEAE, n (%):	15 (15.8)	43 (18.3)	35 (14.6)
Subjects with TEAEs (by MedDRA Primary System Organ Class)	*n (%) [n considered drug-related by the Investigator]*		
Ear and labyrinth disorders	1 (1.1) [0]	0	0
Eye disorders	3 (3.2) [0]	2 (0.9) [0]	2 (0.8) [0]
Gastrointestinal disorders	2 (2.1) [0]	8 (3.4) [4]	3 (1.3) [1]
General disorders and administration site conditions	3 (3.2) [2]	6 (2.6) [3]	5 (2.1) [3]
Immune system disorders	0	1 (0.4) [0]	0
Infections and infestations	2 (2.1) [0]	3 (1.3) [1]	0
Injury, poisoning and procedural complications	0	1 (0.4) [0]	1 (0.4) [0]
Investigations	1 (1.1) [0]	4 (1.7) [2]	0
Musculoskeletal and connective tissue disorders	0	2 (0.9) [0]	4 (1.7) [0]
Nervous system disorders	7 (7.4) [1]	21 (8.9) [9]	16 (6.7) [1]
Psychiatric disorders	0	1 (0.4) [0]	0
Reproductive system and breast disorders	1 (1.1) [0]	1 (0.4) [0]	1 (0.4) [0]
Respiratory, thoracic and mediastinal disorders	2 (2.1) [0]	3 (1.3) [1]	4 (1.7) [0]
Skin and subcutaneous tissue disorders	1 (1.1) [1]	0	2 (0.8) [1]
Vascular disorders	0	1 (0.4)	0

Primary Outcomes:

The mean changes from baseline in MSC scores for LCTZ (-7.64) and CTZ (-7.30) were significantly greater than those for PBO (-2.42). The difference between LCTZ and PBO (-5.22), and between CTZ and PBO (-4.88) were statistically significant ($p < 0.001$). The difference between LCTZ and CTZ was -0.35 (95% CI: -1.31; 0.62), and was not statistically significant.

Publication Reference(s) based on the study: none

Date of report: 20-Jul-2007