

A patient preference and satisfaction study of ciclesonide nasal aerosol and mometasone furoate aqueous nasal spray in patients with perennial allergic rhinitis

William E. Berger, M.D.,¹ Bruce Prenner, M.D.,² Ralph Turner, Ph.D., M.P.H.,³ and Eli O. Meltzer, M.D.⁴

ABSTRACT

Patients' preference and satisfaction with their nasal allergy medications may be influenced by their sensory attributes. This study evaluates patient preference and satisfaction with ciclesonide hydrofluoroalkane nasal aerosol (CIC-HFA) compared with mometasone furoate aqueous nasal spray (MFNS). Symptomatic subjects with perennial allergic rhinitis (PAR) were randomized to CIC-HFA at 74 micrograms or MFNS at 200 micrograms q.d. in an open-label, two-period, crossover study. Subject preference was recorded as total preference score (TPS; average of 17 individual preference items) at the end of treatment period 2, and satisfaction was assessed with a 76-item, self-administered instrument at baseline and at the end of each 2-week treatment period. The primary assessments were TPS and regimen attributes composite satisfaction score composed of two of nine satisfaction subscales: sensory impact (including medication running out of the nose, medication running down the throat, and impact on smell and taste) and regimen management (comprised of issues relating to dosing and ability to remember to take medication). Two hundred ninety-four subjects completed the study. A total of 68.1% of subjects preferred CIC-HFA ($p < 0.0001$ versus MFNS), with a mean TPS of 68.3 versus 31.7 for the MFNS group. The regimen attributes composite satisfaction score significantly ($p < 0.0001$ for each treatment period) favored CIC-HFA versus MFNS at the end of treatment period 1 (85.5 vs 77.6) and treatment period 2 (83.0 versus 73.5), respectively. In this study, subjects reported higher preference for and satisfaction with CIC-HFA compared with MFNS, suggesting significant differences in patient perception of attributes in favor of CIC-HFA. Clinical trial registration URL and registration number: www.clinicaltrials.gov/ct2/show/NCT01401465

(Allergy Asthma Proc 34:542–550, 2013; doi: 10.2500/aap.2013.34.3705)

Clinical trials in subjects with allergic rhinitis (AR) have indicated that intranasal corticosteroids (INSs) display similar efficacy.^{1–5} However, subjects in clinical trials are carefully monitored and, as a result, adherence rates tend to be much higher than in the actual clinical setting, especially for chronic diseases such as AR.⁶ In addition, clinical studies have revealed an inverse relationship between patient preference for and anticipated adherence to an INS therapy and the intensity of certain sensory characteristics of INS sprays.^{7–10}

After the implementation of the Montreal Protocol on Substances That Deplete the Ozone Layer banning

the use of chlorofluorocarbon propellants, only aqueous-based INS formulation sprays were available.^{11,12} Two nasal intranasal steroid aerosol treatments are now available.¹³ The majority of aqueous intranasal steroid sprays are administered in volumes of ≈ 100 μL /spray. Because of this amount of fluid, aqueous intranasal steroid sprays may cause throat rundown, which is generally not preferred by patients, when compared with aerosolized INS formulations administered at ≈ 50 μL /spray.¹¹

The corticosteroid prodrug, ciclesonide (CIC), has been formulated as a nasal aerosol containing a hydrofluoroalkane (HFA) propellant and delivered *via* a metered-dose device. CIC-HFA nasal aerosol (Zetonna; Sunovion Pharmaceuticals, Marlborough, MA) at 74 μg q.d., is approved by the U.S. Food and Drug Administration for the treatment of symptoms associated with seasonal AR and perennial AR (PAR) in patients ≥ 12 years old administered as 1 spray/nostril (37 μg /actuation, one actuation per nostril per day).¹⁴ The objective of this study was to compare patient preference and satisfaction with CIC-HFA (74 μg given as 1 spray/nostril daily) and mometasone furoate aqueous nasal spray (MFNS; 200 μg given as 2 sprays/nostril daily) in PAR subjects using a new patient-reported tool, the Allergic Rhinitis Treatment Satisfaction and

From the ¹Allergy and Asthma Associates of Southern California, Mission Viejo, California, ²Allergy Associates Medical Group, Inc., San Diego, California, ³Phase V Technologies, Inc., Wellesley Hills, Massachusetts, and ⁴Allergy and Asthma Medical Group and Research Center, San Diego, California

Funded by Sunovion Pharmaceuticals, Inc.

WE Berger is a research grant recipient, consultant and/or speaker for Alcon, AstraZeneca, Meda, Teva, GlaxoSmithKline, Merck and Sunovion. B Prenner is a research grant recipient, consultant, and/or speaker for Merck, Genentech, Mylan, Teva and Sunovion. R Turner receives research grants from Sunovion. EO Meltzer is a research grant recipient, consultant and/or speaker for Alcon, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Merck, Meda, Mylan, Sunovion, and Teva

Address correspondence to William E. Berger, M.D., Allergy and Asthma Associates of Southern California, 27800 Medical Center Road, Mission Viejo, CA 92691

E-mail address: weberger@hs.uci.edu

Published online September 27, 2013

Copyright © 2013, OceanSide Publications, Inc., U.S.A.

