Triamcinolone Acetonide in the Treatment of Perennial Allergic Rhinitis: A post hoc Efficacy Analysis of a Phase III Study Performed in Russia

Alexander V. Karaulov^a Natalia I. Ilina^b Natalia Shartanova^c
Aleksandr Maslakov^c Luiz Lucio^d

^aDepartment of Clinical Immunology and Allergology of I.M. Sechenov First Moscow State Medical University, Moscow, Russia; ^bNational Research Centre, Institute of Immunology Federal Medical-Biological Agency of Russia, Moscow, Russia; ^cMedical Department, Sanofi Consumer Healthcare, Medical Affairs, Moscow, Russia; ^dMedical Department, Sanofi Consumer Healthcare, São Paulo, Brazil

Keywords

Allergic rhinitis · Triamcinolone acetonide · Fluticasone propionate · Perennial allergic rhinitis · Reflective total nasal symptom score

Abstract

Introduction: Allergic rhinitis (AR) is a disease which affects >24% of the population in Russia. Triamcinolone acetonide (TAA) is a corticosteroid used for treating AR. This post hoc analysis assesses the efficacy of intranasal TAA in improving perennial AR (PAR) symptom scores over 4 weeks. **Methods:** NASANIF (NCT03317015) was a double-blind, parallel-group, multicenter, prospective, non-inferiority, phase III clinical trial in which patients with PAR were randomized (1:1) to receive TAA or fluticasone propionate (FP) over 4 weeks. Our post hoc analysis evaluates weekly change in PAR symptoms using the reflective Total Nasal Symptom Score (rTNSS), overall and for individual symptoms (sneezing, nasal itching, rhinorrhoea, and nasal obstruction). Proportion of patients and time to achieve a ≥ 50 or $\geq 75\%$ reduction in rTNSS were assessed. For rTNSS endpoints, a linear mixed-model methodology was used; for time-to-event endpoints, cumulative incidence functions were estimated using the Kaplan-Meier

method, in the per-protocol population. **Results:** Of 260 patients, 128 each completed the study and were randomized to receive TAA or FP. From baseline to week 4, the changes in total rTNSS were -7.78 (95% CI: -8.1701 to -7.3967 ; $p < 0.001$) and -7.52 (-7.9053 to -7.1320 ; $p < 0.001$) for TAA and FP, respectively. Individual symptoms improved significantly from baseline. The proportion of patients achieving ≥ 50 and $\geq 75\%$ reductions in total rTNSS was 88.0 and 67.2%, respectively in the TAA group. No significant differences were observed between the TAA and FP in any analyses. **Conclusions:** TAA produced effective and prolonged improvement of PAR symptoms over a 4-week treatment period.

© 2021 The Author(s)
Published by S. Karger AG, Basel

Introduction

Allergic rhinitis (AR) is a major health issue which currently affects up to 24% of the population in Russia [1]. The majority (80%) of individuals with AR develop symptoms before the age of 20 years. AR is a multifactorial dis-

Edited by: H.-U. Simon, Bern.

ease that can be classified by symptom frequency, as intermittent (symptoms on <4 days/week or for <4 consecutive weeks/year) or persistent (symptoms on >4 days/week and >4 consecutive weeks/year) [2], or by the temporal pattern of environmental exposure to the triggering allergen, as seasonal (e.g., from pollens) or perennial (e.g., dust mites) [3]. Regardless of classification, typical symptoms are nasal congestion, nasal itch, rhinorrhea, and sneezing [4]. AR can be further classified by severity. In mild AR, sleep is normal and there is no impairment of daily activities [5], whereas in severe AR there can be significant impairment in quality of life, sleep, and work performance [4]. AR can be challenging to treat, with many patients experiencing persistent symptoms and becoming polysensitized. Furthermore, difficult-to-treat phenotypes, such as mixed rhinitis and severe chronic upper airways disease, have recently emerged [6].

