# Control of allergic rhinitis with MP-AzeFlu: a non-interventional study of a Swedish cohort*

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**Background**: The European Union has prioritised allergic rhinitis (AR) control. A visual analogue scale (VAS) has been endorsed as the AR control language and embedded into the most recent MACVIA-ARIA guideline. This study assessed the effectiveness and safety of MP-AzeFlu using a VAS in a real-life study in Sweden.

**Methods**: Patients (N = 431) aged ≥12 years with ARIA-defined moderate to severe AR were included in this multicentre, prospective, non-interventional study and prescribed MP-AzeFlu. Patients assessed symptom severity using a VAS from 0 (not at all bothersome) to 100 mm (very bothersome) on Days 0, 1, 3 and 7, and after ≈14 days in the morning before using MP-AzeFlu. Patients' perceived level of disease control was assessed on Day 3. The proportion of patients who achieved a defined VAS score cutoff for well- and partly controlled AR was also calculated.

**Results**: MP-AzeFlu reduced mean (SD) VAS score from 67.9 (16.1) mm at baseline to 32.1 (22.8) mm on the last day. Results were consistent irrespective of severity, phenotype, patient age class or previous treatment. By Day 3, 84.0% of patients reported well- or partly controlled symptoms. Overall, 17.7%, 32.2%, 53.8% and 64.2% of patients achieved a ≤38 mm "well-controlled" VAS score cutoff on Day 1, 3 and 7 and last day, respectively.

**Conclusions**: MP-AzeFlu provided rapid, effective and sustained symptom control in patients with AR from Sweden in a real-world setting, aligning with EU and MACVIA-ARIA initiatives and supporting the effectiveness of MP-AzeFlu for AR treatment in real life.

**Key words**: rhinitis, health status, quality of life, nose diseases

## Introduction

More than one-quarter of individuals in Sweden live with allergic rhinitis (AR), placing a substantial burden on both sufferers and society [1, 2]. Over the past 10 years, the prevalence of AR in Sweden appears to have plateaued [1]. However, the total cost of AR in Sweden is estimated at €1.3 billion per year, with the majority of the economic burden due to lost work productivity [2]. Existing mono- and multitherapy treatment regimens provide suboptimal symptom relief for many patients with AR [3, 4]. Uncontrolled AR symptoms have a negative impact on patients' sleep, general well-being and quality of life [3, 5]. This results in a high level of patient dissatisfaction with current treatments [6].

AR control has now been prioritised at the European Union government level [7]. MACVIA-ARIA (Contre les Maladies Chroniques pour un Vieillissement Actif-Allergic Rhinitis and its Impact on Asthma) has developed an updated AR treatment algorithm, called the AR clinical decision support system (CDSS), using disease control rather than symptom severity to guide treatment decisions [8]. A visual analogue scale (VAS) has been endorsed as the new language of AR control and embedded within this AR CDSS; a VAS score cutoff of 5/10 is being used to assess AR control and guide treatment decisions [8]. In addition, MACVIA-ARIA describes a patient-defined VAS score of ≤55 mm as partly controlled disease and ≤38 mm as well-controlled disease [9]. Although the VAS is a relatively simple tool, it

correlates well with more conventional AR outcome measures [10, 11] and is sensitive enough to discriminate according to disease severity [12, 13] and treatment effect [14]. At the same time, the need for high-quality data obtained from real-life respiratory research is slowly being recognised [15, 16]. Such data are valuable, being generalisable to a heterogeneous patient population and should be used to help qualify guideline recommendations, complementary to data from randomised controlled trials (RCTs) [15].

Provision of a common language and treatment aim is one way to improve AR control; another is to provide more effective therapies. MP-AzeFlu (Meda, a Mylan company, Canonsburg, PA, US) comprises a novel formulation of an intranasal antihistamine (azelastine hydrochloride), an intranasal corticosteroid (INS; fluticasone propionate) and excipients delivered in a single spray. In an RCT setting, MP-AzeFlu provided more effective and rapid AR symptom relief than an INS or intranasal antihistamine, providing twice the overall nasal and ocular symptom relief than either monotherapy [17]. Among patients treated with MP-AzeFlu, 18% with moderate to severe seasonal AR (SAR) (vs. 8 to 9% of those treated with fluticasone propionate, azelastine or placebo) and 73% with mild to moderate perennial AR (PAR) (vs. 64% of patients treated with fluticasone propionate) achieved complete or near-complete symptom relief in the first 14 days and 1 month of treatment, respectively, and achieved this response many days faster than INS or intranasal antihistamine monotherapy [17, 18]. However, the generalisability of data from clinical studies to the Swedish population is unknown, particularly because the eligibility criteria for participation in clinical studies excludes many patients seen in primary and secondary care in real life [19].

