

Two-week comparison study of olopatadine hydrochloride nasal spray 0.6% versus azelastine hydrochloride nasal spray 0.1% in patients with vasomotor rhinitis

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ABSTRACT

Olopatadine hydrochloride nasal spray 0.6% (OLO) and azelastine nasal spray 137 micrograms (AZE) are effective in treating allergic rhinitis and AZE is indicated for nonallergic vasomotor rhinitis (VMR). This study evaluates the relative safety and efficacy of OLO and AZE in patients with VMR. This randomized, double-blind, parallel-group, multicenter study compared OLO (an investigational use) with AZE over 14 days in patients ($n = 129$) ≥ 12 years of age with chronic VMR. Efficacy included the severity of nasal symptom scores. Safety included adverse events (AEs) and nasal examinations. Patient perceptions of treatment satisfaction and changes in allergy condition were determined using the Treatment Satisfaction Questionnaire for Medication and Patient Global Assessment scores. In the OLO and AZE groups, reflective scores for individual nasal symptoms (nasal congestion, rhinorrhea, postnasal drip, and sneezing) and total nasal VMR symptom scores decreased significantly from baseline to day 14 ($p < 0.05$). No significant between-group differences were observed ($p > 0.05$). No serious AEs were reported in either group. Overall, 22 and 20 AEs were reported in the OLO and AZE groups, respectively. The most common AE was taste disturbance, reported by three (5.3%) and six (10.3%) patients in the OLO and AZE groups, respectively. Patients in both groups reported similar treatment satisfaction scores and a majority of patients in both groups perceived an overall improvement in their rhinitis condition. OLO has a similar efficacy and safety profile to AZE for the management of VMR in patients ≥ 12 years of age.

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Vasomotor rhinitis (VMR; perennial nonallergic rhinitis) is a chronic, noninfectious condition that affects between 5 and 10% of the general population.^{1,2} The clinical presentation of VMR and allergic rhinitis share overlapping symptoms, including varying degrees of nasal congestion, rhinorrhea, postnasal drip, sneezing, and nasal itching.¹ However, unlike allergic rhinitis that is provoked by specific antigens, VMR is not related to allergen exposure and may be triggered by environmental factors such as changes in temperature and/or humidity, strong odors, and airborne irritants, as well as hormonal changes and the ingestion of spicy foods or alcoholic beverages.^{3,4} Because VMR and allergic rhinitis have similar clinical presentations, a diagnosis of VMR is established by patient history

and confirmed by negative allergy skin tests to local aeroallergens.^{1,3,5}

The management of VMR consists of the avoidance of environmental triggers in combination with medication, including intranasal antihistamines, anticholinergics, and/or corticosteroids.¹ Intranasal antihistamines, in particular, are an effective option for the treatment of nonallergic VMR.³

Olopatadine hydrochloride nasal spray 0.6% (OLO; Patanase; Alcon Laboratories, Fort Worth, TX) and azelastine HCl nasal spray 0.1% (AZE; Astelin; Meda Pharmaceuticals, Somerset, NJ) are intranasal antihistamines. OLO is indicated for the relief of the symptoms of seasonal allergic rhinitis in adults and children ≥ 6 years of age, and AZE is indicated for the treatment of nasal symptoms of seasonal allergic rhinitis (patients ≥ 5 years of age) and nonallergic VMR (patients ≥ 12 years of age).^{6,7} Results from clinical studies with OLO have indicated the efficacy of OLO in the treatment of the nasal symptoms of seasonal allergic rhinitis.^{8–13} Although a recent clinical study reported OLO as effective as AZE in providing relief from the nasal symptoms of seasonal allergic rhinitis, OLO has not been previously evaluated for the treatment of VMR.^{13,14} Thus, the current randomized, double-blind, parallel-group, multicenter study was designed to evaluate the efficacy of OLO (an investigational use) relative to AZE

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when administered twice daily for 2 weeks in patients ≥ 12 years of age with a diagnosis of VMR.