A comprehensive review of the literature has shown that the therapies commonly used in clinical practice for the treatment of AR include antihistamines, corticosteroids, leukotriene modifiers, mast cell stabilizers, and decongestants [7]. Symptoms of AR can be targeted using specific therapies that modulate acute- or late-phase allergic reactions, and patient preferences are usually considered during treatment selection. Most current treatments are directed at symptomatic relief of nasal congestion, itching and sneezing. AR diagnosis (and the subsequent design of a treatment plan) usually consists of an in-depth analysis of patient history, a physical exam, and a skin-prick test to confirm reactivity to aero-allergens [8].

Intranasal corticosteroids are recognized as the most effective treatment modality for relieving both early (sneezing, nasal itching, and rhinorrhoea)- and late-phase AR symptoms (nasal congestion/obstruction), due to their ability to modulate the pathophysiology of AR including the release of cytokines and other pro-inflammatory mediators [9, 10]. Intranasal administration ensures the delivery of corticosteroids directly to the nasal mucosa, enhancing their local anti-inflammatory and anti-allergic effects, while also minimizing systemic exposure to therapy [6]. The symptom control provided by intranasal corticosteroids positively impacts quality of life by improving sleep quality, work productivity, and the ability to perform daily activities [11] and is the standard recommended first-line treatment for patients with moderate-to-severe AR [12].

Triamcinolone acetonide (TAA) is a synthetic fluorinated corticosteroid that is used for the treatment of AR in both adults and paediatric patients [13]. TAA has been

compared with fluticasone propionate (FP) in a Phase III study in 260 adults with persistent perennial AR (PAR) (NASANIF; NCT03317015) [14]. TAA was found to be non-inferior to FP in terms of change in reflective Total Nasal Symptom Score (rTNSS) from baseline to the end of week 4 [14]. Due to the profound detrimental impact of AR on patient quality of life, emotional well-being and ability to perform daily activities, it is important for AR patients to experience a reduction in symptoms as early as possible [3, 11]. It is therefore important to determine the efficacy of TAA treatment on a weekly basis in order to determine how quickly symptom relief can occur. Our study focuses on the weekly improvement in rTNSS. The objective of this post hoc analysis of the NASANIF trial is to further investigate and characterize changes in total and individual symptom scores in patients with PAR at each week over the 4 weeks of treatment with either TAA or FP.

Methods

Study Design and Objectives

The NASANIF trial was a randomized (1:1), double-blind, parallel-group, multicentre prospective, non-inferiority, Phase III study conducted between November 30, 2016, and July 10, 2017, at 12 study centres in Russia. The study design has been described previously [14]. In summary, 260 patients with previously diagnosed PAR with a positive skin-prick test were randomized to receive either intranasal TAA (220 µg once daily, administered as 2 × 55 µg sprays in each nostril) or FP (200 µg once daily, administered as 2 × 50 µg sprays in each nostril) for 4 weeks.

In this analysis, for both treatments, efficacy was assessed as follows: (i) the change in weekly rTNSS (both overall [i.e., total score] and for the 4 individual component symptoms [sneezing, nasal itching, rhinorrhoea, and nasal obstruction]) and (ii) the proportion of patients achieving a minimum 50 or 75% reduction in rTNSS, both overall and for individual symptoms. The time taken to achieve these reduction milestones was also assessed.

Each symptom included in the rTNSS is scored according to a 5-point scale from 0 to 4: 0, absent; 1, mild (symptom present, but not annoying or troublesome); 2, moderate (symptom frequently troublesome, but not interfering with normal daily activities or sleep); 3, severe (symptom sufficiently troublesome to interfere with normal daily activity or sleep); and 4, very severe (symptom severe enough to warrant an immediate visit to a physician). Total rTNSS is the sum of scores for each individual symptom, and thus ranges from zero to a maximum of 16.

Statistical Analysis

Standard descriptive summary statistics (arithmetic mean, standard deviation, minimum value, lower quartile, median, upper quartile, and maximum value) were calculated for continuous variables. The initial linear mixed model for change from baseline for rTNSS included, as fixed effects, the continuous time variable (indicating the corresponding days of rTNSS measurement, the treatment indicator, and the interaction effects between treatment

Fig. 1. LS mean change from baseline in total rTNSS (PP population). Error bars indicate standard deviation. FP, fluticasone propionate; rTNSS, reflective Total Nasal Symptom Score; TAA, triamcinolone acetonide; LS, least-squares; PP, per-protocol.

arm and time). For random effects, initially both intercept and slope were considered. Additionally, to estimate and compare least-squares (LS) means, a mixed model with categorical time (weekly visits), random intercept, treatment, and time treatment interaction term were estimated. No simplification or building strategy was applied to these models.

