Effect Of Loratadine Tablets on the Symptomatic Control Of Seasonal Allergic Rhinitis in Adults Challenged with Ragweed Pollen in the Environmental Exposure Unit in Compassion with Azelastine Nasal Spray with Loratadine Tablets, Cetirizine Tablets, and Placebo: A Post Hoc Analysis of Total Symptom Score

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Abstract

Loratadine is a second-generation, non-sedating antihistamine used for the relief of allergic rhinitis symptoms. Previous studies reported that when loratadine was encapsulated, the onset of action for symptom relief was 180 min. However, unmodified loratadine tablets were not evaluated at that time. Using data from a previously published Environmental Exposure Unit (EEU) study comparing azelastine nasal spray with loratadine tablets, cetirizine tablets, and placebo, this post hoc analysis determines the onset of action of loratadine tablets, by analyzing the total symptom score for the relief of nasal and ocular seasonal allergic rhinitis (SAR) symptoms.

Keywords: Allergic rhinitis, Environmental Exposure, Loratadine, Commencement of action,

Ragweed pollen, Seasonal allergies, Outdoor allergy.

Introduction

A Phase IV, randomized, single-center, double-blind, placebo-controlled, double-dummy, four-way crossover study was conducted in the EEU. Seventy participants were randomized sequentially into one of the four treatments during ragweed pollen exposure. Nasal and ocular symptom scores were self-reported by the participants and recorded. The original study analysis was carried out by evaluating the nasal symptom scores only. For this post hoc analysis, both nasal and ocular data from the loratadine and placebo treatment arms were analyzed. The primary endpoint for this analysis was the Commencement of action of loratadine as measured

by the change in total symptom score (TSS) from baseline in comparison to placebo. The onset of ocular symptom relief using the total ocular symptom score (TOSS) was also reported.

Method of study Design and Treatment:

The study was conducted in the EEU and was comprised of a screening visit, a priming period, and four dosing / exposure periods with a 13-day washout between periods (Fig.I). After eligibility was determined, qualifying participants were randomized to a treatment sequence comprised of one dose of each of the four study medications, azelastine, nasal spray, loratadine tablet, cetirizine tablet, and placebo. All study treatments were administered as a combination of an oral tablet (active or placebo) and nasal spray (active or placebo) to maintain study blinding.