PATIENTS AND METHODS

Inclusion and Exclusion Criteria

Eligible for inclusion in this study were patients ≥ 12 years of age with a diagnosis of VMR and at least a 2-year history of chronic rhinitis symptoms related to defined triggers (*e.g.*, changes in climate, strong smells, and tobacco smoke). Patients must have had a positive histamine skin-prick test and a history of negative responses to panel tests of seasonal and perennial allergens common to the local geographic area. Patients also must have been symptomatic, with a total VMR symptom score (TVSS) satisfying a threshold level of ≥ 6 and must not have had any significant anatomic abnormalities, infections, bleeding, or mucosal ulcerations of the nose. Patients must not have had any concurrent diseases that might have interfered with the evaluation of the study medication, required the use of prohibited medications, or had a history of asthma more severe than mild-intermittent. Patients were excluded if they used inhaled or ocular corticosteroids within 14 days before study entry; used systemic corticosteroids within 30 days before study entry; did not complete the appropriate washout period; used long-acting antihistamines; or chronically or intermittently used inhaled, oral, intramuscular, *i.v.*, dermal potent, or super potent topical corticosteroids. Patients who used either OLO or AZE must have discontinued use at least 7 days before the study randomization visit.

Test Articles

The study medications (OLO and AZE) were supplied in commercial packaging with foil overwraps specifically designed to mask the test articles to the patients and all study personnel. Patients were instructed not to discuss the appearance or any other aspects of their treatments with the investigator or study staff. Patients administered 2 sprays of study medication (OLO or AZE) into each nostril twice daily (morning and evening) for 2 weeks (14 days).

Study Design

This was a randomized, double-blind, parallel-group, multicenter study comparing OLO versus AZE in patients with VMR. Approximately 120 patients were planned for enrollment at 8–12 sites in the United States. This study included four in-office visits.

At the screening visit (visit 1), patients provided informed consent; were evaluated for eligibility; described their VMR symptoms, medical histories, and concomitant medication usages; underwent diagnostic allergy tests if not previously performed within the last 2 years; and had brief physical examinations. At the

conclusion of the visit, eligible patients began a washout period for prohibited medications. If no washout was needed, visit 2 procedures may have been conducted on the same day.

At visit 2 (day 0), patients were rescreened for eligibility and medical histories and concomitant medication usages were updated. Patients then underwent a nasal examination to confirm the absence of significant anatomic anomalies. After the examination, patients rated each of their current nasal VMR symptoms (rhinorrhea, postnasal drip, nasal congestion, and sneezing) on a scale ranging from 0 (absent) to 3 (severe). Based on these individual symptom scores, the investigators calculated the TVSS. Eligible patients were randomly assigned to treatments in a 1:1 ratio and in sequential order to study medication (OLO or AZE) in accordance with an electronically generated schedule that was blocked within sites to ensure a balance of treatment assignments. Finally, at this visit, patients received diaries in which they recorded the severity of their nasal VMR symptoms twice daily before dosing (on awakening and before bedtime) for 14 days. Symptoms were reported both instantaneously (*i.e.*, as experienced at that moment) and reflectively (*i.e.*, as experienced since the last dose of study medication).

During visit 3 (day 7) and visit 4 (day 14), patients were asked about changes in concomitant medication use and adverse events (AEs). Diary pages were collected and reviewed for completeness. Before exiting the study at visit 4, a nasal examination was conducted. At visit 4 only, patients completed a Treatment Satisfaction Questionnaire for Medication (TSQM) and a Patient Global Assessment (PGA). The TSQM elicited the patient's evaluation of their general satisfaction with the treatment and yielded scores within each of four domains (effectiveness, side effects, convenience, and global satisfaction); higher scores indicated greater satisfaction.¹⁵ For the PGA, patients provided their overall assessment of change in their rhinitis condition using a 7-point Likert scale, with responses ranging from "very much worse" to "very much better."

The study was conducted in accordance with Good Clinical Practices and the ethical principles described within the Declaration of Helsinki. All participating patients gave written informed consent. A parent or legal guardian signed the consent document for children < 18 years of age; the individual patient may have separately signed or otherwise marked an assent form as required by local regulations.

