

An integrated analysis of the efficacy of fluticasone furoate nasal spray versus placebo on the nasal symptoms of perennial allergic rhinitis

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ABSTRACT

Intranasal corticosteroids are widely prescribed for the treatment of perennial allergic rhinitis (PAR). The aim of this analysis was to determine whether the beneficial effects of once-daily (q.d.) fluticasone furoate nasal spray (FFNS) effectively improved individual nasal symptoms of PAR. An integrated analysis was performed on data from three randomized, double-blind, placebo-controlled, parallel-group trials designed to evaluate the efficacy and safety of FFNS at 110 micrograms, q.d. in subjects with PAR. The analysis included 460 subjects who received FFNS and 459 who received placebo for 4 weeks. All subjects evaluated the severity of individual nasal symptoms of nasal congestion, nasal itching, rhinorrhea, and sneezing on a four-point categorical scale. The main efficacy measures included change from baseline in daily reflective total nasal symptom score (rTNSS), reflective daily scores for each individual symptom, and predose instantaneous TNSS (iTNSS). Over 4 weeks of treatment, FFNS significantly improved rTNSS, iTNSS, and the reflective scores for each individual symptom compared with placebo. The least squares (LS) mean treatment difference over weeks 1–4 between FFNS and placebo for rTNSS was -0.93 , ranging from -0.20 to -0.28 for the individual nasal symptoms ($p < 0.001$ for all versus placebo). For the iTNSS, the LS mean treatment difference between FFNS and placebo over weeks 1–4 was -0.95 (95% CI, -1.24 , -0.66 ; $p < 0.001$). FFNS at 110 micrograms q.d. effectively relieved all nasal symptoms of PAR including nasal congestion over a 24-hour period.

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Allergic rhinitis (AR) is a highly prevalent chronic condition that may be seasonal or perennial, depending on the timing of exposure to the causative allergens.¹ Perennial AR (PAR) is caused by exposure to year-round allergens such as animal dander, molds, and dust mites.^{2,3} The symptoms of PAR include chronic or chronic intermittent nasal symptoms including congestion, rhinorrhea, itching and sneezing, and, less commonly, ocular symptoms.⁴ Although symptom intensity may vary from one patient to another, nasal symptoms, by definition, occur in all patients.^{5,6}

The prevalence of PAR has increased steadily for many years, possibly as part of a worldwide increase in the prevalence of allergic disease and owing to greater allergen exposure.⁷ In the United States, perennial symptoms affect ~10–20% of the general population,⁸

and European epidemiological studies indicate that incidence rates vary from 4.1 to 13% in adults aged 18–65 years.⁹ In other regions of the globe, there is a large diversity in prevalence rates but high prevalence has been established in older children and adolescents.^{10,11} A World Health Organization workshop on “Allergic Rhinitis and Its Impact on Asthma” (ARIA) suggested a new classification of AR based on frequency and severity of symptoms because these are the major factors involved in determining treatment. ARIA reclassified AR as mild/moderate–severe and intermittent/persistent.⁹ However, a clinical classification of seasonal and perennial rhinitis is useful in clinical practice, especially for diagnosis and immunotherapy, and can be used alongside the ARIA classification.¹²

Avoidance of perennial allergens is often impractical or impossible; therefore, pharmacotherapy is a mainstay of treatment for PAR. Intranasal corticosteroids (INs) are well recognized for their efficacy in controlling the nasal symptoms of AR and, as a consequence, are recommended as the first line of pharmacotherapy for rhinitis with prominent nasal congestion in both the American Academy of Allergy, Asthma, and Immunology guidelines and the ARIA guidelines.^{13–15}

Fluticasone furoate nasal spray (FFNS), a high-affinity corticosteroid with potent anti-inflammatory activity and low (<0.5%) absolute bioavailability,¹⁶ has been shown to be well tolerated and significantly more

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Table 1 Details of the studies included in the integrated analysis

