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Clinical Study Summary

DEV/CCM/03162.2007

CT Registry ID#: NCT 00291642
Study No.: A00412

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Based on Clinical Study Report document reference code: RRCE06C0837

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

Name of Sponsor/Company: UCB PHARMA SA

Title of Study:
Double blind, double-dummy, five parallel groups, randomized, exploratory clinical trial to compare the efficacy of single dose of levocetirizine 2.5 mg oral drops (5 mg/mL), levocetirizine 5 mg oral tablets, cetirizine 5 mg oral drops (10 mg/mL) and cetirizine 10 mg oral tablets to placebo in reducing symptoms of seasonal allergic rhinitis (SAR) in ragweed sensitive subjects exposed to ragweed pollen in an Environmental Exposure Unit (EEU).

Investigator(s) (number only): 1

Study Center(s) (number only): 1

Length of Study:
Date first patient enrolled: 31-Jan-2006
Date last patient completed: 15-Apr-2006

Phase of Development: Phase II (therapeutic exploratory)

Abstract:
The primary objective was to compare the efficacy of levocetirizine (LCTZ) 2.5 mg, LCTZ 5 mg, cetirizine (CTZ) 5 mg and CTZ 10 mg versus placebo (PBO) as measured by the mean change from baseline in Major Symptoms Complex (MSC) score over Period 1, defined as the first 10 half-hourly post-dose measurements on Day 1 of study Phase III. Subjects were male or female ≥ 16 years with seasonal allergic rhinitis for the last 2 consecutive years (i.e., 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 combined 3 half-hourly pre-treatment evaluations during the pollen challenge. Subjects were given either LCTZ, CTZ, PBO matching LCTZ, or PBO matching CTZ as a single oral dose on Day 1 of study Phase III. An analysis of covariance (ANCOVA) was fitted on the change from baseline in MSC score including treatment as factor and the baseline score as a covariate. Safety was assessed by changes from predose to postdose for vital signs and physical examination results, as well as by incidence of adverse events (AE).

Number of Subjects:	**PBO**	**LCTZ 2.5 mg**	**LCTZ 5 mg**	**CTZ 5 mg**	**CTZ 10 mg**
Planned, N:	77	116	116	116	116
Enrolled, N:	78	116	119	119	119
Completed, n (%):	76 (97.4)	116 (100)	117 (98.3)	119 (100)	118 (99.2)
Number of Subjects Withdrawn, n (%):	2 (2.6)	0	2 (1.7)	0	1 (0.8)
Withdrawn due to Adverse Events, n (%):	1 (1.3)[a]	0	1 (0.8)	0	1 (0.8)
Withdrawn for Other Reasons, n (%):	1 (1.3)	0	1 (0.8)	0	0

[a] Pre-treatment AE

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Demography:	**PBO (N=78)**	**LCTZ 2.5 mg (N=116)**	**LCTZ 5 mg (N=119)**	**CTZ 5 mg (N=119)**	**CTZ 10 mg (N=119)**
Gender (Females/Males):	42/36	65/51	68/51	65/54	72/47
Age (months), mean (SD):	33.7 (12.5)	33.5 (11.3)	34.4 (12.8)	32.9 (11.3)	34.3 (11.7)
Race, n (%):					
Caucasian	74 (94.9)	108 (93.1)	116 (97.5)	112 (94.1)	116 (97.5)
African/American	1 (1.3)	2 (1.7)	1 (0.8)	1 (0.8)	1 (0.8)
Other/mixed race	1 (1.3)	4 (3.4)	1 (0.8)	2 (1.7)	1 (0.8)
Asian/Pacific	2 (2.6)	2 (1.7)	1 (0.8)	4 (3.4)	1 (0.8)

Safety Outcomes:

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

During the treatment period, 10 subjects (8.6%) in the LCTZ 2.5 mg group, 9 subjects (7.6%) in the LCTZ 5 mg group, 13 subjects (10.9%) in the CTZ 5 mg group, 7 subjects (5.9%) in the CTZ 10 mg group, and 5 subjects (6.4%) in the PBO group experienced a treatment-emergent (TE)AE. The most frequently occurring AEs during the treatment period were gastrointestinal disorders (overall incidence 2.7%), nervous system disorders (overall incidence 2.2%), and respiratory, thoracic and mediastinal disorders (overall incidence 1.8%). There were no deaths or serious (S)AEs reported during the study. Three subjects discontinued the study due to an AE: one subject (0.8%) in the LCTZ 5 mg group, one subject (0.8%) in the CTZ 10 mg group, and 1 subject (1.3%) in the PBO group. The AE in the PBO group occurred pre-treatment. These AEs were considered not related to the study medication. For mean heart rate, diastolic and systolic blood pressure, no clinically relevant difference was observed overall and in each treatment group when comparing pre-treatment and post-treatment value.

Primary & Secondary Outcomes:

The adjusted mean change from baseline in MSC score was -7.15, -7.05, -7.93 and -7.54 in the levocetirizine 2.5 mg, levocetirizine 5 mg, cetirizine 5 mg and cetirizine 10 mg groups, respectively. In the placebo group the change from baseline was -3.80. The individual comparisons of each active treatment versus placebo were also highly statistically significant ($p < 0.001$).

Publication Reference(s) based on the study: None

Date of Report : 20-Jul-2007