The main objective of this non-interventional study (NIS) was to assess the degree to which MP-AzeFlu prescribed by physicians in routine clinical practice achieved AR control in a cohort of patients in Sweden. Control was assessed using a VAS, the MACVIA-ARIA–endorsed language of AR control.

## Material and Methods

### Study design

This was a multicentre, prospective NIS conducted in Sweden between October 2013 and June 2014. It consisted of an inclusion visit (at Day 0) and an optional follow-up visit approximately 14 days later, allowing some flexibility depending on usual clinical practice. Visits took place in the physician's office. At the inclusion visit, a prescription for MP-AzeFlu and instructions for use (one spray in each nostril twice daily) were provided. Concomitant use of ritonavir or of fluticasone propionate (an active ingredient of MP-AzeFlu) was to be avoided, and caution was advised with the use of sedatives or centrally active medications. Otherwise, there were no restrictions regarding concomitant treatments; for example, patients could continue use of oral or intranasal anti-allergic medications or decongestants. As this was a NIS, there was no control group or randomization assignment.

As an alternative to the follow-up visit, patients were permitted to return their completed diary card by mail to the physician after finishing the study. The study was carried out in accordance with current Swedish laws and guidelines [20, 21]. An ethics committee in Lund provided approval of the study documents.

### Physicians

The physicians in this study were involved in the management of patients with AR and included general practitioners; allergists; ear, nose and throat specialists and paediatricians.

### Patients

*Inclusion criteria*

Physicians considered patients' suitability for entry to this study independently from and after the decision to prescribe MP-AzeFlu had been made. Patients who were eligible to receive treatment with MP-AzeFlu according to its approved indication in Sweden could enter this study (i.e. those aged ≥12 years with moderate to severe SAR or PAR for whom monotherapy with either an intranasal antihistamine or glucocorticoid was not considered sufficient). Patients were required to have acute AR symptoms on the day of inclusion, defined as a recommended VAS score >50 mm, or to have symptoms rated by the physician as moderate to severe (regardless of VAS score). Patients with rhinitis medicamentosa were not excluded.

*Exclusion criteria*

Patients were excluded if they had hypersensitivity to MP-AzeFlu or any of its excipients. Female patients who were pregnant or breastfeeding could receive MP-AzeFlu if benefits outweighed risks. All patients provided written informed consent before participating in the study, and if younger than 18 years of age, their caregiver also provided signed consent.

### Data collection and assessments

*MP-AzeFlu use in routine clinical practice*

Physicians recorded information on patient demographics, clinical symptoms and previous AR treatments at the inclusion visit. Physicians also logged information on AR history, number of physician visits in the current calendar year due to AR, predominant symptoms and ARIA-defined AR severity. SAR was defined as allergy to at least one pollen allergen (i.e. spring, summer and/or autumn pollen) but no non-pollen allergens; PAR was defined as allergy to at least one non-pollen allergen (i.e. dust mites, pet dander and/or mould) but no pollen allergens; SAR + PAR was defined as allergy to at least one pollen and at least one

non-pollen allergen; and AR of unknown origin was defined as allergy to other allergens (i.e. not one of the allergens listed above) or unknown allergens (i.e. rhinitis indicated from history but not from specific immunoglobulin-E data). Physicians recorded the reason for the patient's visit ("acute AR symptoms," "expected allergen exposure in near future" or "other") and the reason for prescribing MP-AzeFlu ("other therapies were not sufficient in the past," "other therapies are not considered to be sufficient to treat acute symptoms" or "other"). All data were recorded by physicians in an English-language electronic case report form (eCRF; Trium Analysis Online GmbH, München, Germany).