GlaxoSmithKline Study No. and clinitrial.gov.uk No.	Countries and Study Dates	Design and Duration	No. of Subjects	Citation for Original Research
FFR30002; NCT00103454	Canada and United States (45 sites); January–May 2005	Placebo controlled, 4-wk, double-blind, randomized, parallel group	Placebo, $n = 153$; FFNS at 110 μg , $n = 149$	Nathan <i>et al.</i> ²²
FFR106080; NCT00289198	Australia, Canada, Estonia, Germany, Latvia, Lithuania, New Zealand, Russia, and United States (40 sites); February–June 2006	Placebo controlled, 6-wk, double-blind, randomized, parallel group	Placebo, $n = 151$; FFNS at 110 μg , $n = 151$	Vasar <i>et al.</i> ²³
FFU111439; NCT00609674	Canada, Estonia, Germany, Slovakia, Hungary, Russia, and United States (34 sites); January–June 2008	Placebo controlled, 4-wk, double-blind, randomized, parallel group	Placebo, $n = 155$; FFNS at 110 μg , $n = 160$	Given <i>et al.</i> ²⁹

effective than placebo at relieving symptoms of AR in children, adolescents, and adults with both PAR and seasonal AR (SAR) in double-blind, controlled clinical studies investigating once-daily (q.d.) treatment.^{17–24} FFNS has established efficacy against both nasal and ocular symptoms in SAR.²⁵

Nasal congestion is typically the most troublesome symptom of PAR and is often the primary cause of nocturnal sleep disturbance and daytime fatigue among these patients.^{5,6,26,27} PAR is also reported to manifest with greater intensity during the morning (A.M.) hours, highlighting the need for effective treatment strategies with 24-hour symptom control.²⁸

In three separate clinical studies FFNS has proven to be efficacious in relieving the nasal symptoms associated with PAR. Treatment with FFNS at 110 μg q.d. for 4 or 6 weeks consistently improved both nasal and ocular symptoms.^{22,23,29} Although an overall change in total symptom score has often been used as a primary efficacy measure for the majority of INs in AR patients and, undoubtedly, provides a useful indicator of efficacy, this measure does not provide specific information on the effect of treatment on individual symptoms. The aim of this integrated analysis was to determine whether the beneficial effects of FFNS consistently improved individual nasal symptoms of PAR.

METHODS

Integrated analyses were performed on combined data from three trials (FFR30002, FFR106080, and FFU111439)^{22,23,29} evaluating the efficacy and safety of

q.d. administration of FFNS in adult and adolescent subjects ≥ 12 years old (Table 1). Subjects had a clinical history of PAR defined as a 2-year medical history and past treatment of AR characterized by year-round symptoms that could have included nasal congestion, rhinorrhea, nasal itching, and sneezing. Subjects were also required to have a positive skin test (*i.e.*, wheal of ≥ 3 mm larger than the diluent control for prick testing) to a perennial allergen such as dust mites, animal dander, mold, or cockroach within 12 months before screening. Subjects with significant concomitant medical conditions, a severe physical obstruction of the nose, rhinitis medicamentosa, sinusitis, glaucoma, cataracts or ocular herpes simplex, or asthma, with the exception of mild intermittent asthma were excluded from these studies.

The three PAR studies were randomized, double-blind, placebo-controlled, parallel-group, multicenter trials of similar study design (Table 1). Studies FFR30002 and FFU111439 were of 4 weeks duration and study FFR106080 was of 6 weeks duration. The studies consisted of a 7- to 14-day screening period followed by a 4- or 6-week treatment period. Clinic visits were scheduled on the 1st day of the screening period, the day of randomization (day 1), at the end of each treatment week, and, if applicable, at early withdrawal.