The proportions of patients who achieved a minimum 50 or 75% reduction in rTNSS at any time-point were assessed using descriptive statistics, by presenting the cumulative proportion of responders achieving these response thresholds for the first time. Time to event was calculated as the time from baseline to the end of the week in which the response threshold (50 or 75% reduction in rTNSS) was met, or to the date of the last visit (for censored data). Only the first achievement of a 50 or 75% reduction from baseline was considered. Cumulative incidence functions were performed using the Kaplan-Meier method for total score and for each symptom separately. A log-rank test and cumulative incidence function, along with associated 95% confidence intervals (CIs), were provided to assess differences between treatment groups.

The main analyses were conducted on data from the per-protocol (PP) population, whereas sensitivity analyses were conducted using data from the intent-to-treat (ITT) population. The significance level was stated at 5% using 2-sided *p* values, and all statistical analyses were performed using SAS® Version 9.4 (Cary, NC, USA).

Results

The study population has been described in detail previously [14]. Briefly, of 260 PAR intention-to-treat patients, 129 patients were randomised into the TAA treat-

ment group, while 131 were randomized into the FP group. Three patients discontinued the study prematurely (one in the TAA group and 2 in the FP group), and 1 patient was excluded by deviation, resulting in a total of 256 patients completing the study (128 in each treatment group), constituting the PP population.

In the TAA arm, the LS mean changes in total rTNSS from baseline (day 0) were -2.43 (95% CI: -2.82 to -2.05) at week 1, -5.15 (95% CI: -5.53 to -4.76) at week 2, -6.75 (95% CI: -7.13 to -6.36) at week 3, and -7.78 (95% CI: -8.17 to -7.40) at week 4 (Fig. 1). Changes versus baseline were statistically significant at all study visits (*p* < 0.001). Similar reductions in total rTNSS were observed in the FP arm, and no significant between-group differences were observed at any visit. The results obtained for the ITT population were similar to those obtained for the PP population (data not shown).

Mean scores for individual symptoms decreased progressively each week (Fig. 2). In both treatment groups, the difference from baseline was statistically significant (*p* < 0.001) for all 4 symptoms and for all treatment weeks. For TAA, LS mean changes from baseline to week 4 were -1.80 (95% CI: -1.94 to -1.67) for sneezing, -1.87 (95% CI: -2.00 to -1.75) for nasal itching, -2.01 (95% CI: -2.14 to -1.88) for rhinorrhea, and -2.10 (95% CI: -2.22 to -1.97) for nasal obstruction. No significant differences were observed between TAA and FP at any time-point.

Fig. 2. LS mean change from baseline in individual symptom scores for: sneezing (a); nasal itching (b); rhinorrhea (c); nasal obstruction (PP population) (d). * $p < 0.001$ versus baseline. Error bars indicate standard deviation. FP, fluticasone propionate; rTNSS, reflective Total Nasal Symptom Score; TAA, triamcinolone acetate; LS, least-squares; PP, per-protocol.

The proportion of patients in the TAA group who achieved at least a 50% reduction in total rTNSS was 63.0% at week 2 and 88.0% at week 4 (Table 1), versus 62.4 and 91.2%, respectively, with FP. The proportions of patients achieving at least a 75% reduction in total rTNSS were 36.2% after 2 weeks and 67.2% after 4 weeks in the TAA arm, versus 27.2 and 68.8%, respectively, in the FP arm (Table 2). No significant differences were observed between the TAA and FP groups in the achievement of either of the response thresholds at any time-point (data not shown).

The probability of achieving at least a 50% reduction in total rTNSS increased from 0.0 at baseline to approximately 0.90–0.95 after 4 weeks of treatment (Fig. 3). Similarly, the probability of achieving a 75% reduction in rTNSS increased from 0.0 at baseline to approximately 0.81 for TAA and 0.7 for FP after 4 weeks (Fig. 4). No significant differences were observed between TAA and FP in the probability of achieving either response threshold. The results obtained for the ITT population were similar to those obtained for the PP population (data not shown).