*MP-AzeFlu effectiveness assessment*

Data on AR symptom severity and disease control were recorded by the patient on a patient card (in the Swedish language), which was handed back to the physician at the follow-up visit or returned by mail. During the inclusion visit, on Days 1, 3 and 7 after the start of treatment and on the last day, patients evaluated how bothersome their current symptoms had been in the previous 24 hours on a VAS scale ranging from 0 mm (not at all bothersome) to 100 mm (very bothersome) in response to the statement: "Please reflect on how bothersome your symptoms were within the previous 24 hours." Assessments were made in the morning before administration of MP-AzeFlu. Patients also rated their level of disease control within the previous 24 hours on Day 3 of treatment as "well-controlled," "partly controlled" or "uncontrolled" (referred to as patient-reported disease control). Upon receipt of patient cards, physicians transcribed the information into the eCRF. Data were electronically signed by the physicians and saved in the study database located at Trium Analysis Online GmbH.

### Safety

All suspected adverse drug reactions (ADRs) and special situations (i.e. pregnancy; breastfeeding; any overdose, abuse, off-label use, misuse or medication error; adverse reaction related to occupational exposure; lack of efficacy) were documented by the physician and recorded in the eCRF. An ADR was defined as an adverse event (AE) with a reasonable possibility that the event may have been caused by MP-AzeFlu. AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA) coding system (Version 17.0).

### Statistics

It was planned to include up to 400 patients, which was considered sufficient to provide insight into the effectiveness of MP-AzeFlu in real-life clinical practice in Sweden. All baseline and efficacy analyses were based on the safety population, defined as all patients who received at least one dose of MP-AzeFlu and whose physician provided an electronic signature to confirm data accuracy. All data were reported using descriptive statistics with analyses performed by Syneed Medidata GmbH (Konstanz, Germany), using SAS Version 9.1.3 (Cary, NC, US).

Mean VAS score changes from baseline on Days 0, 1, 3 and 7 and last day were calculated for the total population (N = 431), according to phenotype, age group, baseline AR severity and previous therapy. Patients' perception of symptom control 3 days after starting MP-AzeFlu (at Day 3) was calculated for the total population and according to phenotype, excluding patients with missing data on symptom control from the analysis (n = 69).

### Post-hoc analyses

Definitions of "well-controlled" and "partly controlled" AR were determined by a weighted mean of the country-specific VAS

Table 1. Patient demographics and baseline clinical characteristics (N = 431).

| Characteristic | |
|---|---|
| Gender, n (%) | |
| Female | 232 (53.8) |
| Age, y, n (%) | |
| 12-17 | 18 (4.2) |
| 18-65 | 377 (87.5) |
| >65 | 36 (8.4) |
| Duration of rhinitis,* y (mean [SD]) | 18.6 (14.1) |
| Type (phenotype) of rhinitis, n (%) | |
| SAR | 106 (24.6) |
| PAR | 60 (13.9) |
| SAR + PAR | 220 (51.0) |
| Unknown origin | 45 (10.4) |
| Severity of AR†, n (%) | |
| Troublesome symptoms | 301 (69.8) |
| Impairment of daily activities/leisure/sport | 211 (49.0) |
| Impairment of school/work | 151 (35.0) |
| Sleep disturbance | 221 (51.3) |
| At least one criterion | 429 (99.5) |
| Predominant symptoms, n (%) | |
| Nasal congestion | 272 (63.1) |
| Rhinorrhoea | 61 (14.2) |
| Sneezing | 30 (7.0) |
| Nasal pruritus | 57 (13.2) |
| Unknown | 11 (2.6) |
| Concomitant ocular symptoms, n (%) | 204 (47.3) |

*n = 313. †Moderate to severe AR if at least one criterion was met.
AR = allergic rhinitis, PAR = perennial AR, SAR = seasonal AR, SD = standard deviation, y = years.