Patients

To be eligible for randomization, subjects were required to have both an average reflective daily total nasal symptom score (rTNSS) of ≥ 6 and an average reflective daily nasal congestion score of ≥ 2 based on

the average of the last eight A.M. and evening (P.M.) assessments including the A.M. assessment on the A.M. of the randomization visit. Patients meeting these criteria were randomized 1:1 on day 1 to receive either FFNS at 110 μ g q.d. or vehicle placebo nasal spray q.d. Study medication was taken each A.M. for 4 or 6 weeks. Except for study medication, antiallergy and antirhinitis medications were prohibited throughout the treatment period.

Efficacy Assessments

All efficacy measures for nasal symptoms, including rhinorrhea, nasal congestion, nasal itching, and sneezing, were based on subject-rated, individual symptom assessments evaluated on a four-point categorical scale: 0 indicating none (no sign or symptom evident); 1, mild (sign or symptom clearly present but causing minimal awareness and easily tolerated); 2, moderate (definite awareness of sign or symptom that is bothersome but tolerable); and 3, severe (sign or symptom that is hard to tolerate and causes interference with activities of daily living and/or sleeping).

Subjects were asked to score their symptoms in a reflective manner and an instantaneous manner on a diary card. The reflective rating represented how the subject had been feeling over the preceding 12 hours. This assessment provided information on how effective the treatment was throughout a 12-hour period of time and was performed twice daily (A.M. and P.M.). The A.M. assessment was performed in the A.M. before administering the dose of study drug and assessed how the subject felt during the night. The P.M. assessment was performed ~12 hours after dosing and before bedtime and assessed how the subject felt during the day.

The instantaneous rating represented how the subject felt at the time of the assessment, or at that “instant.” The instantaneous assessment was performed q.d., in the A.M. before administering the dose of study drug. This assessment provided information on the efficacy of the treatment at the end of the 24-hour dosing interval.

For the three studies, the primary efficacy end point was the mean change from baseline over the entire treatment period in daily rTNSS. The TNSS is the sum of four individual symptom scores for rhinorrhea, nasal congestion, nasal itching, and sneezing. The secondary efficacy end points include the mean change from baseline over the entire treatment period in A.M., predose, instantaneous TNSS (iTNSS), and the mean change from baseline over the entire treatment period in both individual daily reflective nasal symptom scores and A.M. predose instantaneous nasal symptom scores for rhinorrhea, nasal congestion, nasal itching, and sneezing.

Safety Assessment

In each study, adverse events were recorded. This data have not been integrated for analysis.

Statistical Analysis

The integrated analysis was based on the intent-to-treat population, defined as all randomized subjects who received at least one dose of study drug. All data from these three studies were used in the analysis model. Analysis of covariance was used for the comparison of treatment groups (FFNS at 110 μ g versus placebo), adjusting for study, baseline symptom score, age, and gender. The two-sided 95% CIs were constructed for the treatment difference between FFNS at 110 μ g and placebo to provide an overall estimate of the treatment effect size.

Comparisons between FFNS and placebo were performed on the mean change from baseline over weeks 1–4 in daily rTNSS, in reflective individual nasal symptom scores for rhinorrhea, nasal congestion, nasal itching, and sneezing, in A.M. predose iTNSS and instantaneous individual nasal symptom scores.

RESULTS

Patient Demographics and Baseline

The intent-to-treat population comprised 919 subjects ($n = 460$ FFNS at 110 μ g; $n = 459$ placebo) who were randomized and received at least one dose of study medication. In each treatment group, 89% of subjects completed the study (Fig. 1). The most common reason for withdrawal was a protocol violation that accounted for 2% of early withdrawals in each group. Demographic and baseline characteristics were similar between treatment groups. Over one-half of the subjects had suffered PAR for at least 10 years and the baseline nasal symptoms were similar between treatment groups (Table 2).