Preference (ARTSP) instrument developed consistent with the U.S. Food and Drug Administration Guidance on Patient Reported Outcome measures.¹⁵ Specifically, the psychometric properties of the ARTSP module were validated in a previous, open-label crossover trial (unpublished data, 2012; clinicaltrials.gov identifier: NCT01287364),¹⁶ where 185 PAR patients received 7 days of treatment with nasal CIC-HFA aerosol (1 spray/nostril; 80 μ g q.d.) and MFNS (2 sprays/nostril; 200 μ g q.d.).^{14,17} Validation of the instrument in this trial included assessing reliability, responsiveness, and sensitivity of the instrument to discern subject satisfaction with and preference for an INS.¹⁵ The statistical validation performed allowed for grouping of the 76 satisfaction items into 9 satisfaction subscales, as well as grouping of 17 preference items into two preference composites (Table 1). In addition, this validation allowed for the designation of the two co-primary end points in this trial: total preference score (TPS), composed of the sum of all 17 individual preference items, and regimen attributes composite score, composed of two subscales out of 9 satisfaction subscales (Table 1); sensory impact subscale (including medication running out of the nose, medication running down the throat, and impact on smell and taste) and regimen management subscale (comprised of issues relating to dosing—i.e., number of times and the time required to dose—and ability to remember to take medication).

METHODS

Subjects

Symptomatic (at trial entry) subjects at least 12 years of age with a history of PAR requiring treatment (continuous or intermittent) for a minimum of 2 years immediately preceding study entry who were expected to require INS treatment throughout the study were included. At least one treatment for PAR during the 6 months preceding study treatment was required to be a prescription nasal spray. Subjects were required to show sensitivity to a minimum of one allergen known to induce PAR—house-dust mite, cockroach, molds, and animal dander—based on positive skin test, defined as a wheal diameter at least 3 mm larger than the negative control wheal (normal saline). Subjects who had a history of nasal pathology, including nasal polyps, clinically significant respiratory tract malformations, recent nasal biopsy, nasal trauma, nasal ulcers or perforations, nasal surgery (any prior nasal surgery), atrophic rhinitis, rhinitis medicamentosa, or active asthma requiring routine β -agonists, or controller therapy (including corticosteroids) were excluded. Subjects who had used intranasal mometasone furoate within 3 months of the study or CIC nasal aerosol at any time before the study were excluded.

This study was approved by the Institutional Review Board (Seattle, WA) and was conducted in accordance with the principles of the Declaration of Helsinki.¹⁸

Study Design

This open-label, randomized, two-period, crossover study (clinicaltrials.gov identifier: NCT01401465) was composed of a screening period of 18–21 days, including a 7-day baseline period, two 14-day treatment periods separated by a 14-day washout period, and a follow-up period of 7–9 days (Fig. 1). Subjects were randomized to either of the following treatment sequences:

Treatment Sequence A. CIC-HFA at 74 μ g (1 actuation/nostril, 37 μ g/actuation) for 14 days, followed by a 14-day washout period, and then MFNS at 200 μ g (2 actuations/nostril, 50 μ g/actuation) q.d. in the morning (A.M.) for 14 days.

Treatment Sequence B. MFNS at 200 μ g (2 actuations/nostril, 50 μ g/actuation) q.d. in the A.M. for 14 days, followed by a 14-day washout period, and then CIC-HFA at 74 μ g (1 actuation/nostril, 37 μ g/actuation) for 14 days.

Randomization and Continuation Criteria. Randomization was based on reflective total nasal symptom score (rTNSS) assessments. Subjects were asked to assess reflective symptoms over the preceding 12 hours, calculated as the sum of four nasal symptoms (runny nose, itchy nose, sneezing, and nasal congestion), each on a scale from 0 (no signs/symptoms evident) to 3 (severe symptoms). Subjects who had a minimum cumulative rTNSS of 28 (out of a maximum of 84) and a minimum cumulative score for runny nose or nasal congestion of ≥ 7 (out of a maximum of 21) over any combination of A.M. or evening (P.M.) scores during 3 of the 7 days of the baseline period (including A.M. assessment on the current day) were randomized. For continuation in the study, subjects were required to meet the same symptom criteria at the end of the washout period. Compliance with study drug administration was measured throughout the study based on subject self-report of study medication administration date and time.

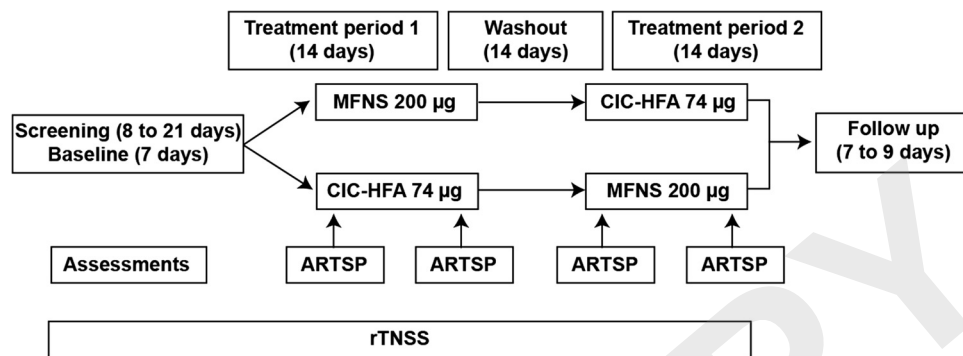
Preference Assessments. Preference was evaluated with a 17-item, binary choice, self-report instrument from the validated ARTSP instrument. The ARTSP instrument was adapted to AR from the Phase V e-Health Outcomes Information System (Phase V Technologies, Inc., Wellesley Hills, MA) treatment satisfaction conceptual framework. A TPS was scored using a forced choice model in which subjects chose either