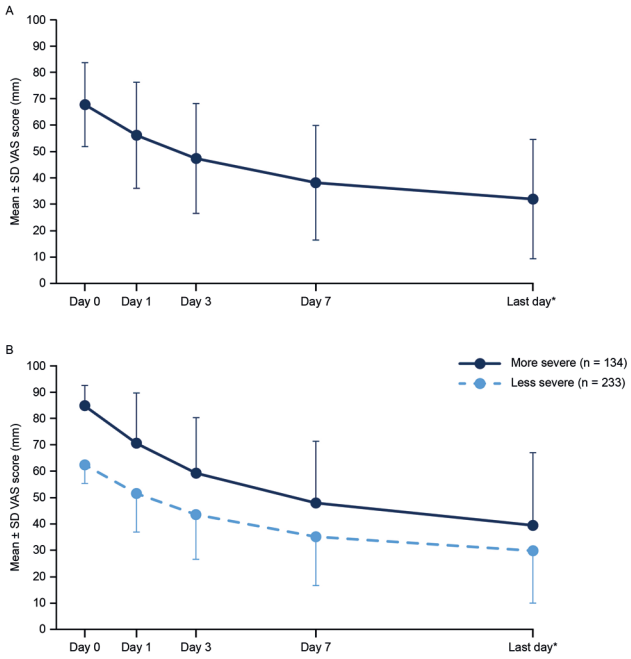


Figure 1. Effect of MP-AzeFlu on visual analogue scale (VAS) score over time in (A) the total population (N = 431) and (B) according to baseline severity. Less severe: baseline VAS score 50-74 mm; more severe: baseline VAS score 75-100 mm. Data are presented as mean and standard deviation (SD). *Mean of last day corresponds to Day 16.8.

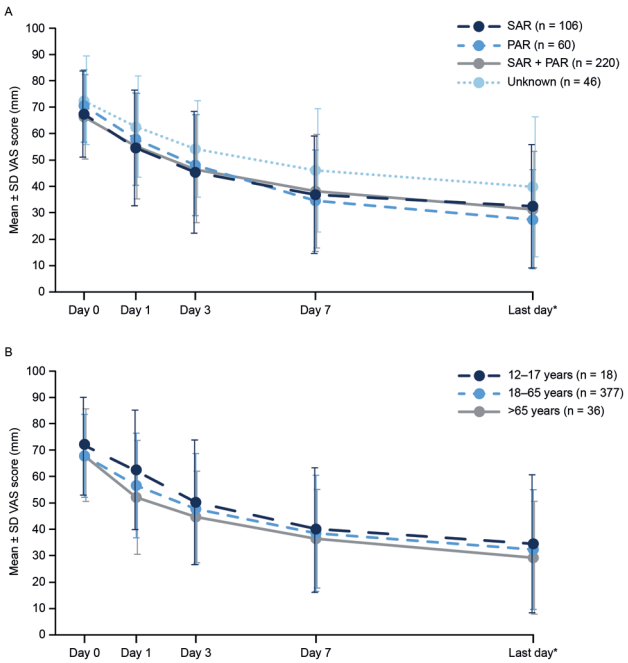


Figure 2. Effect of MP-AzeFlu on visual analogue scale (VAS) score over time according to (A) allergic rhinitis phenotype and (B) patient age class. PAR = perennial allergic rhinitis, SAR = seasonal allergic rhinitis. Data are presented as mean and standard deviation (SD). *Mean of last day corresponds to Day 16.8.

cutoffs (Youden index), calculated from a pooled data set incorporating data from Germany, Sweden, Denmark, Norway and Romania [22] and were 38 mm and 55 mm, respectively. Responder rates for achieving these cutoff values at Day 0, 1, 3 and 7 and last day were derived from time to response analysis as Kaplan-Meier estimates and referred to as VAS-determined disease control. Time at which patients achieved the AR CDSS-defined well-controlled VAS score threshold (i.e. 50 mm) was also assessed.

## Results

### Patient disposition

Overall, 57 Swedish physicians enrolled 449 patients into this study. Eighteen patients were excluded from the analysis: 17 due to unconfirmed data documentation and one who did not take any MP-AzeFlu after being prescribed the treatment. The safety population therefore included 431 patients.

### Patient demographic and baseline characteristics

Patient demographic and baseline clinical characteristics are presented in Table 1. A slightly greater proportion of the population was female (53.8%). Most participants were adults aged 18 to 65 years (87.5%); mean age was 42.0 (15.6) years. About three-quarters of the patients had SAR (either SAR alone or SAR + PAR), with only 13.9% diagnosed with PAR only. In total, 367 patients (85.2%) had a baseline VAS score ≥50 mm (VAS of 50 to 74 mm, n = 233; VAS of 75 to 100 mm, n = 134), 429 patients (99.5%) had moderate to severe AR, according to the ARIA classification. Nasal congestion was patients' most frequent predominant symptom (63.1%). Nearly half of all patients had concomitant ocular symptoms.