Efficacy End Points

The mean daily rTNSSs were similar between groups at baseline. The integrated analysis of the three studies showed that FFNS significantly improved the total daily rTNSS compared with placebo (Table 3). The improvement was statistically significant for FFNS versus placebo at each week of treatment. Over weeks 1–4 the least squares (LS) mean treatment difference between FFNS and placebo was -0.93 (95% CI, -1.21 , -0.64 ; $p < 0.001$; Fig. 2).

FFNS also significantly improved all four daily reflective individual nasal symptoms of PAR compared with placebo over weeks 1–4 of the treatment period (Table 4; Fig. 3). The most improved symptom was sneezing with an LS mean treatment difference between FFNS and placebo of -0.28 (95% CI, -0.36 ,

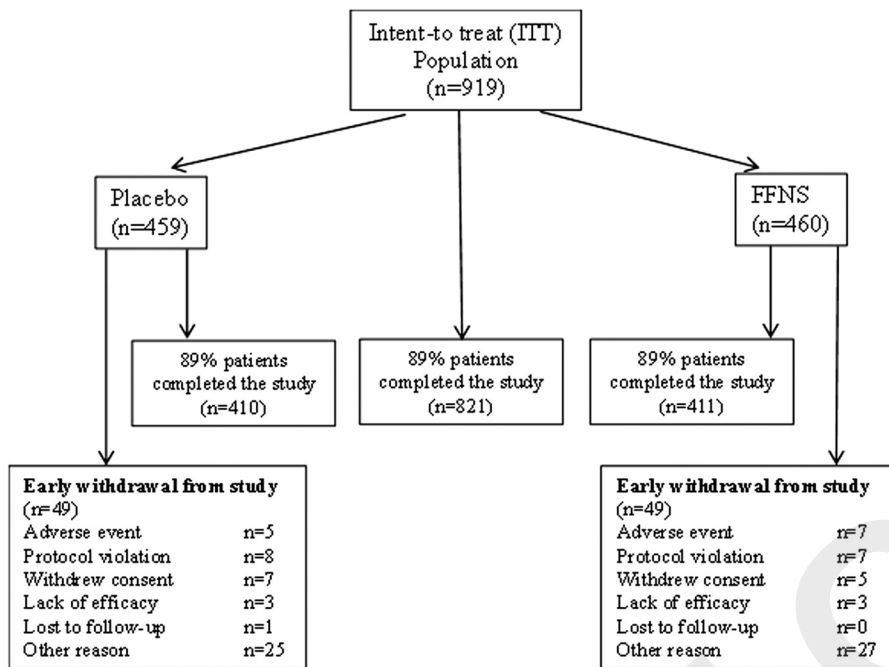


Figure 1. Disposition of patients whose data were used for the integrated analysis.

Table 2 Demographic and baseline characteristics of subjects

	FFNS <i>n</i> = 460	Placebo <i>n</i> = 459	Total <i>n</i> = 919
Mean age (range)	37.6 (12–80)	37.4 (12–77)	37.5 (12–80)
Males, <i>n</i> (%)	167 (36%)	179 (39%)	346 (38%)
Height (cm), mean (SD)	168.6 (9.5)	169.0 (9.1)	168.8 (9.3)
Weight (kg), mean (SD)	77.1 (21.0)	76.9 (19.4)	77.0 (20.2)
Duration of PAR, <i>n</i> (%)			
≥2 to <5 yr	85 (18%)	77 (17%)	162 (18%)
≥5 to <10 yr	108 (23%)	113 (25%)	221 (24%)
≥10 yr	267 (58%)	269 (59%)	536 (58%)
PAR positive test, <i>n</i> (%)			
Mold	153 (33%)	140 (31%)	293 (32%)
Animal danders	231 (50%)	252 (55%)	483 (53%)
Dust mites	386 (84%)	385 (84%)	771 (84%)
Cockroaches	69 (15%)	75 (16%)	144 (16%)
History of SAR	158 (34%)	153 (33%)	311 (34%)
TNSS, mean (SD)			
Daily reflective	8.9 (1.8)	8.8 (1.6)	8.8 (1.7)
A.M. instantaneous	8.5 (2.1)	8.4 (2.0)	8.5 (2.1)
A.M. reflective	8.8 (1.8)	8.7 (1.7)	8.8 (1.8)
P.M. reflective	8.9 (1.8)	8.8 (1.6)	8.9 (1.7)

PAR = perennial allergic rhinitis; SAR = seasonal allergic rhinitis; FFNS = fluticasone furoate nasal spray; TNSS = total nasal symptom score; A.M. = morning; P.M. = evening.

