A novel intranasal therapy of azelastine with fluticasone for the treatment of allergic rhinitis

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Background: Moderate-to-severe allergic rhinitis (AR) is a challenge to treat, with many patients using multiple therapies and achieving limited symptom control. More effective therapies must be developed and tested in well-controlled, randomized, prospective studies with a direct comparison to current standards.

Objectives: The aim of these studies was to investigate the efficacy of MP29-02 (a novel formulation of azelastine and fluticasone propionate [FP]) in patients with moderate-to-severe seasonal allergic rhinitis (SAR) and to compare its efficacy with 2 first-line therapies (ie, intranasal azelastine and intranasal FP) in this population.

Methods: Three thousand three hundred ninety-eight patients (≥12 years old) with moderate-to-severe SAR were enrolled into 3 multicenter, randomized, double-blind, placebo- and active-controlled, parallel-group trials (MP4002 [NCT00651118], MP4004 [NCT00740792], and MP4006 [NCT00883168]). Each trial was conducted for 14 days during different allergy seasons. The primary efficacy variable was the sum of the morning and evening change from baseline in reflective total nasal symptom score (range, 0-24) over the treatment period. Outcomes for the meta-analysis included efficacy according to disease severity and time to response in relevant responder criteria.

Results: In the meta-analysis MP29-02 reduced the mean reflective total nasal symptom score from baseline (−5.7 [SD, 5.3]) more than FP (−5.1 [SD, 4.9], $P < .001$), azelastine (−4.4 [SD, 4.8], $P < .001$), or placebo (−3.0 [SD, 4.2], $P < .001$). This benefit was observed from the first day of assessment, with improvement in each individual nasal symptom, even in the patients with the most severe disease. MP29-02 achieved response consistently days earlier and showed greater efficacy in patients with moderate-to-severe rhinitis than FP and azelastine.

Conclusions: MP29-02 represents a novel therapy that demonstrated superiority to 2 first-line therapies for AR. Patients with moderate-to-severe SAR achieved better control, and their symptoms were controlled earlier with MP29-02 than with recommended medications according to guidelines. (J Allergy Clin Immunol 2012;129:1282-9.)

Key words: *Allergic rhinitis, azelastine, fluticasone propionate, MP29-02, moderate-to-severe*

Allergic rhinitis (AR) occurs in more than 500 million persons around the world and is a global health problem that causes major illness and disability.[1,2] The effects of AR are far reaching and easily underestimated, with its negative effects affecting patient's quality of life (QoL)[3] and school and work performance.[4,5] It is also a costly disease, estimated at €4260 per patient per year in Europe,[6] and $3.4 billion annually in the United States in direct medical costs alone.[7]

AR is a challenge to treat because many patients do not respond

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Abbreviations used
ANCOVA: Analysis of covariance
AR: Allergic rhinitis
FP: Fluticasone propionate
iTNSS: Instantaneous total nasal symptom score
QoL: Quality of life
RQLQ: Rhinitis Quality of Life Questionnaire
rTNSS: Reflective total nasal symptom score
rTOSS: Reflective total ocular symptom score
SAR: Seasonal allergic rhinitis

underestimated and, consequently, inadequately treated.[8] Most patients have moderate-to-severe disease,[3,9] frequently experience severe symptoms while receiving therapy, and are dissatisfied and noncompliant with currently available therapy.[10,11] Patients use multiple therapies (as many as 74.4% of patients) in an attempt to achieve symptom control,[3,9,12-14] despite the limited evidence to support this practice.[2]

Given this unmet medical need, more effective therapies for the management of AR are clearly required. Current guideline-based therapy for AR includes oral and intranasal antihistamines and intranasal corticosteroids. Although intranasal corticosteroids are considered the most effective therapy, especially for more severe cases,[2,15] they need some time to become effective. In contrast, intranasal H_1-antihistamines, such as azelastine, have a rapid onset of action.