The mean (standard deviation [SD]) number of physician visits due to AR (prior to MP-AzeFlu prescription) in the current calendar year was 1.8 (4.4) (with median [range] of 1 [0, 40]). Almost half (47.6%) of patients had visited their physician at least once in the current calendar year due to their AR before inclusion in the study: 20.4% (n = 88) of patients had attended once before; 9.3% (n = 40) had attended twice before; 5.6% (n = 24) three times; and 12.3% (n = 53) four or more times prior to the current visit. The most frequent reasons for physician visit were acute AR symptoms (n = 190; 44.1%), expected allergen exposure in the near future (n = 57; 13.2%) and other (n = 195; 45.2%). The most common reason for prescribing MP-AzeFlu was "other therapies were not sufficient in the past" (n = 295; 68.4%). For the remaining patients, other reasons, including "other therapies were not considered sufficient to treat acute symptoms" were cited.

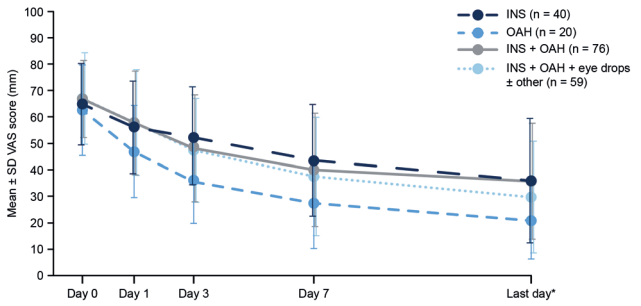


Figure 3. Effect of MP-AzeFlu on visual analogue scale (VAS) score over time according to AR treatment history. AR = allergic rhinitis, INS = intranasal corticosteroid monotherapy, OAH = oral antihistamine monotherapy. Data are presented as mean and standard deviation (SD). *Mean of last day corresponds to Day 16.8.

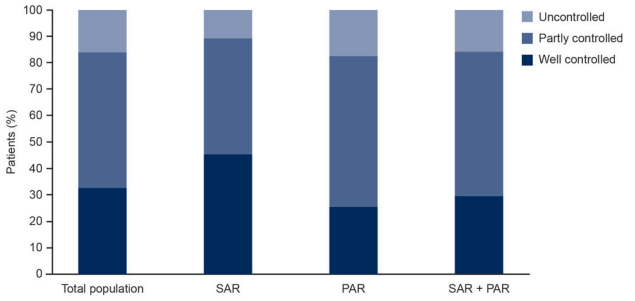


Figure 4. Patient-reported allergic rhinitis (AR) control on Day 3 for the total population with recorded control status (n = 362) and according to AR phenotype (i.e. seasonal AR [SAR; n = 84], perennial AR [PAR; n = 51], SAR + PAR [n = 190]). Unknown origin [n = 37]) not shown.

### AR treatments since the last year

The most commonly used AR medications since the last year were INS (n = 318; 73.8%), oral antihistamine (OAH; n = 294; 68.2%) and intranasal/oral decongestants (n = 119; 27.6%) (supplementary Table 1). Approximately one quarter of patients (n = 109; 25.3%) had used eye drops since the last year, either in the form of an antihistamine or mast cell stabiliser. Regarding combinations of therapy, 40 patients used INS monotherapy, 20 patients used OAH monotherapy, 76 patients used INS + OAH and 59 patients used INS + OAH + eye drops ± other treatment. In total, 318 patients (73.8%) had used multiple AR treatments since the last year. At the time of the inclusion visit, 38 patients (8.8%) were undergoing immunotherapy and 33 (7.7%) had previously received immunotherapy.

### Effectiveness

The mean (SD) time period between treatment initiation and the VAS assessment on the last visit (or the day the patient returned his or her card) was 16.8 (8.1) days (median 14 days; first quartile, 14 days; third quartile, 15 days). MP-AzeFlu was shown to reduce mean (SD) VAS score from 67.9 (16.1) mm at baseline (n = 391) to 32.1 (22.8) mm on the last day (n = 372), a reduction of 36.1 (24.0) mm (n = 370) (Figure 1A). Similar results were obtained in patients with more and less severe disease at baseline (Figure 1B), in those with SAR, PAR, SAR + PAR or AR of unknown origin (Figure 2A) and in those aged 12-17 years, 18-65 years and >65 years (Figure 2B).

Patients treated with MP-AzeFlu experienced a reduction in mean (SD) VAS score whether previous treatment was with INS monotherapy (28.8 [26.0] mm reduction); OAH monotherapy (41.4 [19.9] mm reduction); INS + OAH (31.2 [24.6] mm reduction) or INS + OAH + eye drops ± other (38.0 [21.0] mm reduction) (Figure 3).