–0.20; $p < 0.001$). A significant difference was also seen between the treatment groups for nasal congestion with an LS mean treatment difference between FFNS and placebo of –0.20 (95% CI, –0.28, –0.12; $p < 0.001$).

The integrated analysis showed that FFNS at 110 μg also resulted in significantly greater improvements in A.M. predose iTNSS. The LS mean treatment difference

between FFNS and placebo over weeks 1–4 was –0.95 (95% CI, –1.24, –0.66; $p < 0.001$; Fig. 4). The improvements in the A.M. predose instantaneous individual nasal symptom scores over weeks 1–4 were also significant compared with placebo (Table 5), with sneezing the most improved symptom with an LS mean treatment difference between FFNS and placebo over weeks 1–4 of –0.25

Table 3 Analysis of mean change from baseline in daily rTNSS over wk 1–4

	FFNS (<i>n</i> = 460)	Placebo (<i>n</i> = 459)
Baseline		
<i>n</i>	460	459
LS mean (SE)	8.9 (0.08)	8.8 (0.07)
Week 1		
<i>n</i>	458	456
LS mean (SE)	−2.12 (0.09)	−1.54 (0.09)
LS mean difference	−0.58	
The <i>p</i> value vs placebo (95% CI)	<0.001 (−0.83, −0.33)	
Week 2		
<i>n</i>	454	449
LS mean (SE)	−3.19 (0.11)	−2.29 (0.11)
LS mean difference	−0.89	
The <i>p</i> value vs placebo (95% CI)	<0.001 (−1.20, −0.59)	
Week 3		
<i>n</i>	448	441
LS mean (SE)	−3.75 (0.12)	−2.61 (0.12)
LS mean difference	−1.14	
The <i>p</i> value vs placebo (95% CI)	<0.001 (−1.47, −0.80)	
Week 4		
<i>n</i>	441	435
LS mean (SE)	−4.01 (0.13)	−2.93 (0.13)
LS mean difference	−1.09	
The <i>p</i> value vs placebo (95% CI)	<0.001 (−1.44, −0.73)	
Week 1–4		
<i>n</i>	460	457
LS mean (SE)	−3.22 (0.10)	−2.29 (0.10)
LS mean difference	−0.93	
The <i>p</i> value vs placebo (95% CI)	<0.001 (−1.21, −0.64)	

FFNS = fluticasone furoate nasal spray; rTNSS = reflective total nasal symptom score; LS = least squares; SE = standard error.

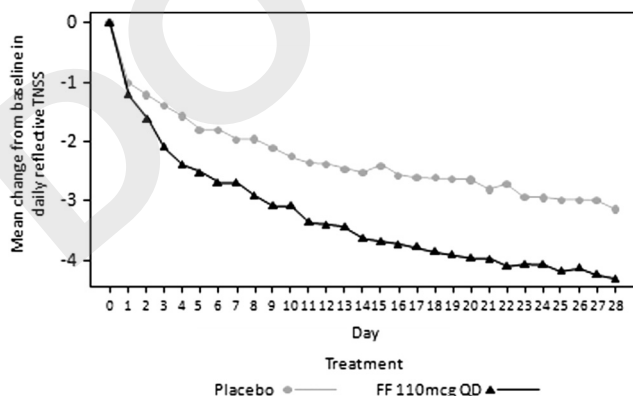


Figure 2. Mean change from baseline in daily reflective total nasal symptom scores (rTNSS).