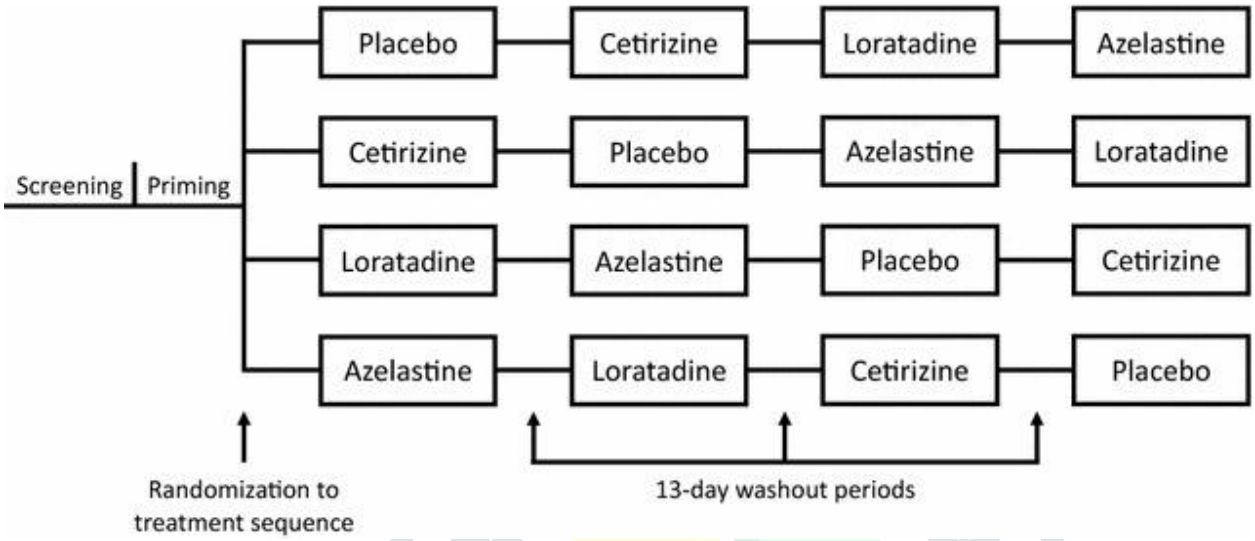

Fig: I Study Diagram

Each dosing period consisted of an 8-h ragweed pollen challenge in the EEU (mean pollen levels of 3500 ± 500 grains/m^3). The level of pollen used is consistent with other EEU studies used to determine the onset of allergy products and provides consistent symptomatic responses in a predictable time frame at a relevant pollen exposure level. Participants were administered their assigned treatment 2 h into the challenge. Nasal and ocular symptom severity was recorded by each participant at designated time points during the challenge. Symptom severity was rated on a scale of 0-3 (0= none, 1= mild, 2= moderate, 3= severe.) (Table: I). Appropriate combinations of symptoms comprised the total nasal symptom score **(TNSS).** total ocular symptom score **(TOSS).** and total symptom score **(TSS) are** an omnibus score comprised of all nasal and ocular symptoms are given in Fig:2

Table: I

Rating scale for symptoms of seasonal allergic rhinitis

Score	Grade	Guideline
0	None	No sign/symptom is evident
1	Mild	Sign/symptom clearly present, but minimal awareness; easily tolerated
2	Moderate	Definite awareness of sign/symptom that is bothersome, but tolerable
3	Severe	Sign/symptom are hard to tolerate, causes interference in session activity

Table: II

Total Nasal and **Total Ocular** symptoms of seasonal allergic rhinitis

Symptom	TNSS	TOSS	TSS
Runny Nose	X		X
Sneezing	X		X
Nasal Itching	X		X
Itchy/red/gritty eye		X	X
Watery eyes		X	X

TNSS total nasal symptom score, TOSS total ocular symptom score, TSS total symptom score

Total scores were the sum of each individual symptom score (rated between 0 and 3); TNSS (0–9), TOSS (0–6), TSS (0–15)

Results

Participant demographics

A total of 70 participants were randomized into the study. Four participants did not complete all four dosing periods and were excluded from the PP population. Briefly, the mean age (SD) was 35 (9.9) years and the majority of participants were Caucasian (97%) (Table 3). Nasal and ocular composite symptom scores were measured at baseline and summarized in Table 4.

Table: III

Summary of participant demographics

Characteristics	Overall (n = 66)
Mean age in years (SD)	35.0 (9.9)
Female (%)	39 (59)
Race (%)	
Caucasian	64 (97)
Black	0 (0)
Asian	2 (3)
American Indian/Alaska Native	0 (0)
Native	0 (0)

Hawaiian/Other Pacific Islander	
Other	0 (0)

Table: IV

Baseline symptom scores

Baseline symptom scores (SD)[a]	**Loratadine (n = 66)**	**Placebo (n = 66)**
TNSS	6.9 (1.7)	6.5 (1.8)
TOSS	4.0 (1.5)	3.7 (1.7)
TSS	10.9 (2.6)	10.2 (3.0)

Baseline symptom scores were collected immediately prior to dosing (i.e. 2 h after the start of allergen challenge on study day)

Safety

In this study, loratadine was well tolerated. Sixty-eight and 69 participants received one dose of loratadine and placebo respectively. Serious adverse events or deaths were not reported during the dosing periods. A total of 12 and 5 adverse events (AEs) were reported in the loratadine (4 mild and 8 moderate) and placebo (2 mild and 3 moderate) groups respectively. Only one report of mild urticaria was considered possibly related to the study medication (loratadine) (Table5).

Table: V

	Loratadine (n = 68)	**Placebo (n = 69)**
Number of participants reporting ≥ 1 AEs (%)		7 (10)
Number of AEs reported	12	5
Serious (%)		
No	12 (100)	5 (100)
Yes	0 (0)	0 (0)
Severity of AE (%)		
Mild	4 (33)	2 (40)
Moderate	8 (67)	3 (60)
Severe	0 (0)	0 (0)
Possible relationship to study medication (%)		
Not possibly related	11 (92)	5 (100)
Possibly related	1 (8)	0 (0)

Conclusion

The current post hoc analysis demonstrated an onset of action of 75 min for unmodified loratadine tablets. The longer onset of action previously reported by Day et al. is most likely attributed to a delayed release of loratadine from an over-encapsulated tablet that was evaluated in the study. As bioequivalence cannot be assumed between loratadine dosage forms, and since the active is a BCS Class II drug, one must be mindful when interpreting onset data generated with dosage forms that have been altered from their origin.

Abbreviations Used

AR allergic rhinitis

BCS Biopharmaceutics Classification System

EEU Environmental Exposure Unit

SAR seasonal allergic rhinitis

TNSS total nasal symptom score

TOSS total ocular symptom score

TSS total symptom score

PP per protocol

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