Table 1 ARTSP treatment preference and satisfaction composite scales and subscales

Preference	
Preference items	Ease of use, convenience, flexibility in daily activities, taste, use in public (related to having to act after administration of nasal spray, such as using a tissue or having to “sniff” product after sprayed), smell, fewer problems with medication running out of the subject’s nose, perceived longer relief, fewer problems with medication dripping down the subject’s throat, perceived symptom relief, price, feeling better about appearance, fewer problems with nose irritation, faster relief, number of sprays per dose, how the medication makes the subject’s nose feel, overall feeling, and overall preference
Total preference score	The sum of all 17 preference items (1 = prefer ciclesonide; 0 = prefer mometasone)
Preference subscale composites	
Treatment process composite (pertaining to the drug delivery process)	Reflects preference on items related to ease of use, convenience, flexibility in daily activities, taste, use in public, smell, fewer problems with medication running out of the nose, fewer problems with medication dripping down throat, and number of sprays per dose
Treatment outcomes composite (pertaining to perceived drug effectiveness)	Reflects preference on items concerned with perceived longer relief, symptom relief, preference if both were the same price, feeling better about your appearance, and fewer problems with irritation to nose; faster relief, how it makes your nose feel
Satisfaction	
Scale	Assessment
Interference	Degree to which allergy symptoms or side effects of the nasal spray interfered with daily routine, meals, recreation, family life, sleep schedules, energy levels, making plans, traveling, having fun, and overall quality of life
Regimen adaptation	Convenience of the treatment, whether the treatment was one that the subject would recommend to other persons with the same condition, and the level of satisfaction with the current treatment
Role limitation	Degree of interference with social interactions with family, friends, travel, having fun, problems in performing work or social roles, and how flexible the treatment was with scheduling life activities
Regimen difficulties	Degree of pain, discomfort, and side effects perceived to be associated with treatment, and the extent to which pain and discomfort were bothersome
Sensory impact	Sensory attributes, including medication running out of the nose, medication running down the throat, and impact on smell and taste; issues regarding skipping the medication because of the way the nose feels and wanting to try other medications to find a better one
Hassle	Amount of bother and hassle of the treatment regimen, including coordinating activities, dosing, carrying supplies, rubbing nose or eyes, blowing nose repeatedly, or facial puffiness
Burden	Level of degree of burden that treatment for allergic rhinitis imposes on a number of areas, including adherence to the treatment regimen, exercise, performing daily activities, social activities, and enjoying life
Regimen management	Issues relating to dosing (number of times and the time required to dose) and ability to remember to take medication
Perceived relief	Perceived level of relief along with the degree of satisfaction associated with that amount of relief
Subscale composites	
Treatment functional impact composite	Interference, role limitation, and burden
Regimen acceptance composite	Perceived relief and regimen adaptation
Regimen attributes composite	Sensory impact and regimen management

ARTSP = Allergic Rhinitis Treatment Satisfaction and Preference instrument.

Figure 1. Study design. ARTSP, Allergic Rhinitis Treatment Satisfaction and Preference instrument; CIC-HFA, ciclesonide hydrofluoroalkane nasal aerosol; MFNS, mometasone furoate aqueous nasal spray; rTNSS, reflective total nasal symptom score.



CIC-HFA or MFNS for each preference item (Table 1). In addition, there were two composite scores which had been created and validated in a previous study. Specifically, these were

Treatment process composite score—composed of items pertaining to drug delivery process—ease of use, convenience, flexibility in daily activities, taste, use in public, smell, fewer problems with medication running out of the nose, fewer problems with medication dripping down the throat, and number of sprays per dose.

Treatment outcomes composite score—composed of items pertaining to perceived drug effectiveness—longer relief, symptom relief, preference if both medications were the same price, feeling better about personal appearance, and fewer problems with nasal irritation; faster relief, how it makes the nose feel (Table 1).

Satisfaction Assessments. The ARTSP instrument evaluated treatment satisfaction using 76 items assigned to nine subscales (Table 1). All subscales were standardized to range from 0 (lower satisfaction) to 100 (higher satisfaction). Three satisfaction composite scores of regimen attribute composite score, treatment functional impact score, and regimen acceptance score were created (unpublished data, 2012).¹⁶

Efficacy and Safety

Change from baseline in rTNSS was used to confirm that both treatments were equally effective for purposes of evaluating the ARTSP instrument. Adverse events (AEs) were monitored and recorded throughout the study.