(95% CI, −0.33, −0.17; *p* < 0.001). A significant difference was also seen between the treatment groups for nasal congestion with an LS mean treatment difference between FFNS and placebo of −0.24 (95% CI, −0.32, −0.16;

p < 0.001), and for nasal itching and rhinorrhea with an LS mean treatment difference of −0.23 (95% CI, −0.31, −0.15; *p* < 0.001) and 0.24 (95% CI, −0.32, −0.15; *p* < 0.001), respectively.

Safety

In each study, FFNS was well tolerated, and the type and incidence of adverse events were similar to those in the placebo group. Events that were reported at an incidence of >3% and, more commonly, in FFNS patients than in placebo patients are shown in Table 6.

DISCUSSION

AR can considerably impair patients' quality of life, reduce functional ability, and is associated with high direct and indirect costs.^{5,30} AR impairs work productivity to a greater magnitude than other common diseases such as hypertension.³¹ Although PAR appears to be less common than SAR, PAR contributes disproportionately to the clinical and economic burdens of

Table 4 Analysis of mean change from baseline in daily reflective individual nasal symptom scores over wk 1–4 of the treatment period

	FFNS (n = 460)	Placebo (n = 459)
Rhinorrhea		
n	460	457
Baseline mean (SD)	2.3 (0.54)	2.3 (0.54)
LS mean (SE) change from baseline	−0.78 (0.03)	−0.57 (0.03)
LS mean difference vs placebo	−0.21	
The p value vs placebo (95% CI)	<0.001 (−0.29, −0.13)	
Nasal congestion		
n	460	457
Baseline mean (SD)	2.5 (0.38)	2.6 (0.37)
LS mean (SE) change from baseline	−0.80 (0.03)	−0.60 (0.03)
LS mean difference vs placebo	−0.20	
The p value vs placebo (95% CI)	<0.001 (−0.28, −0.12)	
Nasal itching		
n	460	457
Baseline mean (SD)	2.1 (0.63)	2.1 (0.63)
LS mean (SE) change from baseline	−0.80 (0.03)	−0.57 (0.03)
LS mean difference vs placebo	−0.23	
The p value vs placebo (95% CI)	<0.001 (−0.31, −0.15)	
Sneezing		
n	460	457
Baseline mean (SD)	1.9 (0.72)	1.9 (0.68)
LS mean (SE) change from baseline	−0.84 (0.03)	−0.56 (0.03)
LS mean difference vs placebo	−0.28	
The p value vs placebo (95% CI)	<0.001 (−0.36, −0.20)	

FFNS = fluticasone furoate nasal spray; LS = least squares; SE = standard error; SD = standard deviation.

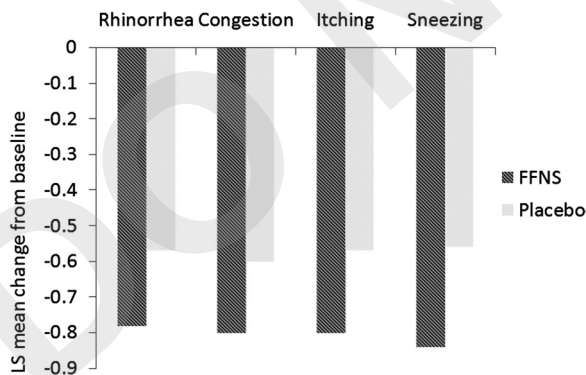


Figure 3. Least square (LS) mean change from baseline in reflective individual nasal symptom scores.