Efficacy and Safety Analyses

Statistical analyses of the efficacy and safety parameters were conducted using all patients who completed the 2-week treatment period without protocol deviations. The last observation carried for-

Table 1 Demographics (analysis population)

Variable	OLO (n = 57)	AZE (n = 58)	Total (n = 115)	p value
Age (yr)				0.134*
<30	15 (26.3)	20 (34.5)	35 (30.4)	
30–39	7 (12.3)	4 (6.9)	11 (9.6)	
40–49	19 (33.3)	12 (20.7)	31 (27.0)	
50–59	8 (14.0)	17 (29.3)	25 (21.7)	
≥60	8 (14.0)	5 (8.6)	13 (11.3)	
Sex, n (%)				0.184*
Male	18 (31.6)	12 (20.7)	30 (26.1)	
Female	39 (68.4)	46 (79.3)	85 (73.9)	
Race, n (%)				0.302#
White	43 (75.4)	47 (81.0)	90 (78.3)	
Black	5 (8.8)	8 (13.8)	13 (11.3)	
Hispanic/Latino	6 (10.5)	3 (5.2)	9 (7.8)	
Asian	1 (1.8)	0 (0.0)	1 (0.9)	
Other	2 (3.5)	0 (0.0)	2 (1.7)	

*The p values of between-group comparisons using Fisher's exact test.

#The p values of between-group comparisons using chi-square test.

AZE = azelastine hydrochloride nasal spray 0.1%; OLO = olopatadine hydrochloride nasal spray 0.6%.

ward method was used to impute missing efficacy data. Statistical analyses were conducted using SAS (SAS Institute, Cary, NC), with inferences drawn at the 0.05 α -level.

The primary efficacy variable was the mean change from baseline to day 14 in the reflective TVSS (rTVSS). The rTVSS was an indication of how the patient felt since the last symptom assessment and was calculated as the sum of the individual nasal symptom scores reported at each time-point (*i.e.*, every morning and evening); the scores were averaged across days. Secondary endpoints included the mean absolute changes from baseline in the reflective and instantaneous individual nasal VMR symptom scores. For these evaluations, the average of the morning and evening scores from each patient was used and the absolute change from baseline for each patient was computed and averaged for each study day. In each evaluation, Student's *t*-tests were used to assess differences between OLO and AZE and to compare baseline and day 14 scores. Other outcomes included the satisfaction scores from the TSQM and the proportions of patients in each treatment group who reported an improved rhinitis condition in the PGA. Between-group comparisons were conducted using Student's *t*-tests (TSQM) or chi-square tests (PGA). The evaluation of safety included AEs and nasal examination results.

RESULTS

Patient Disposition

A total of 129 patients were enrolled at 10 study sites in the United States between September and Novem-

ber 2009. Of the enrolled patients, 63 were randomly assigned to the OLO group and 66 to the AZE group. A total of 115 patients (89%) were included in the analysis population (57 patients in the OLO group; 58 patients in the AZE group).

Patient Demographic and Baseline Characteristics

Overall, there were no statistically significant differences in demographic or baseline characteristics between patients in the OLO and AZE groups (Tables 1 and 2). In the analysis population, 73.9% of the patients were female, 67.0% were ≤ 49 years of age, and the majority of the patients were white (78.3%; Table 1). On day 0, patients reported mean scores between 1 and 3 for each individual nasal symptom, indicating that they experienced mild to severe symptom intensity before study drug administration. Baseline instantaneous scores, obtained from day 1 morning nasal symptom assessments, were considerably lower than the baseline reflective scores; however, the scores were similar between groups (Table 2).

