UCB reference No.: RXCE06E1643

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Clinical Study Summary

DEV/CCM/03156.2007

CT Registry ID#: NCT00521040
Study No.: A00306

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: **RRCE04M0203**

Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
Xyzal® Tablets	Levocetirizine dihydrochloride	Seasonal allergic rhinitis associated with pollen-induced asthma

Name of Sponsor/Company: UCB Pharma SA

Title of Study:
A double-blind, parallel, placebo-controlled, 3 arms, randomized study: evaluation of the efficacy and safety of levocetirizine 5 mg oral tablets, administered during 8 weeks preceding and during 8 weeks following the anticipated onset of the grass pollen season, in subjects suffering from seasonal allergic rhinitis associated with pollen-induced asthma

Investigator(s) (number only): 53

Study Center(s) (number only): 53

Length of Study:
Date first patient enrolled: 21-Feb-2004
Date last patient completed: 31-Jul-2004

Phase of Development: II (therapeutic exploratory)

Abstract:
The primary objective of the study was to evaluate the efficacy of levocetirizine 5 mg/day (LCTZ), as an early started treatment, versus placebo (PBO), to reduce the symptoms of rhinitis observed over a 12-week period following randomization. Evaluation of the efficacy was performed by the analysis of the Total 4 Symptoms Score (T4SS; sum of the scores of the severity of sneezing, rhinorrhea, nasal pruritus and ocular pruritus). Subjects were male or female, ≥ 12 years of age, with a ≥ 2 year history of seasonal allergic rhinitis that became symptomatic during the annual grass pollen season, a documented hypersensitivity to grass pollen, without an acute ongoing exacerbation of asthma or allergic rhinitis present at the study entry, no continuous ongoing treatment for rhinitis or asthma, and a documented pollen-induced asthma (clear exacerbation of symptoms at the grass pollen season) with ≥1 asthma exacerbation over the past 3 years. Subjects were treated for a total of 16 weeks starting 8 weeks before the anticipated onset of the grass pollen season. There were 3 treatment groups: subjects in the PBO/PBO group received PBO for 16 weeks; subjects in the LCTZ/LCTZ group received LCTZ for 16 weeks; and subjects in the PBO/LCTZ group received PBO for 8 weeks followed by LCTZ for 8 weeks. All statistical tests were 2-tailed at the 5% level of significance, unless otherwise stated. The primary efficacy variable was analyzed on the intention-to-treat (ITT) population as weekly mean T4SS using a repeated measures model including terms for treatment (PBO/PBO and LCTZ/LCTZ), week (week 1 up to 16), treatment by week, and center with an unstructured variance-covariance matrix. The treatment comparison was performed via a contrast over the first 12 weeks. Safety assessments were made by collection of adverse events (AEs) and physical examination abnormalities.

Number of Subjects:	**PBO/PBO**	**LCTZ/LCTZ**	**PBO/LCTZ**
Planned, N:	100	100	100
Enrolled (randomized and treated), N:	156	150	153
Completed, n (%):	133 (85.5)	127 (84.7)	131 (85.6)
Number of Subjects Withdrawn, n (%):	23 (14.7)	23 (15.3)	22 (14.4)
Withdrawn due to Adverse Events, n (%):	5 (3.2)	9 (6.0)	5 (3.3)
Withdrawn for Other Reasons, n (%):	18 (11.5)	14 (9.3)	17 (11.1)

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Demography:	**PBO/PBO (N=156)**	**LCTZ/LCTZ (N=150)**	**PBO/LCTZ (N=153)**
Gender (Females/Males):	72/84	86/64	98/55
Age (years), mean (SD):	30 (11.5)	32 (12.4)	31 (11.4)
Race, n (%):			
Caucasian	151 (96.8)	143 (95.3)	144 (94.1)
African/American	2 (1.3)	5 (3.3)	7 (4.6)
Asian/Pacific Islander	2 (1.3)	2 (1.3)	1 (0.7)
Other/mixed Race	1 (0.6)	0	1 (0.7)

Safety Outcomes:

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

During the treatment period, 83 subjects (53.2%) in the PBO/PBO group, 90 subjects (60.0%) in the LCTZ/LCTZ group and 77 subjects (50.3%) in the PBO/LCTZ group experienced treatment emergent (TE)AEs. The most frequently reported TEAEs according to SOC (≥ 20% of subjects) were infections and infestations and nervous system disorders. The most frequently reported drug-related TEAEs (≥ 3% according to SOC) were nervous system disorders and general disorders and administration site conditions and gastrointestinal disorders. There were no deaths during the study. Serious AEs were reported by 3 subjects during the study (2 subjects [1.3%] in the LCTZ/LCTZ group and 1 subject [0.65%] in the PBO/LCTZ group), none were considered drug related. A total of 19 subjects (4.1%) discontinued study drug due to TEAEs; 5 subjects (3.2%) in the PBO/PBO group, 9 subjects (6.0%) in the LCTZ/LCTZ group and 5 subjects (3.3%) in the PBO/LCTZ group.