Table 1. Cumulative proportion of patients achieving at least a 50% reduction from baseline in rTNSS both overall and for individual symptoms

Symptoms	Treatment group	Week 1, n/N (%)	Week 2, n/N (%)	Week 3, n/N (%)	Week 4, n/N (%)
Total rTNSS	TAA FP	39/127 (30.7) 40/126 (31.8)	80/127 (63.0) 78/125 (62.4)	102/125 (81.6) 95/125 (76)	110/125 (88.0) 114/125 (91.2)
Sneezing	TAA FP	68/127 (53.5) 57/126 (45.2)	92/127 (72.4) 86/125 (68.8)	112/125 (89.6) 100/125 (80.0)	113/125 (90.4) 116/125 (92.8)
Nasal itching	TAA FP	65/127 (51.2) 64/126 (50.8)	100/127 (78.7) 93/125 (74.4)	110/125 (88.0) 109/125 (87.2)	114/125 (91.2) 119/125 (95.2)
Rhinorrhea	TAA FP	41/127 (32.3) 42/126 (33.3)	85/127 (66.9) 81/125 (64.8)	96/125 (76.8) 99/125 (79.2)	111/125 (88.8) 111/125 (88.8)
Nasal obstruction	TAA FP	35/127 (27.6) 33/126 (26.2)	77/127 (60.6) 73/125 (58.4)	92/125 (73.6) 94/125 (75.2)	104/125 (83.2) 110/125 (88.0)

Data are presented as the cumulative number and percentage of patients achieving the specified response threshold within each treatment group at each time-point. FP, fluticasone propionate; TAA, triamcinolone acetone; rTNSS, reflective Total Nasal Symptom Score.

Table 2. Cumulative proportion of patients achieving at least a 75% reduction from baseline in rTNSS both overall and for individual symptoms

Symptoms	Treatment group	Week 1, n/N (%)	Week 2, n/N (%)	Week 3, n/N (%)	Week 4, n/N (%)
Total rTNSS	TA FP	11/127 (8.7) 13/126 (10.3)	46/127 (36.2) 34/125 (27.2)	57/125 (45.6) 58/125 (46.4)	84/125 (67.2) 86/125 (68.8)
Sneezing	TA FP	26/127 (20.5) 24/126 (19.1)	52/127 (40.9) 46/125 (36.8)	65/125 (52.0) 62/125 (49.6)	86/125 (68.8) 82/125 (65.6)
Nasal itching	TA FP	24/127 (18.9) 25/126 (19.8)	54/127 (42.5) 46/125 (36.8)	69/125 (55.2) 66/125 (52.8)	85/125 (68.0) 90/125 (72.0)
Rhinorrhea	TAA FP	8/127 (6.3) 9/126 (7.1)	37/127 (29.1) 30/125 (24.0)	60/125 (48.0) 48/125 (38.4)	76/125 (60.8) 72/125 (57.6)
Nasal obstruction	TAA FP	9/127 (7.1) 11/126 (8.7)	28/127 (22.1) 20/125 (16.0)	46/125 (36.8) 44/125 (35.2)	67/125 (53.6) 68/125 (54.4)

N (%), number and percentage of patients; FP, fluticasone propionate; TAA, triamcinolone acetone; rTNSS, reflective Total Nasal Symptom Score.

Discussion

Intranasal administration of TAA significantly improved both overall and rTNSS and individual symptoms scores from baseline to the end of study treatment in PAR patients with the changes in rTNSS recorded at each week versus baseline being statistically significant. Similar results were observed for participants in the FP group. In the TAA group, 88.0 and 67.2% of patients achieved ≥ 50

and $\geq 75\%$ reductions in total rTNSS, respectively, with similar results observed in the FP group.

The focus of this post hoc analysis was the change in total and individual nasal symptom scores over 4 weeks in patients with PAR who were randomized to receive either TAA or FP. TAA was demonstrated to be efficacious in reducing the total rTNSS and scores for individual symptoms, with a continuous improvement being seen through week 4, the last time-point at which symptoms were assessed.