Primary Efficacy: Change from Baseline in rTVSS

In the OLO and the AZE groups, the rTVSS decreased significantly from baseline to day 14 (Fig. 1). Specifically, in the OLO group, the mean (standard deviation [SD]) rTVSS was 8.0 U (SD = 1.8) at day 0, which decreased to 1.6 U (SD = 1.8) at day 14 (mean change = 5.9 U [SD = 3.0]; $p < 0.001$). In the AZE group, the mean rTVSS was 8.4 U (SD = 1.6) at day 0,

Table 2 Baseline characteristics—Nasal symptom scores (analysis population)

	OLO <i>n</i> = 57 Mean (SD)	AZE <i>n</i> = 58 Mean (SD)	<i>p</i> value*
Reflective score			
<i>n</i>	44	43	
Rhinorrhea	1.9 (1.0)	1.7 (0.9)	0.257
Postnasal drip	2.2 (0.9)	2.3 (0.7)	0.569
Nasal congestion	2.2 (0.8)	2.5 (0.6)	0.076
Sneezing	1.7 (0.8)	1.9 (0.7)	0.162
rTVSS	8.0 (1.8)	8.4 (1.6)	0.309
Instantaneous score			
<i>n</i>	44	40	
Rhinorrhea	0.8 (0.9)	0.7 (0.8)	0.701
Postnasal drip	1.3 (1.0)	1.1 (0.9)	0.263
Nasal congestion	1.3 (0.9)	1.4 (0.7)	0.545
Sneezing	0.5 (0.7)	0.6 (0.7)	0.544
iTVSS	3.8 (2.8)	3.7 (2.4)	0.901

Note: The baseline values for reflective scores were obtained from the day 0 patient evaluations of their nasal symptom scores before dosing. Instantaneous scores were obtained from the patients' day 1 morning nasal symptom assessments. Because dosing with study drug occurred on the evening of day 0, baseline instantaneous scores were considerably lower than the baseline reflective scores.

*The *p* values of between-group comparisons (OLO vs AZE) using Student's *t*-test.

AZE = azelastine hydrochloride nasal spray 0.1%; OLO = olopatadine hydrochloride nasal spray 0.6%; iTVSS = instantaneous total VMR symptom score; rTVSS = reflective total VMR symptom score; VMR = vasomotor rhinitis.

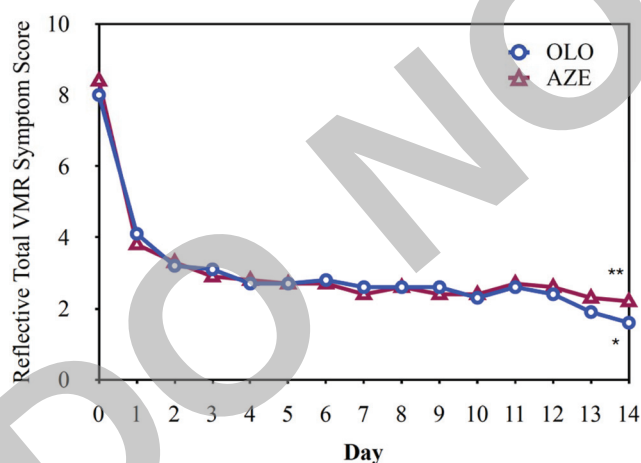


Figure 1. Mean reflective total vasomotor rhinitis (VMR) symptom scores by day (analysis population). *Significant difference from baseline to day 14 in the olopatadine hydrochloride nasal spray 0.6% (OLO) group; $p < 0.001$ using Student's *t*-test. **Significant difference from baseline to day 14 in the azelastine hydrochloride nasal spray 0.1% (AZE) group; $p < 0.001$ using Student's *t*-test. Note that between-group comparisons (OLO versus AZE) were conducted using Student's *t*-test ($p = 0.354$).

which decreased to 2.2 U (SD = 2.2) at day 14 (mean change = 6.5 U [SD = 2.3]; $p < 0.001$). However, there were no significant differences between the OLO and AZE groups in the mean change from baseline to day 14 in the rTVSS ($p = 0.354$; Table 3).

Secondary Efficacy End Points: Changes from Baseline in Individual Nasal Symptom Scores

In the OLO and the AZE groups, the scores for each of the individual reflective symptoms (nasal congestion, rhinorrhea, postnasal drip, and sneezing) decreased significantly from baseline to day 14 (Fig. 2). Similar results were also observed for the instantaneous individual symptom scores, although changes from baseline in the scores for rhinorrhea and sneezing in the OLO group were not significant (Table 3). Additionally, there were no significant differences between the OLO and AZE groups in the mean reflective or instantaneous scores for any individual nasal symptom at any assessment time point during the 2-week treatment period (i.e., $p > 0.05$ for each comparison between treatment groups; Table 3).

