IS FLUTICASONE FUROATE EFFECTIVE IN TREATING ALL 7 INDIVIDUAL NASAL AND OCULAR SYMPTOMS OF SEASONAL ALLERGIC RHINITIS?

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ABSTRACT

Background: 70% of allergic rhinitis (AR) patients across Europe experience both nasal and ocular symptoms. It is therefore important for a treatment to provide effective relief for all symptoms of seasonal AR (SAR), including the 4 individual nasal symptoms (nasal itching; sneeze; congestion; rhinorrhoea) and 3 ocular symptoms (eye itching/burning; eye tearing/watering; eye redness) present within the rTNSS (reflective total nasal symptom score) and rTOSS (reflective total ocular symptom score). Patients do not measure their condition in terms of rTNSS or rTOSS but complain of individual symptoms; therefore, efficacy against these specific symptoms is important. The enhanced-affinity corticosteroid fluticasone furoate nasal spray (FFNS), delivered via a unique side-activated device, has previously shown consistent nasal and ocular efficacy across all four trials in patients with SAR. Data from these trials have been combined in an integrated analysis designed to evaluate the magnitude of effect for each symptom.

Methods: All four GlaxoSmithKline funded studies (FFR20001; FFR30003; FFR103841; FFR104861) were randomised; double-blind; placebo-controlled; parallel-group; multi-centred; and designed to evaluate the efficacy and safety of once daily FFNS for 14 days in adult and adolescent subjects (≥12 years) with SAR. Randomised patients (n=1142) received either FFNS 110 µg (n=571) or vehicle placebo nasal spray (n=570) once daily. Patients rated the severity of their nasal and ocular symptoms on a 4-point categorical scale (0=none, 3=severe) twice daily in a reflective manner. Comparisons between FFNS and placebo were performed on the mean change from baseline in daily reflective individual nasal and ocular symptoms using the analysis of covariance (ANCOVA), adjusting for baseline value, based on the integrated database.

Results: The integrated analysis demonstrated that FFNS significantly improved all 7 nasal and ocular symptoms of SAR compared with placebo. The LS mean treatment difference ranged from -0.43 to -0.33 (*P*<0.0001) for the individual nasal symptoms and from -0.21 to -0.22 (*P*<0.0001) for the individual ocular symptoms. FFNS also significantly improved rTNSS and rTOSS versus placebo with LS mean treatment differences of -1.47 and -0.65 (*P*<0.001 for both comparisons), respectively.

Conclusion: FFNS 110 µg once daily was effective in relieving all 7 individual nasal and ocular symptoms of SAR in adult and adolescent patients.

BACKGROUND

- Approximately one quarter of the population of Western Europe has seasonal allergic rhinitis (SAR),[1] and more than 70% of these individuals experience both nasal and ocular symptoms, which are moderate-to-severe in one third of cases.[2] These symptoms have a profound impact on quality of life as well as incurring substantial healthcare costs.
- It is therefore important to provide effective relief from all SAR symptoms. In clinical studies SAR symptoms are usually individualised as four nasal symptoms (nasal itching, sneezing, congestion, rhinorrhoea) and three ocular symptoms (eye itching/burning, eye tearing/watering, eye redness). These are included within the reflective total nasal symptom score (rTNSS) and reflective total ocular symptom score (rTOSS), respectively.
- Patients do not measure their condition in terms of rTNSS or rTOSS but complain of individual symptoms; therefore, efficacy against these specific symptoms – not only against the combined symptom scores – is important.
- Intranasal corticosteroids (INS) demonstrate consistent efficacy against the nasal symptoms of SAR;[3] however, until recently, the evidence for an ocular effect has been inconsistent for any one INS across a range of placebo-controlled studies.[4]
- Fluticasone furoate nasal spray (FFNS) is an enhanced-affinity corticosteroid, delivered via a unique side-activated device, which has recently shown consistent nasal and ocular efficacy across four rigorously controlled trials in adult and adolescent patients with SAR as assessed by rTOSS and instantaneous TOSS (iTOSS).[5-8]

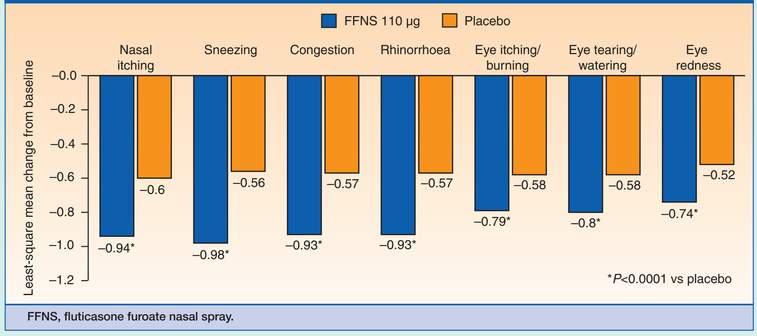
OBJECTIVE

- The objective of this analysis was to evaluate the magnitude of effect of FFNS on each of the seven individual nasal and ocular SAR symptoms, as assessed by combined data from an integrated analysis of four randomised studies.

STUDY DESIGN

- All four trials (one Phase IIb and three Phase III) were 14-day, randomised, double-blind, placebo-controlled, parallel-group, multicentre studies, conducted during the peak allergy season across different geographical regions.
- The three Phase III studies (US mountain cedar [FFR30003], European grass [FFR103841] and US ragweed [FFR104861]) assessed the safety and efficacy of FFNS 110 µg once daily (od). The Phase IIb dose-ranging study (US mountain cedar [FFR20001]) evaluated the efficacy and safety of FFNS 55 µg, 110 µg, 220 µg and 440 µg od; however, only the results from patients who received 110 µg od were considered for the purposes of this analysis.
- A total of 1141 adult and adolescent patients (aged ≥12 years) with confirmed SAR (defined as a clinical history of nasal allergy symptoms during each of the last two mountain cedar, ragweed or grass-pollen allergy seasons, and a positive skin-prick test to the respective allergen within 12 months prior to screening) were randomised to receive either FFNS 110 µg od (n=571) or placebo od (n=570).