The recently updated Allergic Rhinitis and its Impact on Asthma guidelines[15] highlighted the need for high-quality, direct comparison studies to further substantiate the current treatment recommendations. Three randomized, placebo- and active-controlled, parallel-group trials were performed to directly compare the efficacy and safety of intranasal azelastine, intranasal fluticasone propionate (FP), and intranasal MP29-02 (a novel formulation of azelastine and FP), with all 3 medications using exactly the same formulation, in patients with moderate-to-severe seasonal allergic rhinitis (SAR). Each study aimed to demonstrate and replicate that MP29-02 demonstrated superiority to either monotherapy in a head-to-head fashion. Moreover, in the meta-analysis responder analyses were added to further address relevance in treatment efficacy.

METHODS

Protocol

Individual results and a meta-analysis of 3 phase III, multicenter, randomized, double-blind, parallel-group trials (MP4002 [NCT00651118], MP4004 [NCT00740792], and MP4006 [NCT00883168]) were assessed in patients with moderate-to-severe SAR to determine the efficacy of MP29-02 compared with intranasal H_1-antihistamine (azelastine), corticosteroid (FP), and placebo using the same formulation. Placebo spray comprised exactly the same vehicle/formulation as the active treatments without any active agent. The same treatments and treatment periods and essentially similar protocols were used in the 3 studies. The studies were conducted in accordance with US Food and Drug Administration and European Medicines Agency recommendations,[16,17] and good clinical practice[18] during the 2008-2009 US Spring and Fall allergy seasons. After institutional review board approval, written informed consent was obtained from all patients or legal guardians (subjects aged <18 years).

Participants

Subjects (≥12 years old) with a minimum 2-year history of SAR, significant [illegible] to relevant pollen were randomized. All subjects had moderate-to-severe SAR defined by a reflective total nasal symptom score (rTNSS) of at least 8 of 12, with a congestion score of 2 or 3 during screening. Inclusion criteria for the duration of symptoms for the 3 studies were slightly different. For more information on this and exclusion criteria, see the Methods section in this article's Online Repository at www.jacionline.org. Excluded therapies and medications are summarized in Table E1 in this article's Online Repository at www.jacionline.org.

Planned interventions and timing

Each study comprised a 7-day, single-blind, placebo lead-in period and a 14-day treatment period with 3 study visits at days 1, 7, and 14. On visit 2 (day 1), eligible patients were randomized to 14 days of treatment (1 spray per nostril twice daily) with the following: (1) MP29-02 nasal spray (novel formulation of 137 μg of azelastine/50 μg of FP); (2) azelastine nasal spray (137 μg); (3) FP (50 μg) nasal spray; or (4) vehicle placebo nasal spray. Doses were separated by approximately 12 hours. Patients recorded application times and symptom scores in a diary. Compliance with treatment was assessed (see the Methods section in this article's Online Repository).

Efficacy variables

The primary efficacy variable was the sum of the morning and evening overall change from baseline in 12-hour rTNSSs over the entire 14-day treatment period (sum of the individual nasal symptoms of congestion, itching, rhinorrhea, and sneezing).[16,17] All nasal and ocular symptoms were scored by patients twice daily on each treatment day according to a 4-point scale. For nasal symptoms, a score of 0 was defined as none (no symptoms present), a score of 1 was defined as mild (mild symptoms that do not interfere with any activity), a score of 2 was defined as moderate (slightly bothersome symptoms that slightly interfere with activity/nighttime sleep), and a score of 3 was defined as severe (bothersome symptoms that interfere with activity/nighttime sleep). Therefore the maximum rTNSS or instantaneous total nasal symptom score (iTNSS) was 24 (ie, 4 symptoms × score of 3 × 2 for morning + evening). See the Methods section in this article's Online Repository for calculation of baseline scores.

Secondary efficacy variables included overall change from baseline (treatment period, days 2-14) in the individual reflective nasal symptom score, iTNSS, and reflective total ocular symptom score (rTOSS). For the symptoms of itchy eyes and watery eyes, the same scale was used as for nasal symptoms. For the symptom of red eyes, the following scale was used: 0, none (no redness present); 1, mild (slightly dilated blood vessels and pinkish color compared with the subject's normal color); 2, moderate (more dilation of blood vessels and red color compared with subject's normal color); and 3, severe (large, numerous, dilated blood vessels and deep red color compared with the subject's normal color). The maximum rTOSS was 18 (ie, 3 symptoms × score of 3 × 2 for morning + evening). Onset of action was also determined clinically by means of assessment of iTNSS in the first 4 hours after administration.