Assessments and Statistical Methods

The intent-to-treat population (subjects who received a minimum of 1 dose of the study medication) was used for all measures, and the per-protocol population (completers with no important protocol deviations) was used for evaluating rTNSS. All statistical tests

were two sided and were conducted at the 5% significance level (unless specified otherwise).

The co-primary assessments were TPS (assessed at the end of the study) and the regimen attributes composite score (assessed at the end of each 2-week treatment period). A one-sample signed-rank test was used to test the null hypothesis (no preference) that the median standardized TPS was equal to 50. A linear mixed, random effects model with a response variable of change from baseline in regimen attributes composite score and with factors of treatment, sequence, and period as fixed effects, subject nested within sequence as a random effect, and baseline composite score as a covariate was used to compare the two treatment groups, yielding descriptive statistics and the 95% confidence interval (CI) of the difference in least square means.

The first key secondary assessment was the treatment process composite preference score, which is a composite of patient preference scores reflecting preference on items pertaining to the drug process. Preference for CIC-HFA versus MFNS was assessed by comparing the treatment process composite preference score to a median standardized score of 50, using the signed-rank test at a significance level of 0.05. Values of >50 indicated a greater preference for CIC-HFA.

Changes from baseline in subject-reported A.M. and P.M. rTNSS scores were averaged over the 2-week treatment period. The 95% CI of the least square mean difference between CIC-HFA and MFNS was calculated from the ANCOVA model and the CI upper bound was compared with the noninferiority margin of 0.5, accepted as a minimal clinically important difference in rTNSS.¹⁹

A fixed sequence testing procedure was used to control for multiplicity. Each primary end point was tested at a significance level of 0.025. If both showed statistical significance at the 0.025 level, the first key secondary end point was evaluated at a two-sided significance level of 0.05. If the first key secondary end point was statistically significant, then noninferiority was evaluated for the second key secondary end point using a

Table 2 Demographics and baseline characteristics (intent-to-treat population)

	Treatment Period 1 (<i>n</i> = 165)	Treatment Period 2 (<i>n</i> = 162)	Total (<i>n</i> = 327)
Age (yr), mean (SD)	37.5 (14.78)	35.7 (14.72)	36.6 (14.76)
Male gender, <i>n</i> (%)	63 (38.2)	63 (38.9)	126 (38.5)
Race, <i>n</i> (%)			
White/Caucasian	134 (81.2)	144 (88.9)	278 (85.0)
Black/African American	15 (9.1)	9 (5.6)	24 (7.3)
Asian	5 (3.0)	5 (3.1)	10 (3.1)
American Indian/Alaska Native	2 (1.2)	0	2 (0.6)
Native Hawaiian/other Pacific Islander	0	1 (0.6)	1 (0.3)
Other	3 (1.8)	0	3 (0.9)
Multiple	6 (3.6)	3 (1.9)	9 (2.8)
Positive skin-prick allergy test,* <i>n</i> (%)	164 (100.0)	162 (100.0)	327 (100.0)

*Subjects may have been allergic to multiple allergens.

SD = standard deviation.

95% CI. No other end points were controlled for multiplicity.

Treatment comparisons based on individual treatment preference scores were assessed by calculating the proportion of subjects who preferred either CIC-HFA or MFNS for each question. A binomial test was used to test for greater preference between treatments.

RESULTS

Patient Disposition and Demographics

A total of 294 subjects completed the study. The most common reasons for discontinuation were inability to meet continuation criteria (11 subjects), withdrawal of consent (5), scheduling difficulties (2), moving/relocation (1), and pregnancy (1); 5 subjects discontinued because of an AE, 5 subjects discontinued due to protocol violations, and 1 subject discontinued due to noncompliance with study medication. The per-protocol population consisted of 283 randomized subjects (86.5%). Among those completing the study, mean treatment compliance was >99% (while on study medications) for each treatment. Demographic and baseline characteristics were similar across the two treatment groups (Table 2).

Patient Preference

A mean TPS of 68.3 (standard deviation [SD] = 35.2) was calculated for CIC-HFA, indicating a greater preference for CIC-HFA compared with MFNS (31.7). In addition, a significantly ($p < 0.0001$) higher proportion of subjects (68.1%) indicated a preference for CIC-HFA (201 observations/answers were >50) compared with MFNS (94 observations/answers were >50).

Subjects significantly favored CIC-HFA for 15 of the 17 individual preference questions (88%, $p < 0.0001$ versus MFNS, uncontrolled for multiplicity; Fig. 2). The two remaining preference items that also numerically favored CIC-HFA (differences were not statistically significant) were fewer problems with nose irritation (52.5% for CIC-HFA versus 47.5% for MFNS; $p = 0.4151$, uncontrolled for multiplicity) and how the medication makes the subject's nose feel (53.9% for CIC-HFA versus 46.1% for MFNS; $p = 0.2002$, uncontrolled for multiplicity).