Treatment Emergent AEs:	**PBO/PBO (N=156)**	**LCTZ/LCTZ (N=150)**	**PBO/LCTZ (N=153)**
Subjects with at least 1 TEAE, n (%):	83 (53.2)	90 (60.0)	77 (50.3)
Subjects with TEAEs (by Primary System Organ Class)	*n (%) [n considered drug-related by the Investigator]*		
Infections and infestations	35 (22.4) [1]	41 (27.3) [1]	30 (19.6) [0]
Nervous system disorders	32 (20.5) [5]	31 (20.7) [9]	30 (19.6) [5]
Respiratory, thoracic and mediastinal disorders	19 (12.2) [0]	23 (15.3) [1]	28 (18.3) [1]
Gastrointestinal disorders	14 (9.0) [2]	19 (12.7) [7]	23 (15.0)[7]
General disorders and administration site conditions	11 (7.1) [4]	20 (13.3) [9]	9 (5.9) [4]
Skin and subcutaneous tissue disorders	9 (5.8) [1]	7 (4.7) [3]	9 (5.9) [1]
Musculoskeletal and connective tissue disorders	7 (4.5) [0]	8 (5.3) [1]	8 (5.2) [0]
Psychiatric disorders	4 (2.6) [1]	4 (2.7) [2]	7 (4.6) [1]
Injury and poisoning and procedural complications	4 (2.6) [0]	5 (3.3) [0]	5 (3.3) [0]
Reproductive system and breast disorders	2 (1.3) [0]	6 (4.0) [0]	3 (2.0) [0]
Ear and labyrinth disorders	2 (1.3) [0]	0	6 (3.9) [2]
Investigations	2 (1.3) [1]	3 (2.0) [2]	0
Vascular disorders	4 (2.6) [0]	0	0
Immune system disorders	1 (0.6) [0]	1 (0.7) [0]	1 (0.7) [0]
Cardiac disorders	1 (0.6) [0]	0	1 (0.7) [0]
Eye disorders	1 (0.6) [0]	1 (0.7) [0]	0
Hepatobiliary disorders	0	2 (1.3) [0]	0
Surgical and medical procedures	2 (1.3) [0]	0	0
Endocrine disorders	0	1 (0.7) [0]	0
Social circumstances	0	0	1 (0.7) [0]

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Death and other significant SAEs:	**PBO/PBO (N=156)**	**LCTZ/LCTZ (N=150)**	**PBO/LCTZ (N=153)**
Death, n (%):	0	0	0
Subjects with SAEs, n (%):	0	2 (1.3)	1 (0.7)
Subjects with SAEs (by Primary System Organ Class)	*n (%) [n considered drug-related by the Investigator]*		
Gastrointestinal disorders	0	1 (0.7) [0]	0
Respiratory, thoracic and mediastinal disorders	0	0	1 (0.7) [0]
Reproductive system and breast disorder	0	1 (0.7) [0]	0
Primary Outcomes: **Primary analysis of efficacy:** Early initiation of LCTZ significantly reduced the symptoms of rhinitis compared with PBO over the first 12 weeks of the study; in the primary analysis of efficacy, the adjusted mean difference in T4SS between groups was 0.65 (95% CI: 0.27, 1.03; $p < 0.001$).			
Comparison of mean T4SS over the first 12 weeks of the study - ITT population	**PBO/PBO (N=155)**	**LCTZ/LCTZ (N=148)**	
Descriptive mean (SD)	2.25 (1.72)	1.64 (1.80)	
Inferential adjusted mean (SE)	2.27 (0.15)	1.61 (0.15)	
Difference in adjusted mean (95% CI), LCTZ/LCTZ vs PBO/PBO	0.65 (0.27;1.03)		
p-value	< 0.001		
Publication Reference(s) based on the study: none			
Date of report: 20-Jul-2007			