Figure 1: Least-square mean change from baseline in individual symptoms



FFNS, fluticasone furoate nasal spray.

METHODS

Symptom scoring

- Individual nasal and ocular symptoms were assessed in a reflective manner in all four trials.
- The four individual nasal symptoms were rhinorrhoea, nasal congestion, nasal itching and sneezing. The three individual ocular symptoms were eye itching/burning, eye tearing/watering and eye redness.
- Reflective scores indicated how a patient was feeling during the previous 12 hours and were recorded in the morning and evening.
- Patients rated the severity of each nasal and ocular symptom on a 4-point categorical scale (0=none, 3=severe).
- The total nasal symptom score (TNSS) represented the sum of the four individual symptom scores for rhinorrhoea, nasal congestion, nasal itching and sneezing (maximum score=12).
- The total ocular symptom score (TOSS) referred to the sum of the three individual symptom scores for itching/burning eyes, tearing/watering eyes and eye redness (maximum score=9).

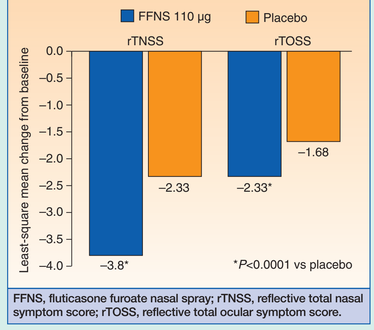
Statistical analysis

- In three of the studies, individual nasal and individual ocular symptom scores were assessed as secondary endpoints. In the fourth study (dose-ranging study [FFR20001]) the individual nasal symptom scores were assessed as a secondary endpoint.
- An integrated analysis of all four studies was conducted for each of the seven individual nasal and ocular symptoms and for rTNSS and rTOSS.
- Mean change from baseline over the entire treatment period in daily reflective individual nasal and ocular symptoms was evaluated and the least-square (LS) mean difference for the individual symptom scores was used to compare the efficacy of FFNS with placebo.
- Comparisons between treatment and placebo groups were carried out using an analysis of covariance (ANCOVA) with adjustments for baseline value.

RESULTS

- The integrated analysis of all four studies demonstrated that FFNS 110 µg od significantly improved all seven reflective individual nasal and ocular symptoms of SAR compared with placebo (*P*<0.0001 in each case) (Table 1, Figure 1).
- The LS mean treatment difference ranged from –0.43 to –0.33 (*P*<0.0001) for the individual nasal symptoms and from –0.22 to –0.21 (*P*<0.0001) for the individual ocular symptoms.
- FFNS also significantly improved rTNSS and rTOSS versus placebo with LS mean treatment differences of –1.47 and –0.65 (*P*<0.001 for both comparisons), respectively (Figure 2).
- Results were consistent across different allergy seasons, including grass, ragweed and mountain cedar seasons, and different geographical locations throughout Europe and the USA.

Figure 2: Least-square mean change from baseline in rTNSS and rTOSS



FFNS, fluticasone furoate nasal spray; rTNSS, reflective total nasal symptom score; rTOSS, reflective total ocular symptom score.

Table 1: Individual reflective nasal and ocular symptom scores

Symptoms	Treatment arms	Change from baseline over treatment period (LS means)	Standard error	Treatment difference	*P*-value	95% CI
Nasal itching	Placebo FFNS 110 µg	–0.6009 –0.9308	0.02810 0.02805	–0.3298	<0.0001	–0.4077 –0.2519
Sneezing	Placebo FFNS 110 µg	–0.5567 –0.9820	0.02777 0.02772	–0.4253	<0.0001	–0.5023 –0.3483
Congestion	Placebo FFNS 110 µg	–0.5695 –0.9265	0.02729 0.02724	–0.3570	<0.0001	–0.4327 –0.2814
Rhinorrhoea	Placebo FFNS 110 µg	–0.5676 –0.9275	0.02860 0.02855	–0.3600	<0.0001	–0.4393 –0.2807
Eye itching/ burning	Placebo FFNS 110 µg	–0.5787 –0.7868	0.02764 0.02760	–0.2080	<0.0001	–0.2847 –0.1314
Eye tearing/ watering	Placebo FFNS 110 µg	–0.5828 –0.8036	0.02790 0.02785	–0.2207	<0.0001	–0.2981 –0.1434
Eye redness	Placebo FFNS 110 µg	–0.5230 –0.7357	0.02800 0.02795	–0.2128	<0.0001	–0.2904 –0.1351

CI, confidence interval; FFNS, fluticasone furoate nasal spray; LS, least square.

CONCLUSIONS

- FFNS 110 µg od demonstrated consistent and clinically meaningful efficacy in the treatment of all seven nasal and ocular symptoms of SAR – as well as rTNSS and rTOSS – in adult and adolescent patients. This indicates that, irrespective of which symptom/collection of symptoms a patient is experiencing, FFNS can be expected to provide effective relief.
- This consistent efficacy occurred over a significant geographical distribution, a variety of allergens and in a large number of patients.

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GlaxoSmithKline

Abstract 721

Research funded by GlaxoSmithKline

Presented at the 29th EAACI Congress London, United Kingdom 5-9 June 2010