Other End Points: TSQM and PGA

Patient perceptions of treatment satisfaction and of changes in their allergy condition were determined by TSQM and the PGA questionnaire scores, respectively. Patients in the OLO and AZE groups reported similar satisfaction scores in the individual TSQM domains of effectiveness (60.7 versus 61.9, respectively; $p = 0.749$), convenience (78.1 versus 81.5, respectively; $p = 0.312$), side effects (89.9 versus 90.9, respectively; $p = 0.747$), and global satisfaction (56.9 versus 58.9, respectively; $p = 0.687$; Fig. 3).

Table 3 Two-week mean absolute changes from baseline in reflective and instantaneous individual VMR symptom scores (analysis population)

	OLO <i>n</i> = 57		AZE <i>n</i> = 58		<i>p</i> value*
	Mean (SD)	<i>p</i> value ^a	Mean (SD)	<i>p</i> value*	
Reflective score					
<i>n</i>	44		43		
Rhinorrhea	1.5 (1.1)	<0.001	1.3 (1.0)	<0.001	0.418
Postnasal drip	1.5 (1.2)	<0.001	1.8 (0.9)	<0.001	0.313
Nasal congestion	1.4 (1.1)	<0.001	1.7 (1.2)	<0.001	0.349
Sneezing	1.4 (0.9)	<0.001	1.7 (0.8)	<0.001	0.143
Instantaneous score					
<i>n</i>	44		40		
Rhinorrhea	0.2 (0.9)	0.077	0.3 (0.7)	0.013	0.727
Postnasal drip	0.5 (1.0)	0.002	0.5 (0.9)	0.002	0.917
Nasal congestion	0.4 (0.8)	0.001	0.6 (0.8)	<0.001	0.280
Sneezing	0.2 (0.6)	0.083	0.3 (0.6)	0.002	0.294

Note: The baseline values for reflective scores were obtained from the day 0 patient evaluations of their nasal symptom scores before dosing. Instantaneous scores were obtained from the patients' day 1 morning nasal symptom assessments. Because dosing occurred on the evening of day 0, baseline instantaneous scores were considerably lower than the baseline reflective scores (see Table 2.). Therefore, despite the fact that the absolute instantaneous and reflective scores in both treatment groups were similar at each assessment, the numerical values for change from baseline to day 14 were lower for instantaneous scores relative to reflective scores.

*The *p* values of comparisons between baseline and day 14 scores using Student's *t*-test.

#The *p* values of between-group comparisons (OLO vs AZE) using Student's *t*-test. AZE = azelastine hydrochloride nasal spray 0.1%; OLO = olopatadine hydrochloride nasal spray 0.6%; VMR = vasomotor rhinitis.