QoL

QoL was assessed before randomization and at the end of the study by using the 28-item Rhinitis Quality of Life Questionnaire (RQLQ) for subjects older than 18 years.[19] Total baseline RQLQ scores were used to categorize patients according to severity.

Safety variables

Safety was assessed based on the incidence, type, and severity of adverse events coded with the Medical Dictionary for Regulatory Activities. At each visit, patients underwent a direct visual nasal examination to determine potential side effects to the nasal mucosa or otherwise clinically relevant intranasal conditions. Vital signs were also measured.

Sample size

For studies MP4002 and MP4004, sample size was determined based on the [illegible][20]

suggested that MP29-02 and FP might reduce the rTNSS by −5.92 and −4.19, respectively, and that a meta-analysis SD of 5 might be a conservative estimate. On the basis of these values, a 2-sided α value of 5%, and a 10% dropout rate, 195 randomized subjects per treatment arm were sufficient to achieve 90% power. Sample size in study MP4006 was determined by excluding a treatment difference of less than 0.6 units in overall reduction in the rTNSS over a 14-day treatment period. Allowing for dropouts, a minimum of 450 subjects per group had to be randomized.

Randomization

Patients were randomized and balanced by study site in blocks of 4. Eligible subjects received the study site's next available randomization number in sequence.

Blinding

Individual nasal spray bottles were identity masked such that both patients and study personnel were blind to treatment assignment. The active controls comprised the individual components of MP29-02 in the same vehicle (ie, contained the same excipients assessed qualitatively and quantitatively), pump volume (0.137 mL per spray), and device (see the Methods section in this article's Online Repository). A blind randomization code was maintained at a central site apart from the sponsor and study centers. Study blinding was preserved at the study sites until all subjects completed the study and the database had been locked.

Statistical analyses

A hierarchical test procedure was implemented to maintain the overall 2-sided type I error level of .05 among the pairwise comparisons. As a first step, changes in combined rTNSSs were compared between patients receiving MP29-02 and placebo. If this was significant, MP29-02 was then compared with azelastine, and if this was also significant, it was then compared with FP.

As prespecified in trial protocols and statistical analysis plans before unblinding, efficacy analyses were performed on the intent-to-treat population of all randomized patients with at least 1 postbaseline observation. An analysis of covariance (ANCOVA) model was applied to the primary efficacy variable of absolute change in combined morning plus evening rTNSSs. The model included the treatment days from day 2 (first day with postdose morning score) to day 14. Fixed effects were treatment group, day, and center, with baseline as a continuous covariate. The covariance matrix of the error terms was left unspecified and allowed to differ among treatment groups, with degrees of freedom calculated by using the Satterthwaite approximation. Treatment differences are presented as differences in least squares means resulting from this applied ANCOVA (ie, estimates are corrected for influence of covariates, such as center or baseline severity [see Methods section in this article's Online Repository]), to account for the applied inferential statistical methods. Change from baseline in iTNSSs, individual reflective nasal symptom scores, rTOSSs, and RQLQ scores were assessed in the same way.

The meta-analysis on efficacy data was conducted *post hoc* and comprised all 3 studies. The statistical models used for the meta-analysis were similar to those used in the individual studies, with an additional fixed effect for study.

In addition, the rTNSS (overall and by day) was assessed based on patient severity. Patients were categorized into 2 severity groups according to their median baseline rTNSSs (ie, ≤18.9 or >18.9) or median baseline RQLQ scores (ie, ≤3.9 or >3.9). Moreover, time to response was analyzed by using Kaplan-Meier estimates. A change from baseline in (1) combined rTNSS of at least 50%[17] or (2) a score of 1 point or less for each nasal symptom (ie, complete or near-complete resolution of each symptom) were used to define response.

