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Clinical Study Summary (CSS)

DEV/SGE/00910.2008

CT Registry ID#: NCT00150761
Study No.: A00380

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Based on Clinical Study Report document reference code: RRCE04F1405

Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
Xyzal® Tablets	Levocetirizine dihydrochloride	Allergy

Name of Sponsor/Company: UCB Pharma SA

Title of Study: A randomized, double-blind, double dummy, placebo controlled, cross-over exploratory trial in healthy male adult subjects. Comparison by means of infrared thermography of the anti-H1 potency of levocetirizine 5 mg and cetirizine 10 mg tablet single oral dose after nasal histamine provocation.

Investigator(s) (number only): 1

Study Center(s) (number only): 1

Length of Study:
Date first patient enrolled: 05-Jul-2004
Date last patient completed: 05-Oct-2004

Phase of Development: Phase IV (human pharmacology)

Abstract:
The objectives of this study were: 1- to compare by means of infrared (IR) thermography the anti-histaminic potency of levocetirizine (LEV) 5 mg (single dose) and cetirizine (CET) 10 mg (single dose), using a placebo (PLC) as control following 2 nasal histamine provocations (NHP) performed 10 min before and 2 hours after study medication intake, respectively. Thermography recordings started 13 min before and ended 135 min after study medication intake; 2- to assess and compare the onset action of LEV 5 mg and CET 10 mg; 3- to explore the predictive value of screening thermography parameters on treatment effect; 4- to collect additional information on the safety of LEV. The pharmacodynamic variables of interest were: 1- the mean and maximum temperature change from baseline post NHP recorded in the intervals 0-110 min and 120-135 min after study medication intake; 2- the mean, minimum, and maximum temperature observed in the intervals 0-110 min and 120-135 min after study medication intake; 3- the shortest time to the maximum temperature change from baseline in the intervals 0-110 min and 120-135 min after study medication intake; 4- the number (percentage) of subjects who experienced temperature changes (decrease in Session 1 and increase in Session 2) of 0.25, 0.50, 0.75, 1.00, 1.25, 1.50, and 1.75 °C from baseline post NHP recorded in the intervals 0-110 min and 120-135 min after study medication intake; the relative change from baseline post NHP in temperature for LEV and CET measured over every minute during each recording interval; 5- the onset of action of LEV and CET (based on relative change from baseline post NHP in temperature); and 6- the baseline temperature before nasal saline provocation and the mean temperature increase from baseline at screening visit measured during the interval 0-15 min after a nasal saline provocation and a nasal histamine provocation. Safety assessments included the monitoring of adverse events (AEs), physical examination, and vital signs. Subjects were to be healthy male subjects, aged between 18 and 55 years inclusive, with a BMI between 19 and 27 kg/m² inclusive, no history of allergy, absence of current acute rhinitis, and no nasal structural abnormalities, hot flushes and other vasomotor disorders, ENT or upper respiratory tract infection, history of immediate-onset hypersensitivity or of laryngeal edema, or any vascular disease (hypertension, vasculitis, and venous disorder. The study consisted of a 21-day screening period and a treatment period which was divided into 3 periods, each lasting 1 day with a washout period of 7 days between the periods. Each subject received one dose of LEV, CET, or PLC at visits V2, V3 and V4 on a random basis. In each treatment period, 2 NHPs were carried out 10 min before and 120 min after study drug intake. For each pharmacodynamic thermography variable, a descriptive analysis was performed. Continuous pharmacodynamic variables (mean temperature

CT Registry ID#: NCT00150761
Study No.: A00380

change from baseline post NHP, maximum temperature change, time to maximum temperature change, and individual onset of action) were evaluated according to a univariate model of ANCOVA, adapted to a 3-way cross-over design. The covariate was the difference in baseline temperature post NHP minus pre NHP (Session 1) or baseline temperature pre NHP (Session 2). Treatment least-squares means (LSM) and 95% confidence intervals of difference of LSM means were calculated. The primary comparison was between LEV and CET. PLC was used as control. Thermography recordings started with the per protocol planned ThermaCAMTM SC500 camera from FLIR SystemsTM. This camera broke down during the study and was replaced by a SC300 model. Since the sensitivity of the SC300 camera was lower than that of the SC500 (0.1°C vs. 0.07°C, respectively) and could therefore potentially jeopardize the results of the study, the trial was stopped before completion.

Number of Subjects:	**Overall**
Planned, N:	60
Enrolled, N:	53
Completed with SC500 camera, n (%):	29 (54.7)
Completed with SC500 and SC300 camera, n (%):	6 (11.3)
Not completed due to premature study stop, n (%):	17 (32.1)
Number of Subjects Withdrawn, n (%):	1 (1.9)
Withdrawn due to Adverse Events, n (%):	1 (1.9)
Demography:	**Overall (N=53)**
Gender (Females/Males):	0/53
Race, n (%):	
Caucasian:	53 (100)

Safety Outcomes:

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

Overall, 9.1%, 15.6% and 20.9% of subjects reported treatment-emergent (TE) AEs during treatment with LEV, CET, and PLC, respectively. The most commonly reported class of TEAEs during treatment with LEV, CET and PLC were nervous system disorders (6.8%, 8.9%, and 4.7% of subjects, respectively), gastrointestinal disorders (0%, 6.7%, and 0% of subjects, respectively), and respitatory, thoracic and mediastinal disorders (0%, 0%, and 4.7% of subjects, respectively). Drug-related TEAEs were reported for 6.8%, 6.7%, and 4.7% of subjects during treatment with LEV, CET, and PLC, respectively.

No serious AEs were reported during the study. One subject permanently discontinued the study due to an AE of migraine after LEV treatment.

Treatment Emergent AEs (TEAE):	**PLC (N=43)**	**LEV (N=44)**	**CET (N=45)**
Subjects with at least one TEAE, n (%):	9 (20.9)	4 (9.1)	7 (15.6)
MedDRA Primary System Organ Class with an incidence of ≥3%:	*n (%) [n considered drug-related by the Investigator]*		
Nervous system disorders	2 (4.7) [2]	3 (6.8) [3]	4 (8.9) [3]
Gastrointestinal disorders	0	0	3 (6.7) [1]
Respiratory, thoracic and mediastinal disorders	2 (4.7) [0]	0	0

CT Registry ID#: NCT00150761
Study No.: A00380

Primary and Secondary Outcomes:

The mean nasal temperature before first NHP was around 31.8°C in all 3 groups. In all groups, a mean nasal temperature increase of about 0.6°C was observed after the first NHP and before study drug intake. In the interval 0-50 min after study drug intake, a mean nasal temperature decrease of about 0.57°C, 0.51°C, and 0.53°C from baseline in the LEV, CET, and PLC groups, respectively was observed. The difference between the treatment groups was not statistically significant. In the interval 60-110 min after study drug intake, the mean nasal temperature decrease was 1.30°C, 1.32°C, and 1.19°C after LEV, CET, and PLC, respectively. No statistical differences were found. LEV and CET profiles were similar.

The results found after the second NHP were similar to those in previous studies. LEV and CET appear to be active about 20 min and beyond 50 min, respectively, after study drug intake. However, no significant differences were found. Beyond 60 min, both anti-H1 drugs were similar.

Publication Reference(s) based on the study: None

Date of report: 29-May-2008