Fig. 3. Kaplan-Meier estimates of the proportion of patients achieving at least a 50% reduction in total rTNSS over time. CIF, cumulative incidence function; FP, fluticasone propionate; PP, per-protocol; rTNSS, reflective Total Nasal Symptom Score; TAA, triamcinolone acetonide.

Fig. 4. Kaplan-Meier estimates of the proportion of patients achieving at least a 75% reduction in total rTNSS over time. CIF, cumulative incidence function; FP, fluticasone propionate; rTNSS, reflective Total Nasal Symptom Score; TAA, triamcinolone acetonide.

Sneezing, nasal itching, and rhinorrhoea are features of the early phase of AR, whereas nasal congestion/obstruction is associated with the late phase. Although it appears some hours after the onset of an allergic reaction, nasal congestion is usually considered to be the most bothersome symptom of AR, and has a considerable impact on quality of life [9]. We found that relief from individual symptoms, including nasal obstruction, was significant from week 1 onwards, and furthermore, that there was a continuous and consistent improvement in symptoms over the course of the study in both treatment groups.

Additionally, over 60% of patients achieved a substantial response to TAA (i.e., a $\geq 50\%$ reduction in total

rTNSS vs. baseline, indicating a halving of symptom burden) after 2 weeks of treatment, and almost 90% achieved this threshold at week 4. An extensive response (i.e., a $\geq 75\%$ reduction in total rTNSS vs. baseline), representing a shift from moderate-to-severe symptoms to mild symptoms, was achieved by 36% of TAA recipients at week 2, and by 67.2% at week 4. Patients treated with FP experienced similar effects on symptom burden. The high proportions of patients achieving ≥ 50 and $\geq 75\%$ symptom improvement with TAA treatment are consistent with the high satisfaction ratings reported in the original NASANIF trial (83.6% of patients and 84.4% of physicians reported satisfaction with TAA treatment) [14].

There were 65 individual adverse events (31 in the TAA group vs. 34 in the FP group) documented in 47 (18.1%; 25 vs. 22) of the 260 (129 vs. 131) treated patients. The most frequently reported single events were nervous system disorders 14 versus 9 AEs in 13 (10.8%) versus 6 patients (4.58%), including headache 13 versus 8 cases; respiratory, thoracic, and mediastinal disorders 6 versus 11 AEs in 6 (4.65%) versus 10 (7.63%) patients. In terms of severity, 27 versus 31 AEs were rated as mild in 41 patients: 21 (16.28%) versus 20 (15.27%) patients. Moderate AEs 3 versus 3 cases were detected in 6 patients: 3 (2.33%) versus 3 (2.29%). Severe AE was detected in a single case in 1 patient (0.78%) in the FP group. All patients who reported adverse events were recovered by the end of the study.

TAA has been demonstrated to have significant effects on symptoms of AR as early as 12 h after the start of treatment, with a maximum effect at 3–5 days [15]. As well as having a rapid onset of action, effective pharmacotherapies for AR must provide symptom improvement that is sustained for the duration of treatment. Furthermore, we have shown that TAA treatment significantly improves the quality of life of PAR patients (Karaulov et al. [16], submitted). This post hoc analysis assessed the improvement of PAR symptom scores in patients treated with TAA or FP over 4 weeks, although further studies will be needed to determine if this effect can be sustained over a longer period despite positive early indications.

Our study adds to a growing body of evidence suggesting that intranasal TAA and FP have comparable efficacy in PAR. Some head-to-head studies have demonstrated that TAA and FP have similar efficacy in seasonal AR [7, 17]. Other studies have shown that the treatments have similar positive effects on quality of life, in both seasonal [9] and perennial [14] AR.

A multitude of factors influences the successful treatment of AR, including patient acceptance and adherence to medication as well as correct administration technique [18]. Patient compliance is important for and correlates with treatment effectiveness [19]. Key factors that influence patient adherence include sensorial attributes such as taste, scent, post-nasal drip, irritation/dryness of the nose/throat, and convenience (how easy it is to carry and use) [20, 21]. TAA has a mild odour and taste and has been formulated in a thixotropic aqueous solution that produces a sensation of moistness in the throat and nose; these attributes should promote patient adherence to treatment [17, 21, 22].