A mean treatment process composite preference score of 74.1 (SD = 33.7) was recorded for CIC-HFA, indicating preference for CIC-HFA versus MFNS (treatment process composite preference score of 25.9). A total of 77.6% (229 observations/answers were >50) of 295 subjects indicated a preference for CIC-HFA versus MFNS (66 observations/answers were >50; $p < 0.0001$). The mean treatment outcomes composite preference score (reflects preference on items concerned with patient perception of drug effectiveness) was 61.6 (SD = 40.8), indicating preference for CIC-HFA versus 38.4 for MFNS. A total of 62.4% (184 observations/answers were >50) of the 295 subjects indicated a preference for CIC-HFA versus MFNS (111 observations/answers were >50).

Patient Satisfaction

The overall mean change from baseline in the regimen attributes (composed of two—sensory impact and regimen management—of the nine satisfaction subscales) composite score was 13.90 (standard error [SE] = 1.36) for CIC-HFA and 4.88 (SE = 1.36) for MFNS ($p < 0.0001$). Overall, in treatment periods 1 and 2, treatment satisfaction scores revealed more favorable

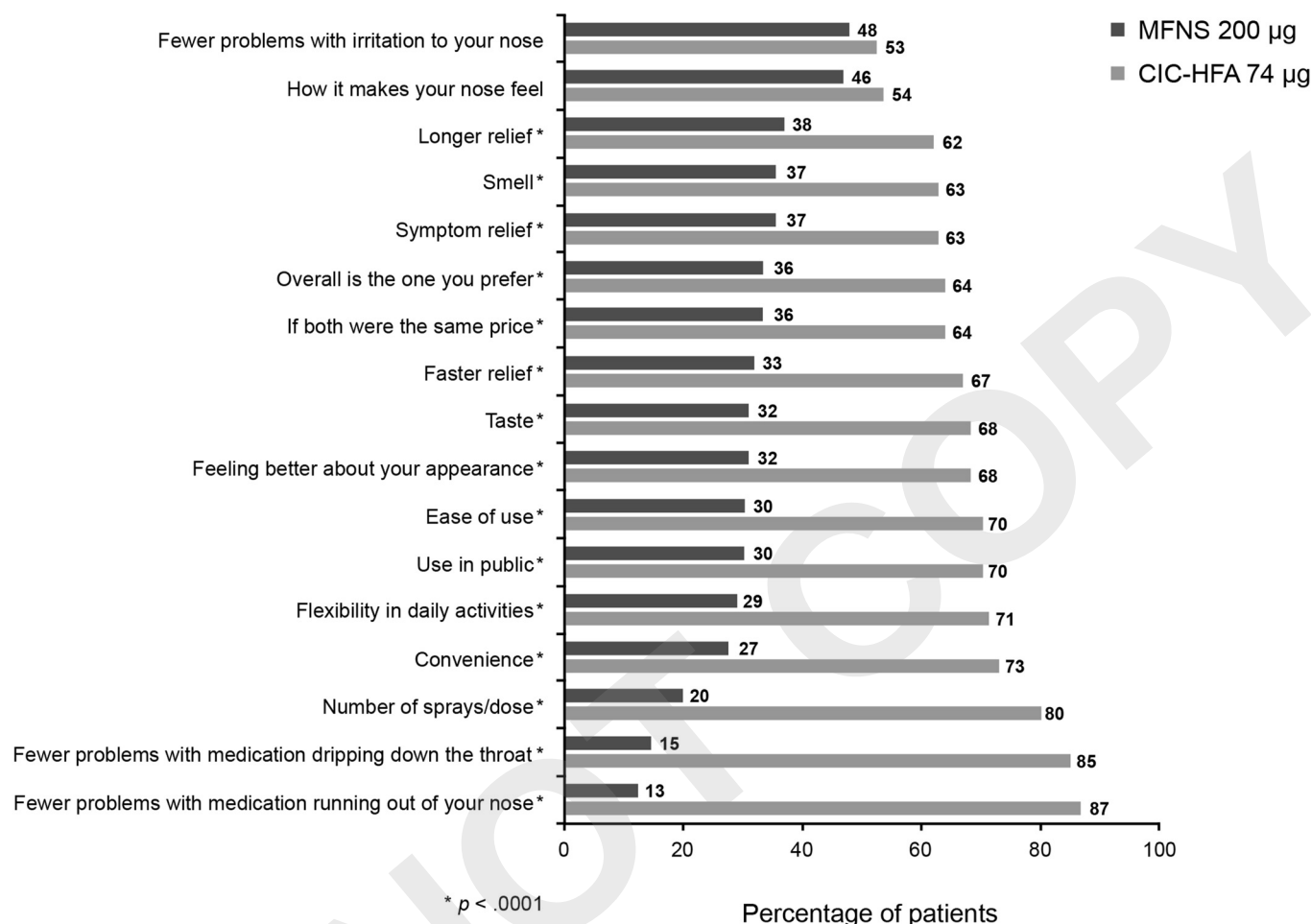


Figure 2. Patient preference results. CIC-HFA, ciclesonide hydrofluoroalkane nasal aerosol; MFNS, mometasone furoate aqueous nasal spray.

responses for CIC-HFA versus MFNS for the following eight of nine satisfaction subscales: interference, regimen adaptation, role limitation, sensory impact, hassle, burden, regimen management, and perceived relief (Table 3). Only the regimen difficulties subscale (composed of items assessing satisfaction related to degree of pain, discomfort, and side effects perceived to be associated with treatment, and the extent to which pain and discomfort were bothersome) significantly favored MFNS ($p < 0.01$; uncontrolled for multiplicity).