RESULTS

Patients

Study completion rates were high (approximately 95%) and similar across studies and across treatment groups (see Table E2 in this article's Online Repository at www.jacionline.org). Dropout rates were negligible (see Table E3 in this article's Online Repository at www.jacionline.org). When data were pooled for meta-analysis, 848, 846, 847, and 857 patients received MP29-02, FP, azelastine, and placebo, respectively. The baseline characteristics of the 4 treatment groups were similar, both within and between studies (Table I). Patients' baseline rTNSSs were well matched and confirmed that the vast majority of these patients had moderate-to-severe AR.

Outcomes

Efficacy in individual studies (primary end point rTNSS). In each study MP29-02 significantly reduced the mean rTNSS from baseline by a greater margin than FP, azelastine, or placebo (Table II and Fig 1). All individual nasal symptoms contributed to the effect (see Tables E4 and E5 in this article's Online Repository at www.jacionline.org). In each study all active treatments were statistically significantly superior to placebo, whereas MP29-02 demonstrated superiority to all other treatment arms.

Safety. For each study, the proportion of subjects with a treatment-emergent adverse event was similar for the active groups (see Table E6 in this article's Online Repository at www.jacionline.org). The higher proportion of treatment-related adverse events observed in the MP29-02 and azelastine treatment groups was due primarily to the taste of azelastine coded as dysgeusia in these patients (2.1% to 4.7% of MP29-02–treated patients and 3.4% to 7.2% of azelastine-treated patients, see Table E7 in this article's Online Repository at www.jacionline.org), but no patient discontinued therapy because of this event. For all studies, changes in vital signs and nasal examination were similar in all groups.

Meta-analysis. *rTNSSs, iTNSSs, individual symptom scores, and rTOSSs: Change from baseline.* Patients treated with MP29-02 experienced significantly greater nasal symptom relief than those treated with either monotherapy. Over the entire 14-day treatment period, MP29-02 reduced the mean rTNSS from baseline (−5.7 [SD, 5.3]) to a significantly greater degree than FP (−5.1 [SD, 4.9], $P < .001$), azelastine (−4.4 [SD, 4.8], $P < .001$), or placebo (−3.0 [SD, 4.2], $P < .001$; Table II and Fig 1). MP29-02 had an onset of action of 30 minutes, and the clinical benefit was observed during the first day of assessment and sustained over the entire course of treatment (see Fig E1 in this article's Online Repository at www.jacionline.org).

MP29-02 reduced the overall iTNSS from baseline to a significantly greater extent than FP ($P = .022$), azelastine ($P < .001$), or placebo ($P < .001$). MP29-02 targeted all of the symptoms of AR (see Tables E4 and E5). Compared with FP or azelastine monotherapy, patients who received MP29-02 had greater relief from their symptoms of nasal congestion ($P = .005$ vs FP and $P < .001$ vs azelastine), nasal itch ($P = .005$ vs FP and $P = .001$ vs azelastine), rhinorrhea ($P = .013$ vs FP and $P < .001$ vs azelastine), and sneezing ($P = .001$ vs FP and $P < .001$ vs azelastine; see Tables E4 and E5). Patients treated with MP29-02 also experienced superior relief from their ocular symptoms than those treated with FP alone. Over the entire 14-day treatment period, MP29-02 reduced the mean rTOSS from baseline (−3.2 [SD, 4.0]) compared with FP (−2.8 [SD, 3.6]), azelastine (−2.9 [SD, 3.8]), or placebo (−1.8 [SD, 3.4]), achieving statistical significance versus FP ($P = .003$) and pla-

TABLE I. Baseline characteristics of study participants included in 3 randomized trials (ITT population)