Our study has some limitations to consider. First of all, this study did not compare the efficacy of TAA versus FP in subgroups of interest defined by age, gender, ethnicity,

or concomitant diseases. Furthermore, as the study duration was limited to 4 weeks, it is unclear to what extent the symptom reduction of perennial AR achieved by TAA therapy can be sustained over a longer time period. Long-term follow-up studies would therefore be informative to assess the longevity of the symptoms reductions induced by TAA treatment. The aim of the primary trial on which this post hoc analysis is based was to compare the efficacy of TAA with that of a known treatment, FP. Therefore, there was not a placebo arm in this study but the inclusion of a placebo arm could be informative in future studies. As eosinophils play a crucial role in the pathogenesis of allergic airway inflammation, previous studies on AR have assessed the impact of serum eosinophil cationic protein levels, eosinophil activation, and eosinophil phenotype on AR disease severity [23, 24]. The primary trial did not assess these factors; therefore, this limitation may be addressed in future work. In conclusion, this post hoc analysis showed that intranasal TAA and FP were similarly efficacious in patients with moderate-to-severe PAR. TAA administered once daily demonstrated effective and sustained control of PAR symptoms, with continuous improvement in total and individual symptom scores over 4 weeks of treatment.

Acknowledgements

Editorial support was provided by Chandara Olgunsoy, MSc, and Ella Palmer, PhD, CMPP, of inScience Communications, Springer Healthcare Ltd., UK, and was funded by Sanofi. The authors would like to thank Beatrice Bois-De Fer and Aurore Allard for their critical examination and proofreading of the manuscript.

Statement of Ethics

This study was conducted in accordance with the Declaration of Helsinki, the International Council for Harmonization (ICH) Good Clinical Practice (GCP) guidelines, and Russian regulations. Informed consent was obtained from all participants prior to their enrolment. The study protocol was approved by the Research Ethics Committees at each study site.

Conflict of Interest Statement

A.M. and L.L. are employees of Sanofi. A.V.K., N.I.I., and N.S. declare no conflict of interest.

Funding Sources

This study was sponsored by Sanofi.

Author Contributions

A.V.K. supervised the design of the study and acted as a clinical trial investigator in the study. All the authors contributed to the preparation and review of the manuscript. All the authors read and approved the final version for submission.

Data Availability Statement

The data that support the findings are not publicly available due to Sanofi policies but are available upon reasonable request.