Efficacy Assessment

Both treatments in this study resulted in comparable improvement in rTNSS (Fig. 3). Least square mean changes from baseline in rTNSS after 2 weeks of treatment were -2.4 and -2.3 for CIC-HFA and MFNS, respectively.

Safety

The overall incidence of treatment-emergent AEs was higher for CIC-HFA than for MFNS (28.9% and 21.5%, respectively; Table 4), as was the incidence of

local AEs (15.1% and 7.1%, respectively). However, most AEs were mild or moderate in severity. Only two subjects (one in each group) experienced an AE that led to treatment discontinuation; neither event was considered related to treatment.

Overall, the types of treatment-emergent AEs reported would be anticipated with treatment with an INS in a symptomatic population of subjects with PAR. The most frequently reported AEs overall were application site pain, headache, and epistaxis. Application site pain (burning on initial application) occurred more frequently with CIC-HFA treatment versus MFNS (6.1% versus 1.0%) and was deemed by the study investigator to be mild in severity, and headache occurred more frequently with MFNS versus CIC-HFA (3.8% versus 2.3%). Epistaxis was reported by a similar percentage of subjects during each treatment (2.3% for CIC-HFA; 1.3% for MFNS).

Two serious AEs were reported during the study, including one death (completed suicide) and one event of chest pain. Both serious AEs were reported during the washout period after treatment period 1 with

Table 3 Overall mean change in treatment satisfaction subscales and composites (intent-to-treat population)

	CIC-HFA at 74 μ g		MFNS at 200 μ g		<i>p</i> Value*
	LSM (SE)	95% CI	LSM (SE)	95% CI	
Treatment satisfaction scores					
Interference	17.31 (2.18)	13.02, 21.59	14.36 (2.18)	10.08, 18.65	0.0148
Regimen adaptation	6.65 (2.69)	1.35, 11.95	2.19 (2.70)	−3.12, 7.49	0.0078
Role limitation	9.35 (1.38)	6.64, 12.06	6.62 (1.38)	3.91, 9.33	0.0006
Regimen difficulties	−7.58 (2.34)	−12.19, −2.97	−0.13 (2.35)	−4.75, 4.48	<0.0001
Sensory impact	21.37 (1.90)	17.64, 25.09	4.41 (1.90)	0.68, 8.13	<0.0001
Hassle	24.70 (2.82)	19.16, 30.24	17.40 (2.82)	11.85, 22.94	<0.0001
Burden	10.45 (1.68)	7.15, 13.75	8.23 (1.68)	4.93, 11.53	0.0144
Regimen management	6.41 (1.32)	3.82, 9.00	5.38 (1.32)	2.79, 7.97	0.1728
Perceived relief	8.05 (3.08)	2.00, 14.10	3.77 (3.08)	−2.28, 9.83	0.0187
Satisfaction subscale composites scores					
Treatment functional impact composite#	12.36 (14.7)	9.47, 15.26	9.70 (1.48)	6.80, 12.60	0.0019
Regimen acceptance composite§	7.34 (2.79)	1.86, 12.83	2.99 (2.79)	−2.50, 8.47	0.0095
Regimen attributes composite¶	13.90 (1.36)	11.22, 16.58	4.88 (1.36)	2.20, 7.56	<0.0001

*From a t-test.

#The treatment functional impact composite combines the interference, role limitation, and burden treatment satisfaction subscales.

§The regimen acceptance composite combines the perceived relief and regimen adaptation treatment satisfaction subscales.

¶The regimen attributes composite, a co-primary end point, combines the sensory impact and regimen management treatment satisfaction subscales.

CI = confidence interval; CIC-HFA = ciclesonide hydrofluoroalkane nasal aerosol; LSM = least square mean; MFNS = mometasone furoate aqueous nasal spray; SE = standard error.

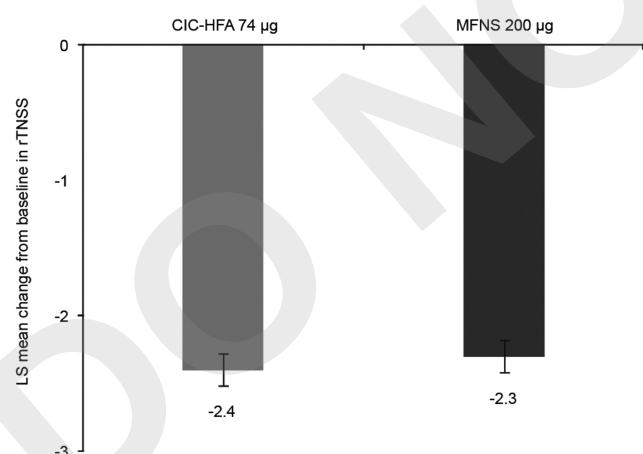


Figure 3. Improvement in rTNSS. Data are mean change from baseline ($\pm$ standard error of the mean). rTNSS, reflective total nasal symptom score; CIC-HFA, ciclesonide hydrofluoroalkane nasal aerosol; LS, least square; MFNS, mometasone furoate aqueous nasal spray.