	Study MP4002			
	MP29-02 (n = 207)	**FP (n = 207)**	**Azelastine (n = 208)**	**Placebo (n = 209)**
Age (y)	37.3 (14.1)	38.6 (14.1)	36.2 (14.6)	37.3 (16.0)
Male sex, no. (%)	65 (31.4)	80 (38.6)	78 (37.5)	77 (36.8)
White race, no. (%)	162 (78.3)	161 (77.8)	162 (77.9)	169 (80.9)
History of SAR (y)	21.7 (13.2)	21.3 (13.5)	21.6 (13.6)	21.2 (14.0)
	Study MP4004			
	MP29-02 (n = 193)	**FP (n = 189)**	**Azelastine (n = 194)**	**Placebo (n = 200)**
Age (y)	38.8 (14.1)	37.0 (13.6)	38.2 (13.5)	37.2 (13.0)
Male sex, no. (%)	67 (34.7)	68 (36.0)	66 (34.0)	81 (40.5)
White race, no. (%)	154 (79.8)	140 (74.1)	153 (78.9)	164 (82.0)
History of SAR (y)	21.5 (13.5)	21.1 (13.7)	19.7 (13.1)	21.0 (12.8)
	Study MP4006			
	MP29-02 (n = 448)	**FP (n = 450)**	**Azelastine (n = 445)**	**Placebo (n = 448)**
Age (y)	35.6 (14.5)	34.2 (14.5)	36.4 (14.8)	34.7 (14.1)
Male sex, no. (%)	171 (38.2)	170 (37.8)	174 (39.1)	179 (40.0)
White race, no. (%)	364 (81.3)	356 (79.1)	357 (80.2)	348 (77.7)
History of SAR (y)	20.4 (13.0)	19.6 (12.5)	19.5 (12.9)	19.6 (12.4)

Data are presented as means (SDs) unless otherwise stated.
ITT, Intent to treat.

TABLE II. Total nasal symptom scores (baseline and change from baseline) for 3 randomized trials and the meta-analysis results (ITT population)

Treatment	No.	Baseline	Change from baseline	Difference	LS mean	95% CI	*P* value
Study MP4002							
MP29-02	207	18.3 (3.0)	−5.5 (5.2)	—	—	—	—
FP	207	18.2 (3.2)	−5.0 (4.7)	MP29-02, FP	−0.9	−1.74 to −0.07	.034
AZE	208	18.2 (3.5)	−4.1 (4.6)	MP29-02, AZE	−1.4	−2.22 to −0.54	.002
Placebo	209	18.6 (3.2)	−2.6 (3.9)	MP29-02, PLA	−2.7	−3.48 to −1.91	<.001
				FP, PLA	−1.8	−2.50 to −1.09	<.001
				AZE, PLA	−1.3	−2.04 to −0.60	.001
Study MP4004							
MP29-02	193	18.2 (3.3)	−5.6 (5.2)	—	—	—	—
FP	189	18.6 (2.9)	−5.0 (5.2)	MP29-02, FP	−1.0	−1.91 to −0.05	.038
AZE	194	18.5 (3.1)	−4.4 (4.6)	MP29-02, AZE	−1.0	−1.90 to −0.09	.032
Placebo	200	18.2 (3.1)	−2.8 (3.9)	MP29-02, PLA	−2.5	−3.33 to −1.67	<.001
				FP, PLA	−1.5	−2.34 to −0.69	.001
				AZE, PLA	−1.5	−2.31 to −0.71	.001
Study MP4006							
MP29-02	448	19.4 (2.4)	−5.6 (5.2)	—	—	—	—
FP	450	19.4 (2.4)	−5.1 (4.7)	MP29-02, FP	−0.6	−1.22 to −0.07	.029
AZE	445	19.5 (2.5)	−4.5 (4.8)	MP29-02, AZE	−0.7	−1.30 to −0.13	.016
Placebo	448	19.5 (2.4)	−3.2 (4.3)	MP29-02, PLA	−2.1	−2.70 to −1.57	<.001
				FP, PLA	−1.5	−2.03 to −0.95	<.001
				AZE, PLA	−1.4	−1.96 to −0.87	<.001
Meta-analysis (studies MP4002, MP4004, and MP4006)							
MP29-02	848	18.8 (2.9)	−5.7 (5.3)	—	—	—	—
FP	846	18.9 (2.8)	−5.1 (4.9)	MP29-02, FP	−0.8	−1.18 to −0.34	.001
AZE	847	18.9 (3.0)	−4.4 (4.8)	MP29-02, AZE	−0.9	−1.37 to −0.52	<.001
Placebo	857	19.0 (2.8)	−3.0 (4.2)	MP29-02, PLA	−2.3	−2.75 to −1.95	<.001
				FP, PLA	−1.6	−1.97 to −1.21	<.001
				AZE, PLA	−1.4	−1.78 to −1.02	<.001

