Clinical Study Summary

DEV/SGE/04568.2007

CT Registry ID#: NCT00315523
Study No.: A00415

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Based on Clinical Study Report document reference code: RRCE07A0404

Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
Xyzal® Tablet	Levocetirizine dihydrochloride	Seasonal Allergic Rhinitis in ragweed sensitive subjects

Name of Sponsor/Company: UCB Pharma S A

Title of Study: Double-blind, three parallel randomized groups, therapeutic confirmatory clinical trial to compare the efficacy of oral levocetirizine 5 mg and montelukast 10 mg to placebo in reducing symptoms of seasonal allergic rhinitis in ragweed sensitive subjects exposed to ragweed pollen in an environmental exposure chamber

Investigator(s) (number only): 1

Study Center(s) (number only): 1

Length of Study:
Date first patient enrolled: 15-Jul-2006
Date last patient completed: 23-Oct-2006

Phase of Development: Phase III (therapeutic confirmatory study)

Abstract:

The primary study objective was to compare the efficacy of levocetirizine 5 mg and montelukast 10 mg as measured by the mean change from Baseline in the Major Symptom Complex (MSC score) over Period I (Day 1, from drug intake to five hours post-treatment).

The Study consisted of three phases: Phase I (Screening visit); Phase II (Priming exposure) and Phase III (Randomization). During Phase II unmedicated response after exposure to ragweed pollen in the environmental exposure unit was assessed by the eligibility criteria. During Phase III eligible subjects were randomized to the double-blind treatment and exposed to pollen (concentration 3500 ± 500 grains/m^3) for seven hours on Day 1 and six hours on Day 2.
The subjects were male or female adults, *i.e.* aged ≥ 18 years with a clinical history of seasonal allergic rhinitis due to ragweed for the last two consecutive years (*i.e.* last two ragweed pollen seasons); a documented seasonal allergy to ragweed pollen (positive skin test ≥ 3 mm larger than the negative control) performed at the Screening Visit or within 12 months of the Screening Visit; and a Total Symptom Complex Score ≥ 18 points over the combined three half-hourly post-pollen evaluations during priming exposure and over the combined three half-hourly pre-treatment evaluations during the pollen challenge.
The subjects were given levocetirizine 5 mg, montelukast 10 mg or placebo on Day 1 and Day 2 of the pollen challenge, 2 hours and 1.5 hours, respectively, after the start of exposure.

The primary efficacy variable was analyzed using an analysis of covariance (ANCOVA) on the Intention-to-Treat (ITT) population. The pair-wise treatment group differences were estimated by the difference in Least Square means together with 95% Confidence Interval (CI).
Safety assessments included physical examinations, adverse events and vital signs on the ITT population.

Number of Subjects:	**LCTZ**	**MLKT**	**PBO**
Planned, N:	151	151	101
Enrolled, N:	152	149	102
Completed, n (%):	151 (99.3%)	145 (97.3%)	100 (98.0%)

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Number of Subjects Withdrawn, n (%):	1 (0.7%)	4 (2.7 %)	2 (2.0%)
Adverse event, n (%):	0 (0.0%)	3 (2.0%)[a]	1 (1.0%)
Other reasons, n (%):	1 (0.7%)[b]	0 (0.0%)	1 (1.0%)[c]
Withdrawal of consent, n (%):	0 (0.0%)	1 (0.7%)	0 (0.0%)

[a] Reason: One was a pre-treatment AE
[b] Reason: "Non compliance (did not meet inclusion criteria #8)"
[c] Reason: "Motor vehicle accident on patient's way in)"

Demography:	**LCTZ**	**MLKT**	**PBO**
Gender (Females/Males):	87/65	86/63	62/40
Age (years), mean (SD):	38.58 (12.70)	34.63 (11.71)	38.24 (14.00)
Caucasian, n (%):	83 (54.6%)	78 (52.3%)	48 (47.1%)

Safety Outcomes:
Summary of treatment emergent adverse events, deaths, other serious adverse events and certain other significant adverse events:
Sixty-three subjects had treatment emergent AEs (TEAEs), among them 24 were in the levocetirizine 5 mg group. In this group, 9.2% of subjects presented TEAEs that were considered related to study medication (compared to 10.8% in the placebo group, and 8.1% in the montelukast 10 mg group). No subject in the levocetirizine 5 mg group reported a TEAE leading to permanent study drug discontinuation (one subject in the placebo group and one in the montelukast 10 mg group). The most frequent AEs that occurred during treatment were 'Headache' and 'Abdominal pain', followed by 'Fatigue'. Neither death nor serious adverse events occurred throughout the study. No clinically relevant changes in vital signs were noted.

Treatment Emergent Adverse Events (ITT population):	**LCTZ (N = 152)**	**MLKT (N = 149)**	**PBO (N = 102)**
Subjects with at least one TEAE, n (%):	24 (15.8%)	19 (12.8%)	20 (19.6%)
Subjects with a TEAE that led to permanent study drug discontinuation, n (%):	0 (0.0%)	1 (0.7%)	1 (1.0%)
Subjects with TEAEs, *n* (%) [*considered drug-related by the Investigator]*: (*by Primary System Organ Class*)	14 (9.2%)	12 (8.1%)*]*	11 (10.8%)
Ear and labyrinth disorders, n (%):	0 (0.0%)	1 (0.7%)	0 (0.0%)
Gastrointestinal Disorders, n (%):	2 (1.3%)	3 (2.0%)	4 (3.9%)
General Disorders and Administration Site Conditions, n (%):	2 (1.3%)	0 (0.0%)	1 (1.0%)
Infections and infestations, n (%):	0 (0.0%)	1 (0.7%)	0 (0.0%)
Nervous System Disorders, n (%):	9 (5.9%)	5 (3.4%)	6 (5.9%)
Respiratory, thoracic and mediastinal disorders n (%):	0 (0.0%)	1 (0.7%)	0 (0.0%)
Skin and Subcutaneous Tissue Disorders, n (%):	2 (1.3%)	4 (2.7%)	1 (1.0%)
Vascular disorders n (%):	0 (0.0%)	0 (0.0%)	2 (2.0%)

Primary Outcome:
The comparison of change from Baseline of the MSC score during Period I indicated a statistically significant difference between levocetirizine 5 mg and montelukast 10 mg and also between levocetirizine 5 mg and placebo, in favor of levocetirizine 5 mg.

ANCOVA on Period I	**Difference LCTZ *vs.* MLKT (ITT population)**	**Difference LCTZ *vs.* PBO (ITT population)**
Adjusted Mean [95% CI]	-2.18 [-3.35;-1.01]	-2.22 [-3.51;-0.92]
p-value	<0.001	<0.001

Publication Reference (s) based on the study: None

Report Date: 13-Dec-2007