AR partly by virtue of its chronicity and because it is more difficult to treat.³² Effective management of PAR often requires year-round anti-inflammatory treatment to control nasal congestion, the cardinal symptom of PAR, and other nasal symptoms.⁶

Data from this analysis showed that q.d. FFNS produced significantly better relief of nasal symptoms of PAR than placebo. Assessment of the effect of treatment on individual nasal symptoms indicated that

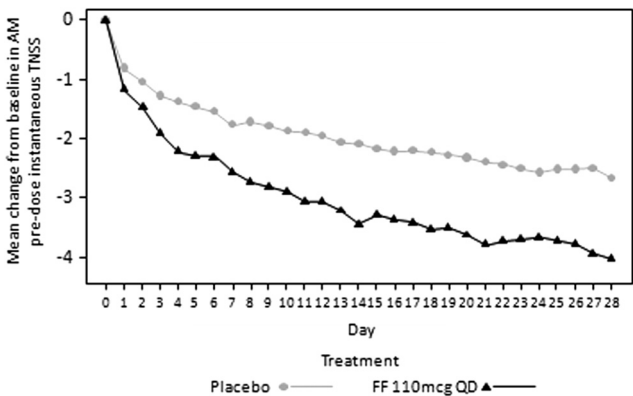


Figure 4. Mean change from baseline in morning (A.M.) predose instantaneous score.

FFNS led to significantly greater decreases from baseline in daily mean reflective scores for congestion, nasal itching, sneezing, and rhinorrhea compared with placebo. FFNS provided a comprehensive reduction of all nasal symptoms throughout the study period. The magnitude of treatment effect was consistent across all four nasal symptoms for both daily reflective scores and A.M. predose instantaneous scores with narrow confidence intervals observed for each symptom.

Table 5. Analysis of mean change from baseline in daily in A.M. predose instantaneous individual nasal symptom scores over wk 1–4 of the treatment period

	Morning (A.M.)	
	FFNS (<i>n</i> = 460)	Placebo (<i>n</i> = 459)
Rhinorrhea		
<i>n</i>	459	456
LS mean (SE)	−0.72 (0.03)	−0.49 (0.03)
LS mean difference	−0.24	
The <i>p</i> value vs placebo (95% CI)	<0.001 (−0.32, −0.15)	
Nasal congestion		
<i>n</i>	459	456
LS mean (SE)	−0.71 (0.03)	−0.47 (0.03)
LS mean difference	−0.24	
The <i>p</i> value vs placebo (95% CI)	<0.001 (−0.32, −0.16)	
Nasal itching		
<i>n</i>	459	456
LS mean (SE)	−0.76 (0.03)	−0.53 (0.03)
LS mean difference	−0.23	
The <i>p</i> value vs placebo (95% CI)	<0.001 (−0.31, −0.15)	
Sneezing		
<i>n</i>	459	456
LS mean (SE)	−0.77 (0.03)	−0.52 (0.03)
LS mean difference	−0.25	
The <i>p</i> value vs placebo (95% CI)	<0.001 (−0.33, −0.17)	

FFNS = fluticasone furoate nasal spray; LS = least squares; SE = standard error.

Table 6 Incidence of adverse events in ≥3% of patients in each individual study

Study	FFNS	Placebo
FFR30002		
Epistaxis	8%	6%
Pharyngolaryngeal pain	5%	3%
Nasal septum ulceration	5%	3%
FFR106080		
Epistaxis	9%	4%
Pharyngolaryngeal pain	9%	4%
Nasopharyngitis	6%	5%
Septum ulceration	4%	1%
FFU111439		
Epistaxis	15%	8%
Nasopharyngitis	5%	1%

FFNS = fluticasone furoate nasal spray.

These findings are important because they provide physicians and patients with information on the effect of FFNS on specific nasal symptoms that are difficult to treat in PAR. Because patients do not always suffer from all symptoms and all symptoms are not equally troublesome, it is important to know that the treatment is effective against all individual symptoms or specific symptoms to optimize therapy in individual patients.

Moreover, patients' preference is often to refer to individual symptom scores rather than total symptom scores because doing so gives them a better perspective of their disease.