Data are expressed as means (SDs). Difference from active treatment is given as LS mean treatment difference with associated 95% CIs and *P* values.
AZE, Azelastine (137 μg per nostril twice daily); *FP,* fluticasone propionate (50 μg per nostril twice daily); *LS,* least squares; *MP29-02,* azelastine/FP (137/50 μg/nostril twice daily); *PLA,* placebo.

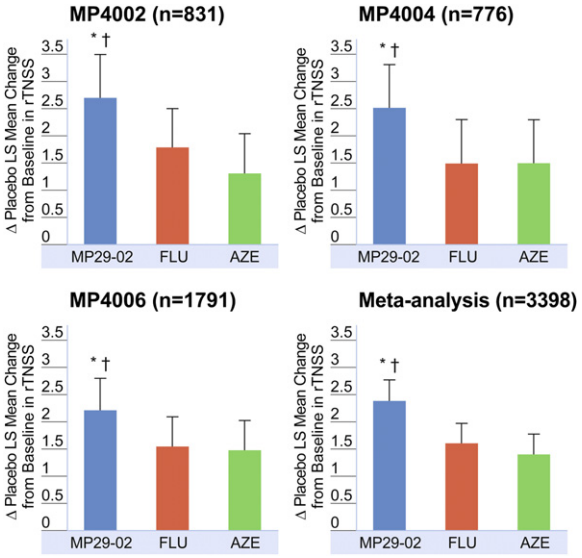

FIG 1. Effect of MP29-02, FP *(FLU)*, and azelastine *(AZE)* on overall rTNSSs (morning plus evening) in patients with moderate-to-severe SAR. Data are presented as least squares *(LS)* mean change from baseline derived by means of ANCOVA minus placebo. The precision of these estimates are indicated by the upper bounds of the respective 95% CIs. *Study MP4002*: n = 831, *P = .034 versus FP; †P = .001 versus AZE; *Study MP4004*: n = 776, *P = .038 versus FP; †P = .032 versus AZE; *Study MP4006*: n = 1791, *P = .029 versus FP; †P = .016 versus AZE; *Meta-analysis*: n = 3398, *P < .001 versus FP; †P < .001 versus AZE.

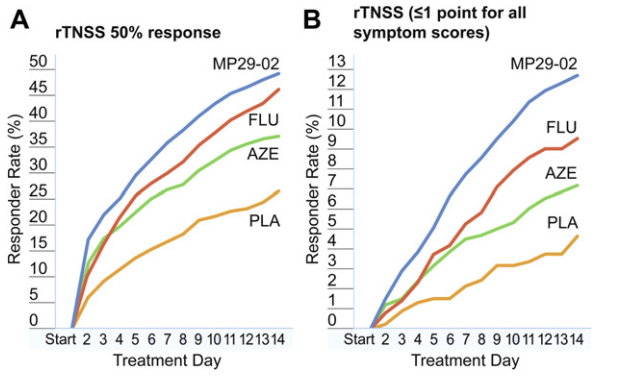

FIG 2. Time-response curves showing the percentage of patients exhibiting 50% improvement in rTNSSs **(A)** or a score of 1 point or less (ie, complete or near-complete resolution) for each nasal symptom **(B)** by treatment day after treatment with MP29-02 (n = 834), FP (*FLU*; n = 846), azelastine (*AZE*; n = 847), or placebo (*PLA*; n = 857). Data are presented as mean proportion of patients for the meta-analysis dataset (studies MP4002, MP4004, and MP4006). Fig 2, *A*, MP29-02 versus FLU: P = .071; MP29-02 versus AZE: P < .001; MP29-02 versus PLA: P < .001. Fig 2, *B*, MP29-02 versus FLU: P = .033; MP29-02 versus AZE: P < .001; MP29-02 versus PLA: P < .001.