MFNS. Both events were assessed by the investigator as not related to study medication.

DISCUSSION

In the current study of equally effective treatments (confirmed by improvements in rTNSS scores), subjects expressed a significant preference for CIC-HFA

Table 4 Treatment-emergent AEs reported by $\geq 2\%$ of subjects overall (intent-to-treat population)

Event	CIC-HFA at 74 µg (n=311)	MFNS at 200 µg (n=312)
	Subjects n (%)	Subjects n (%)
Overall	90 (28.9)	67 (21.5)
Application site pain	19 (6.1)	3 (1.0)
Epistaxis	7 (2.3)	4 (1.3)
Headache	7 (2.3)	12 (3.8)
Oropharyngeal pain	6 (1.9)	6 (1.9)
Upper respiratory tract infection	5 (1.6)	3 (1.0)
Sinus headache	3 (1.0)	4 (1.3)

A treatment-emergent AE was defined as an event with onset date on or after the date of the 1st dose of study medication. A subject with multiple events was counted only once.

CIC-HFA = ciclesonide hydrofluoroalkane nasal aerosol; MFNS = mometasone furoate aqueous nasal spray; AEs = adverse events.

compared with MFNS. All 17 preference items numerically favored CIC-HFA over MFNS, with 15 of the 17 items being statistically significant in favor of CIC-HFA. For the individual preference items, subjects fa-

vored CIC-HFA versus MFNS in terms of smell, aftertaste, ease of use, and convenience, with substantial differences in favor of CIC-HFA noted for items related to medication dripping down the throat or running out of the nose. It is medically plausible that the perceived intensity of certain sensory attributes of an INS, such as odor and aftertaste, nose and throat irritation, ease of administration, and wetness/dryness, can influence patient adherence.²⁰ In a clinical study in which subjects chose between INS products that differed in their sensory attributes—smell, taste, aftertaste, throat run-down, nose run-out, and feel of spray in nose or throat—preference for a particular INS declined as the intensity of each attribute increased, with aftertaste as the most important attribute determining preference.¹⁰ These findings suggest a possible link between the sensory attributes of an INS and the potential for sustained adherence. Patient satisfaction with treatment in this study measured by satisfaction subscale composite scores indicated that patients were more satisfied with CIC-HFA versus MFNS (eight of the nine subscales favored CIC-HFA [$p < 0.02$], with the exception of regimen difficulties subscale, which favored MFNS [$p < 0.01$]). Some of the differences in preference and satisfaction between CIC-HFA and MFNS may have been caused by differences in deposition within the nasal cavity, as well as runoff into the nasopharynx or nose run-out. In a scintigraphy study that compared the nasal deposition of a radiolabeled solution of CIC-HFA aerosol and a radiolabeled aqueous nasal suspension of mometasone in symptomatic PAR or seasonal AR patients, greater sustained deposition of radioactivity within the nasal cavity occurred with CIC-HFA versus MFNS at 2 minutes (99.5% versus 86.3%), with larger amounts retained in the nasal cavity over a 10-minute postdose evaluation (80.81% for CIC-HFA versus 54.09% for MFNS) (unpublished data, 2013; clinicaltrials.gov identifier: NCT01371786).²¹ In this same scintigraphy trial, deposition of radioactivity within the nasopharynx (indicator of runoff of nasal spray down the back of the throat) and on wipes (indicator of nose run-out) was less for radiolabeled CIC-HFA aerosol at 10 minutes compared with radiolabeled MFNS (nasopharynx, 17.59% versus 32.19%; wipes, 1.6% versus 13.74%, clinicaltrials.gov identifier: NCT01371786).

This study was limited because the total per-dose volume of MFNS administered (400 μ L) was substantially higher than that for CIC-HFA (100 μ L), a difference that may have accounted for the higher throat rundown and nose run-out seen with MFNS versus CIC-HFA. Also, this was an open-label study that did not include a dummy nasal HFA and an aqueous placebo group (because of feasibility constraints, where the dummy “placebo” nasal spray may provide symptom improvement and therefore potentially influence

findings). In addition, subjects’ prior experience with mometasone may have influenced findings. Additional studies comparing CIC-HFA with nasal beclomethasone dipropionate HFA aerosol (administered as 2 sprays/nostril q.d.), the only other nasal HFA aerosol, would help discern potential differences between these two nasal HFA aerosol sprays.^{22,23} In this study, both INS formulations were generally well tolerated, and most AEs were mild or moderate in intensity.

In conclusion, the results of this study show that significantly more of these PAR patients preferred and were more satisfied with CIC-HFA compared with MFNS. The difference in satisfaction and preference in favor of CIC-HFA appears to be based on differences in patient perception of sensory attributes.

ACKNOWLEDGMENTS

All authors meet the criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE), were fully responsible for all content and editorial decisions, retained full control over all content of this article, and were involved with all stages of article development. Editorial and writing assistance in the development of this article in the form of drafting and revising content based on specific direction from the authors, collation of author comments, editing, referencing, article formatting, and creation of tables and figures was provided by Connection Healthcare (Newtown, PA).