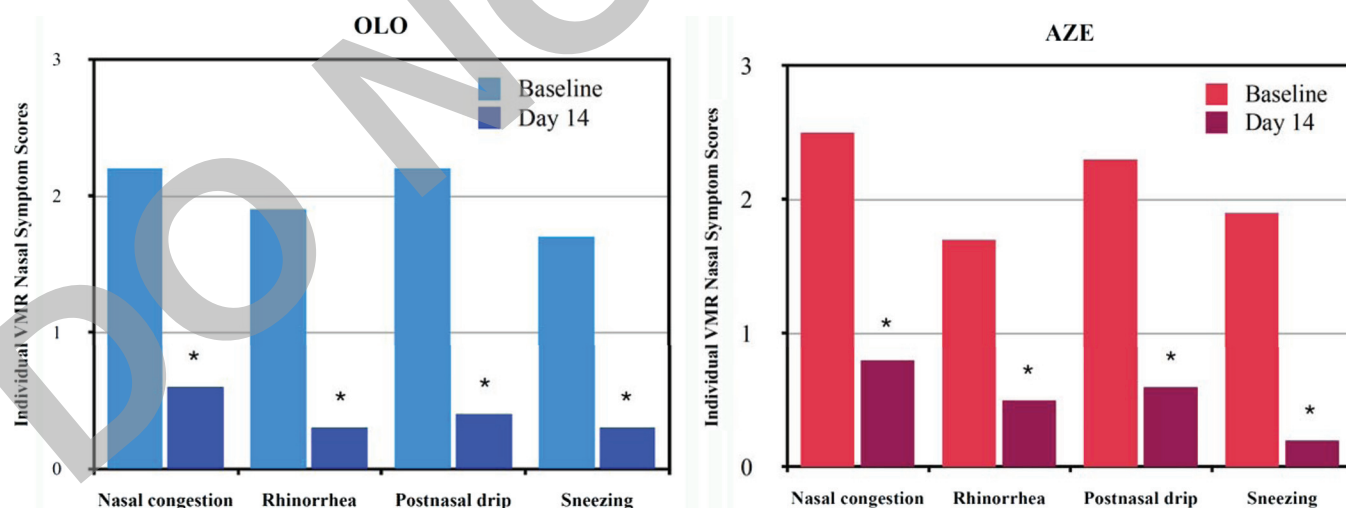


Figure 2. Baseline and day 14 individual reflective vasomotor rhinitis (VMR) nasal symptom scores (analysis population). *Significant difference from baseline using Student's *t*-test; *p* < 0.001 for the comparison of day 14 and baseline scores for each symptom in the olopatadine hydrochloride nasal spray 0.6% (OLO) and azelastine hydrochloride nasal spray 0.1% (AZE) groups. Note that there were no significant between-group differences (*p* values for these OLO versus AZE comparisons are presented in Table 3).

A majority of the patients in both treatment groups perceived an improvement in their rhinitis condition at the end of the study (this included patients who felt a little better, moderately better, and very much better relative to how they felt at the start of the study). Specifically, 82.5 and 75.9% of the patients in the OLO

and AZE groups, respectively, perceived overall improvements in their condition (*p* = 0.384; Fig. 4).

Safety

In this study, 34 (29.6%) patients reported one or more AE (regardless of severity, seriousness, or rela-

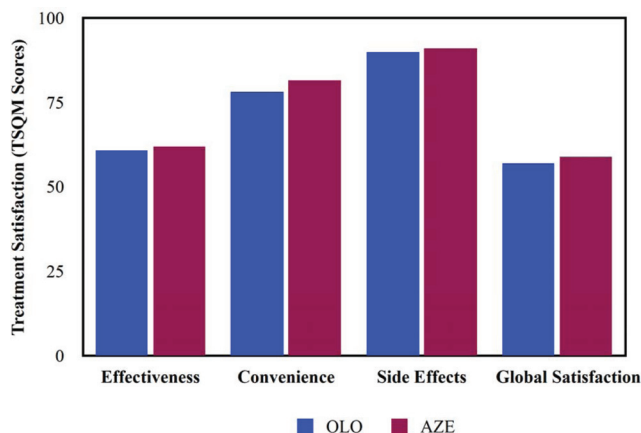


Figure 3. Treatment Satisfaction Questionnaire for Medication (TSQM) scores (analysis population). Between-group comparisons (olopatadine hydrochloride nasal spray 0.6% [OLO] versus azelastine hydrochloride nasal spray 0.1% [AZE]) were conducted using Student's *t*-tests: effectiveness ($p = 0.749$), convenience ($p = 0.312$), side effects ($p = 0.747$), and global satisfaction ($p = 0.687$).