rTNSS responder analyses. Fig 2, *A*, shows the proportion of patients in each treatment group who experienced a 50% or greater reduction in rTNSS over time. The results highlighted a time advantage of MP29-02 over FP (up to 3 days earlier) and azelastine (up to 5 days earlier) monotherapy in producing a clinically meaningful reduction in rTNSS, as well as an increased responder rate with MP29-02 (see Table E8 in this article's Online Repository at www.jacionline.org). More patients treated with MP29-02 (12.4%) also exhibited complete or near-complete elimination of their symptoms (ie, reduction in all nasal symptoms scores to ≤1) than those treated with FP (9.3%), azelastine (7.1%), or placebo (4.2%; Fig 2, *B*). Moreover, this effect was also observed days earlier than either monotherapy: up to 5 days faster than FP (P = .033) and up to 7 days faster than azelastine (P < .001).

rTNSS change from baseline by baseline patient severity. MP29-02 provided benefits for all patients, providing significantly greater symptom relief than FP or azelastine monotherapy regardless of disease severity (Fig 3). When severity was split by median baseline rTNSS, MP29-02 was significantly superior to FP (difference, −0.6; P = .033 [95% CI, −1.16 to −0.05]) and azelastine (difference: −0.8; P = .004 [95% CI, −1.41 to −0.27]) in patients with less severe disease (ie, baseline rTNSS of ≤18.9), with a greater benefit observed in patients with more severe disease (ie, baseline TNSS of >18.9) compared with both FP (difference: −0.8; P = .008 [95% CI, −1.46 to −0.23]) or azelastine (difference: −1.1; P = .001 [95% CI, −1.71 to −0.48]). When severity was alternatively split by median baseline RQLQ score, MP29-02 was again superior to FP and azelastine monotherapy (in terms of rTNSS improvement) in patients with moderate rhinitis (ie, RQLQ: ≤3.9; difference of −0.9 [P = .006; 95% CI, −1.46 to −0.24] vs azelastine) and significantly superior in patients with severe rhinitis (ie, RQLQ: >3.9; difference of −1.0 [P = .004; 95% CI, −1.68 to −0.33] vs FP and difference of −1.1 [P = .001; 95% CI, −1.75 to −0.44] vs azelastine).

QoL. Patients were well matched for QoL impairment, with overall baseline RQLQ scores of 3.9 (SD, 1.0) in the MP29-02, azelastine, and placebo groups and 3.8 (SD, 1.0) in the FP group. By day 14, all active treatments significantly improved patient QoL (MP29-02: −1.6 [SD, 1.3]; FP: −1.5 [SD, 1.3]; azelastine: −1.4 [SD, 1.3]) compared with placebo (−1.0 [SD, 1.2], P < .001).

DISCUSSION

Before MP29-02, no clinical development program had demonstrated additional benefit over 2 currently recommended first-line AR therapies in patients with moderate-to-severe disease. In the present program MP29-02 demonstrated superior efficacy over intranasal FP and intranasal azelastine monotherapy in patients with AR in a set of 3 randomized, double-blind, placebo-controlled clinical studies with active controls by using the same device and formulation. This provides sound clinical evidence, for the first time, that intranasal antihistamines and corticosteroids have complementary pharmacologic effects on the pathogenesis of AR and satisfy the demands of the Allergic Rhinitis and its Impact on Asthma guidelines requesting high-quality direct comparison studies. The consistency of the results among the clinical trials and symptoms contributes to the robustness of the data. Adverse events were similar for all active groups, and only a few patients experienced mild dysgeusia.

The advancement in the treatment of SAR derives from MP29-02 providing consistent and uniform relief from each of the individual nasal symptoms of congestion, itching, rhinorrhea, and sneezing. Whether intranasal corticosteroids are also effective in treating ocular symptoms is an ongoing debate.[21] In this regard MP29-02 has been shown to be more effective than FP, as

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