Nasal symptoms in AR have been strongly linked to sleeping difficulties and consequent impairment in next-day function and well-being.³³ Sleep impairment is a significant problem for patients with AR, and nasal congestion is one of the main causes. In a recent survey of individuals with AR, 68% of respondents with PAR and 48% with SAR reported that their condition interfered with sleep.⁹ Nasal congestion is the symptom patients find most bothersome and would like most to prevent.^{34,35} In this analysis, FFNS significantly reduced nasal congestion from baseline. The treatment difference compared with placebo was statistically significant although a reduction was also seen in the placebo treatment group. A strong placebo effect has commonly been observed in allergic diseases, where the evaluating parameters tend to be physical or subjective³⁶ or is seen in studies of relatively short duration.

According to the ARIA guidelines, corticosteroids are currently the most effective anti-inflammatory medication available for the treatment of rhinitis.⁹ In comparative studies, INs have shown superior efficacy compared with other medications used to treat

nasal congestion. A meta-analysis of 14 controlled trials in patients with AR showed that intranasal steroids provide superior relief of nasal congestion/blockage compared with oral antihistamine.³⁷ Intranasal steroids also showed greater effectiveness than intranasal H₁-antihistamines in improving nasal blockage in a meta-analysis of four studies in patients with AR.³⁸ In addition, several trials have shown superior congestion relief with the intranasal steroid fluticasone propionate versus montelukast in patients with SAR.^{39,40}

The symptoms of AR vary in severity over the course of the day and are often worse in the A.M.. The intensity of nasal congestion, rhinorrhea, and sneezing is greatest early in the A.M. in ~70% of patients^{27,41} with patients diagnosed with PAR reporting symptoms that were most severe in the A.M. significantly more often than those with SAR.⁴¹ Therefore, to maximize the benefits for patients any pharmacologic agent used in the management of AR should be effective in controlling these peak A.M. symptoms. The specific mechanisms underlying the chronobiology of AR are speculative; however, several factors might contribute such as that secretions increase and accumulate overnight, allergen exposure is continuous and cortisol levels are lowest at night, and, hence, inflammatory mediators might be at high levels.⁴² The significant change in A.M. predose iTNSS shows that the beneficial effects of FFNS on nasal symptoms were evident for 24 hours after each dose. This indicates the sustained 24-hour efficacy of FFNS as previously observed in patients with seasonal symptoms.^{18–21} Instantaneous scores may represent a more accurate assessment of 24-hour efficacy than reflective scores.²³

Intranasal fluticasone furoate has also been shown to show consistent efficacy on ocular symptoms along with an improvement in quality of life in SAR patients.²⁵ In this integrated analysis ocular symptoms were not analyzed because ocular symptoms are not as prominent in PAR as SAR.¹ In each individual study used in this analysis the baseline ocular symptoms were low because there was no requirement for ocular symptoms scores at baseline as part of the entry criteria. In addition, ocular symptom scores were only recorded as secondary end points so the studies were not designed or powered to investigate the effect of FFNS on ocular symptoms.

In summary, this integrated analysis resulted in a large and powerful study on the efficacy of FFNS in the treatment of PAR. The analysis shows that treatment with FFNS at a dose of 110 µg q.d. consistently relieves all nasal symptoms of PAR. A significant improvement in all symptom domains of the TNSS was seen at every week. The efficacy has been shown to be sustained over 24 hours which is important to decrease the A.M. peak symptoms. In addition, the reduction in nasal

blockage is important for subjects with PAR because it affects their sleep and quality of life.

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Erratum

In the article *Efficacy and safety of ecallantide in treatment of recurrent attacks of hereditary angioedema: Open-label continuation study* *Allergy Asthma Proc* 34, 155–161, 2013; doi: 10.2500/aap.2013.34.3653, in the footnotes on page 1, a statement in the Conflicts of Interest printed incorrectly. The correct statement is: R Iarrobino, LE Stolz and WE Pullman are employees of Dyax Corp.

The editorial office regrets the error.

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