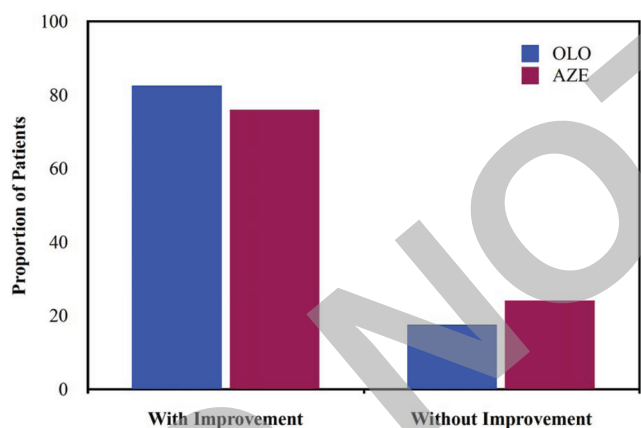


Figure 4. Patient Global Assessment (analysis population) between-group comparisons (olopatadine hydrochloride nasal spray 0.6% [OLO] versus azelastine hydrochloride nasal spray 0.1% [AZE]) were conducted using chi-square test ($p = 0.384$). Note that patients with improvement included patients who recorded their condition as being "very much better," "moderately better," or "a little better" than baseline, and patients without improvement included those who recorded their condition as being "unchanged," "a little worse," or "moderately worse" than baseline.

tionship to the study drug). In the OLO group, 19 patients reported 22 AEs and in the AZE group, 15 patients reported 20 AEs (Table 4). The reported AEs were all mild in severity and none of the patients experienced serious AEs. With two exceptions, no single AE was reported by more than two patients in either treatment group. The two exceptions included taste disturbance (reported by 3/57 [5.3%] patients in the OLO group and 6/58 [10.3%] patients in the AZE group) and nose bleed (reported by 3/57 [5.3%] and 3/58 [5.2%] patients in the OLO and AZE groups,

Table 4 Adverse events (AEs) by treatment group (analysis population)

Verbatim Event	No. of Events	
	OLO $n = 57$	AZE $n = 58$
Taste disturbance	3	6
Nose bleed	3	3
Fatigue	1	2
Nasal irritation	2	1
Nasal redness	1	2
Sore throat	1	2
Headache	1	1
Ankle sprain	1	0
Depression	1	0
Dizziness	1	0
H1N1 flu	1	0
Heart palpitations	0	1
Muscle cramps in leg	1	0
Nasal pain	0	1
Nausea	1	0
Rectal hemorrhoids	1	0
Tachycardia	1	0
Vomiting	1	0

Note: The same patient may have reported more than one AE and patients reporting a particular AE more than once are counted only once for that event.

There were no significant differences between treatment groups in the number of patients who experienced AEs ($p = 0.381$ using chi-square test).

AZE = azelastine hydrochloride nasal spray 0.1%; OLO = olopatadine hydrochloride nasal spray 0.6%.

respectively). Although neither of these specific events led to patient discontinuation from the study, five patients discontinued study participation because of AEs, including two patients in the OLO group and three patients in the AZE group (Table 5).

Overall, 16 patients experienced 21 AEs that were considered treatment related. With the exception of three patients in the AZE group, no patient experienced more than one treatment-related AE. Fewer patients in the OLO group experienced treatment-related AEs than in the AZE group (5 patients versus 11 patients, respectively; $p = 0.039$). Treatment-related AEs reported in the OLO group included nasal irritation (two reports), taste disturbance (two reports), and fatigue. Treatment-related AEs reported in the AZE group included taste disturbance (six reports), fatigue (two reports), nasal redness (two reports), headache, heart palpitations, nasal irritation, nasal pain, nose bleed, and sore throat.

No clinically relevant changes from baseline were observed among either treatment groups in nasal examinations. Similar occurrences of nasal abnormalities

Table 5 Adverse events (AEs) leading to discontinuation (all patients)

Verbatim Event	No. of Events	
	OLO <i>n</i> = 63	AZE <i>n</i> = 66
Fatigue	0	1
Headache	1	0
Rash to bilateral forearms	0	1
Right ankle fracture	1	0
Right tibia fracture	1	0
Sinus infection	1	0
Sore throat	0	1
Tonsil infection	1	0

Note: The same patient may have reported more than one AE and patients reporting a particular AE more than once are counted only once for that event.

There were no significant differences between treatment groups in the number of patients who discontinued due to AEs ($p = 0.686$ using chi-square test).

AZE = azelastine hydrochloride nasal spray 0.1%; OLO = olopatadine hydrochloride nasal spray 0.6%.

were observed in both groups in posttreatment nasal examinations. In the OLO group, nasal bleeding was observed in two patients and mucosal ulceration was noted in one patient. In the AZE group, mucosal ulceration was observed in two patients, and one patient experienced nasal bleeding.