References

- 1 Khaitov R, Ilyna N. Allergy and immunology: national guidance. 2014.
- 2 Dykewicz MS, Wallace DV, Amrol DJ, Baroody FM, Bernstein JA, Craig TJ, et al. Rhinitis 2020: a practice parameter update. *J Allergy Clin Immunol*. 2020;146(4):721–67.
- 3 Meltzer EO, Blaiss MS, Derebery MJ, Mahr TA, Gordon BR, Sheth KK, et al. Burden of allergic rhinitis: results from the pediatric allergies in America survey. *J Allergy Clin Immunol*. 2009;124(3 Suppl 1):S43–70.
- 4 Small P, Keith PK, Kim H. Allergic rhinitis. *Allergy Asthma Clin Immunol*. 2018;14(Suppl 2):51.
- 5 Varshney J, Varshney H. Allergic rhinitis: an overview. *Indian J Otolaryngol Head Neck Surg*. 2015;67(2):143–9.
- 6 Bjerner L, Westman M, Holmström M, Wickman MC. The complex pathophysiology of allergic rhinitis: scientific rationale for the development of an alternative treatment option. *Allergy Asthma Clin Immunol*. 2019;15:24.
- 7 Platt M. Pharmacotherapy for allergic rhinitis. *Int Forum Allergy Rhinol*. 2014;4(Suppl 2):S35–40.
- 8 Hossenbaccus L, Linton S, Garvey S, Ellis AK. Towards definitive management of allergic rhinitis: best use of new and established therapies. *Allergy Asthma Clin Immunol*. 2020;16:39.
- 9 Gross G, Jacobs RL, Woodworth TH, Georges GC, Lim JC. Comparative efficacy, safety, and effect on quality of life of triamcinolone acetonide and fluticasone propionate aqueous nasal sprays in patients with fall seasonal allergic rhinitis. *Ann Allergy Asthma Immunol*. 2002;89(1):56–62.
- 10 May JR, Dolen WK. Management of allergic rhinitis: a review for the community pharmacist. *Clin Ther*. 2017;39(12):2410–9.
- 11 Bridgeman MB. Overcoming barriers to intranasal corticosteroid use in patients with uncontrolled allergic rhinitis. *Integr Pharm Res Pract*. 2017;6:109–19.
- 12 Brozek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic rhinitis and its impact on asthma (ARIA) guidelines – 2016 revision. *J Allergy Clin Immunol*. 2017;140(4):950–8.
- 13 Jeal W, Faulds D. Triamcinolone acetonide. A review of its pharmacological properties and therapeutic efficacy in the management of allergic rhinitis. *Drugs*. 1997;53(2):257–80.
- 14 Karaulov AV, Vylegzhanina T, Ovchinnikov A, Chernikova M, Nenasheva N. Triamcinolone acetonide versus fluticasone propionate in the treatment of perennial allergic rhinitis: a Randomized, Parallel-Group Trial. *Int Arch Allergy Immunol*. 2019;179(2):142–51.
- 15 Settupane G, Korenblat PE, Winder J, Lumry W, Murphree J, Alderfer VB, et al. Triamcinolone acetonide aqueous nasal spray in patients with seasonal ragweed allergic rhinitis: a placebo-controlled, Double-Blind Study. *Clin Ther*. 1995;17(2):252–63.
- 16 Karaulov AV, Nenasheva N, Smolkin Y, Maslakov A, Lucio L. Triamcinolone acetonide in the treatment of perennial allergic rhinitis: a post hoc analysis of quality of life during a Phase III Study. *Int Arch Allergy Immunol*. 2021, submitted.
- 17 Berridge MS, Heald DL, Muswick GJ, Leisure GP, Voelker KW, Miraldi F. Biodistribution and kinetics of nasal carbon-11-triamcinolone acetonide. *J Nucl Med*. 1998;39(11):1972–7.
- 18 Valovirta E, Ryan D. Patient adherence to allergic rhinitis treatment: results from patient surveys. *Medscape J Med*. 2008;10(10):247.
- 19 Loh CY, Chao SS, Chan YH, Wang DY. A clinical survey on compliance in the treatment of rhinitis using nasal steroids. *Allergy*. 2004;59(11):1168–72.
- 20 Meltzer EO, Hadley J, Blaiss M, Benninger M, Kimel M, Kleinman L, et al. Development of questionnaires to measure patient preferences for intranasal corticosteroids in patients with allergic rhinitis. *Otolaryngol Head Neck Surg*. 2005;132(2):197–207.
- 21 Stokes M, Amorosi SL, Thompson D, Dupclay L, Garcia J, Georges G. Evaluation of patients' preferences for triamcinolone acetonide aqueous, fluticasone propionate, and mometasone furoate nasal sprays in patients with allergic rhinitis. *Otolaryngol Head Neck Surg*. 2004;131(3):225–31.
- 22 Bachert C, El-Akkad T. Patient preferences and sensory comparisons of three intranasal corticosteroids for the treatment of allergic rhinitis. *Ann Allergy Asthma Immunol*. 2002;89(3):292–7.
- 23 Ahlstrom-Emanuelsson CA, Greiff L, Andersson M, Persson CG, Erjefält JS. Eosinophil degranulation status in allergic rhinitis: observations before and during seasonal allergen exposure. *Eur Respir J*. 2004;24(5):750–7.
- 24 Chen Y, Yang M, Deng J, Wang K, Shi J, Sun Y. Elevated levels of activated and pathogenic eosinophils characterize moderate-severe house dust mite allergic rhinitis. *J Immunol Res*. 2020;2020:8085615.