REFERENCES

1. Skoner DP. Allergic rhinitis: Definition, epidemiology, pathophysiology, detection, and diagnosis. *J Allergy Clin Immunol* 108:S2–S8, 2001.
2. Bousquet J, van Cauwenberge P, Ait Khaled N, et al. Pharmacologic and anti-IgE treatment of allergic rhinitis ARIA update (in collaboration with GA2LEN). *Allergy* 61:1086–1096, 2006.
3. Sur DK, and Scandale S. Treatment of allergic rhinitis. *Am Fam Physician* 81:1440–1446, 2010.
4. Herman H. Once-daily administration of intranasal corticosteroids for allergic rhinitis: A comparative review of efficacy, safety, patient preference, and cost. *Am J Rhinol* 21:70–79, 2007.
5. Nielsen LP, Mygind N, and Dahl R. Intranasal corticosteroids for allergic rhinitis: superior relief? *Drugs* 61:1563–1579, 2001.
6. Osterberg L, and Blaschke T. Adherence to medication. *N Engl J Med* 353:487–497, 2005.
7. Loh CY, Chao SS, Chan YH, and Wang DY. A clinical survey on compliance in the treatment of rhinitis using nasal steroids. *Allergy* 59:1168–1172, 2004.
8. Stokes M, Amorosi SL, Thompson D, et al. Evaluation of patients’ preferences for triamcinolone acetonide aqueous, fluticasone propionate, and mometasone furoate nasal sprays in patients with allergic rhinitis. *Otolaryngol Head Neck Surg* 131: 225–231, 2004.
9. Meltzer EO, Stahlman JE, Leflein J, et al. Preferences of adult patients with allergic rhinitis for the sensory attributes of fluticasone furoate versus fluticasone propionate nasal sprays: A randomized, multicenter, double-blind, single-dose, crossover study. *Clin Ther* 30:271–279, 2008.
10. Mahadevia PJ, Shah S, Leibman C, et al. Patient preferences for sensory attributes of intranasal corticosteroids and willingness to adhere to prescribed therapy for allergic rhinitis: A conjoint analysis. *Ann Allergy Asthma Immunol* 93:345–350, 2004.

11. Luskin AT, Blaiss MS, Farrar JR, et al. Is there a role for aerosol nasal sprays in the treatment of allergic rhinitis: A white paper. *Allergy Asthma Proc* 32:168–177, 2011.
12. Velders GJM, Andersen SO, Daniel JS, et al. The importance of the Montreal Protocol in protecting climate. *Proc Natl Acad Sci U S A* 104:4814–4819, 2007.
13. In brief: Two intranasal corticosteroid HFA aerosols for allergic rhinitis. *Med Lett Drugs Ther* 54:84, 2012.
14. Sunovion Pharmaceuticals, Inc. Zetonna (ciclesonide) nasal aerosol package insert. Marlborough, MA; January 2012.
15. Food and Drug Administration (FDA). Guidance for industry. Patient-reported outcome measures: Use in medical product development to support labeling claims, 2006. FDA, Harrisburg, PA, 1–39, 2006.
16. National Institute of Health. ClinicalTrials.gov. Evaluation of a novel questionnaire to assess patient satisfaction with and preference of intranasal corticosteroids for the treatment of allergic rhinitis. Available online at www.clinicaltrials.gov/ct2/show/NCT01287364?term=NCT01287364&rank=1 Updated October 31, 2012; accessed May 3, 2013.
17. Merck & Co., Inc. Nasonex (mometasone furoate monohydrate) nasal spray package insert. Whitestation, NJ; March 2013.
18. World Medical Association Declaration of Helsinki, 1989. Available online at www.hhs.gov/ohrp/archive/irb/irb_appendices.htm#j6; accessed September, 18, 2012.
19. Barnes ML, Vaidyanathan S, Williamson PA, and Lipworth BJ. The minimal clinically important difference in allergic rhinitis. *Clin Exp Allergy* 40:242–250, 2010.
20. Blaiss MS, Benninger MS, Fromer L, et al. Expanding choices in intranasal steroid therapy: Summary of a roundtable meeting. *Allergy Asthma Proc* 27:254–264, 2006.
21. National Institute of Health. ClinicalTrials.gov. A phase 1 scintigraphy study to assess nasal deposition of ciclesonide using a novel nasal metered dose inhaler. NCT01371786. Available online at www.clinicaltrials.gov/ct2/show/NCT01371786?term=NCT01371786&rank=1 Updated September 5, 2012; accessed May 3, 2013.
22. Van Bavel JH, Ratner PH, Amar NJ, et al. Efficacy and safety of once-daily treatment with beclomethasone dipropionate nasal aerosol in subjects with seasonal allergic rhinitis. *Allergy Asthma Proc* 33:389–396, 2012.
23. Meltzer EO, Jacobs RL, LaForce CF, et al. Safety and efficacy of once-daily treatment with beclomethasone dipropionate nasal aerosol in subjects with perennial allergic rhinitis. *Allergy Asthma Proc* 33:249–257, 2012. □

Copyright of Allergy & Asthma Proceedings is the property of OceanSide Publications Inc. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.