DISCUSSION

Although OLO has been reported to be as effective as AZE in providing relief from the nasal symptoms of seasonal allergic rhinitis,¹⁴ OLO has not been previously evaluated for the treatment of VMR and is not approved for the treatment of this condition. This study's primary efficacy analysis indicated that OLO is an effective treatment that provides comparable relief to AZE for the nasal symptoms of VMR. In addition, over the 2-week period, the individual reflective nasal symptom scores generally decreased at each visit relative to baseline in both treatment groups; significant reductions were also observed at the end of the treatment period in both groups. The outcomes for rTVSS in this study were comparable with those reported in the literature for AZE. In two clinical trials of patients with VMR, AZE (administered as 2 sprays/nostril two times daily for 3 weeks) significantly decreased rTVSS from baseline.⁴

The pathophysiology of VMR is unknown. Proposed mechanisms include hyperactivity of the parasympathetic nervous system, nonimmune mast cell degranulation, inflammatory cytokine production (e.g., tumor necrosis factor [TNF]- α and various interleukins), and nasal neuropeptide (e.g., neurokinins and substance P)

release in response to environmental stimuli.^{3,4} OLO is a mast cell stabilizer, which prevents mast cell degranulation and inhibits the secretion of histamine, as well as other chemical mediators of inflammation from mast cells.^{16–18} Specifically, OLO has been shown *in vitro* to decrease the expression and secretion of proinflammatory cytokines, including TNF- α , various interleukins, and peptide leukotrienes. In addition, OLO prevents the up-regulation of adhesion molecules such as intercellular adhesion molecule-1.^{16–20} The decrease in the levels of cytokines and adhesion molecules is believed to limit the migration, accumulation, and activation of inflammatory cells (e.g., eosinophils and neutrophils) that may contribute to the pathophysiology of rhinitis.^{17,19,21} Furthermore, OLO has been shown to inhibit tachykinin release from sensory nerve endings in isolated guinea pig bronchi and other experimental models *in vivo*.²⁰ These effects of OLO may contribute to the efficacy of OLO in patients with VMR.

This study was limited with respect to the fact that no placebo control arm was used to provide an "anchor" for evaluation of the treatment effects. This is also important because VMR is a variable condition in which substantial placebo responses are expected. Additionally, the fact that patients were allowed to have used OLO or AZE before entry into the study (although not within 7 days before randomization) could have affected the study assessments. In particular, the results might have been different, especially with regard to patient satisfaction, if the enrolled patients had had no previous experience with either study drug (*i.e.*, were treatment naive). Despite these limitations, the observed efficacy of OLO and AZE were similar to one another in this study.

In addition to the efficacy results, patients reported higher satisfaction scores for OLO relative to AZE. Furthermore, a substantial proportion of patients who used OLO perceived an improvement in their overall rhinitis condition. Reports of taste disturbance were less frequent among patients who received OLO relative to those who received AZE and were consistent with a previous report comparing sensory attributes of OLO with AZE.²² Given the fact that patient perceptions of sensory attributes can influence adherence to intranasal spray regimens,²³ and the association between patient satisfaction, adherence to treatment, and treatment effect,¹⁵ OLO may provide better patient outcomes than AZE.

Nasal bleeding is a common, albeit minor and self-limiting, AE associated with intranasal antihistamines.^{7,24} Ulceration of the nasal mucosa is a side effect of nasal spray use in general.²⁵ In the current study, the overall occurrences of nasal bleeding and mucosal ulceration were low and were reported at similar frequencies in each treatment group. Furthermore, these events were nonserious, mild in severity, usually re-

solved without the need for concomitant therapy, and did not interrupt patient participation in the study.

No safety concerns for changes in nasal examination parameters were observed during the study in either treatment group. In general, the AEs reported by patients in both treatment groups were similar.

CONCLUSIONS

OLO was well tolerated and effective in reducing the nasal symptoms associated with VMR in patients ≥ 12 years of age. No statistically significant differences between the OLO and AZE groups in either rTVSS or individual symptom scores were observed in the 2-week treatment period.

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