Regarding patient-reported disease control, 3 days after the start of MP-AzeFlu treatment, 32.6% of patients (with control status data) considered their symptoms well-controlled and 51.4% reported their symptoms were partly controlled (Figure 4). Only 16.0% of patients indicated their symptoms were still uncontrolled. Overall, 89.2% of those with SAR, 82.4% with PAR, and 84.2% with SAR + PAR reported their symptoms were partly or well-controlled after 3 days of treatment (Figure 4).

Regarding VAS-determined disease control (post hoc analysis), patient perception of "well-controlled" symptoms corresponded to a VAS score cutoff of 38 mm [21]; 17.7% of patients achieved at least this cutoff on Day 1, 32.2% on Day 3, 53.8% on Day 7 and 64.2% on the last day (Figure 5). Similarly, the feeling of "partly controlled" symptoms corresponded to a VAS score cutoff of 55 mm [21], and 49.5%, 68.0%, 81.4% and 86.8% of Swedish patients achieved at least this cutoff on Days 1, 3 and 7 and last day, respectively (Figure 5). These responses were relatively independent of phenotype—a similar proportion of those with SAR, PAR, SAR + PAR and AR of unknown origin achieved these well- and partly controlled VAS score cutoffs on Days 1, 3 and 7 and last day. On average, patients treated with MP-AzeFlu achieved the AR CDSS control cutoff (50 mm) by Day 3.

### Safety

During the course of this study, eight patients (1.9%) reported a total of 12 safety cases (nine AEs and three special situations). Eight of the AEs were considered related to treatment and classified as ADRs; the most frequent of these were dysgeusia (n = 2) and epistaxis (n = 2). None of the AEs was considered serious. Three patients discontinued treatment with MP-AzeFlu due to AEs (dysgeusia, dysgeusia and nausea, cough; each in one patient).

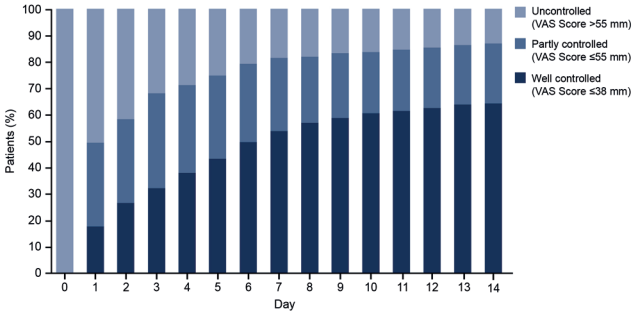


Figure 5. Proportion of patients treated with MP-AzeFlu who had well-controlled (i.e. VAS score ≤38 mm), partly controlled (i.e. VAS score ≤55 mm) and uncontrolled allergic rhinitis over time (VAS-determined disease control). Data are presented as Kaplan-Meier estimates for Days 1, 3 and 7 and last day and interpolated for the other days. VAS = visual analogue scale.

## Discussion

This is the first study to assess the effectiveness of MP-AzeFlu in real-life clinical practice in Sweden. Effectiveness was assessed using the new language of AR control (i.e. VAS), endorsed by MACVIA-ARIA and incorporated into the updated guidelines (AR CDSS) [8]. The results of this study were analysed and reported in the context of a clinical goal of achieving well-controlled disease, both patient- and ARIA-defined.

MP-AzeFlu led to rapid AR symptom relief from the first day of treatment, which was maintained for the duration of the study. Results were consistent irrespective of disease severity, phenotype, patient age class or AR treatment history. Furthermore, 64.2% of patients achieved the patient-defined well-controlled VAS score cutoff (≤38 mm) by last day of MP-AzeFlu treatment. On average, patients treated with MP-AzeFlu achieved the AR CDSS control cutoff (50 mm) [8] by Day 3.

The trial was designed in line with Respiratory Effectiveness Group/European Academy of Allergy and Clinical Immunology recommendations [16]. The real-life data from the current NIS also provide complementary evidence on the effectiveness and safety of MP-AzeFlu to that generated in RCTs [17, 18, 23]. The populations of patients enrolled into RCTs are governed by strict eligibility criteria and may not be fully representative of patients seen in real-life clinical practice [19]. Real-life studies, on the other hand, include broader patient populations and aim to evaluate the effectiveness of treatments in a scenario closer to routine clinical practice [15]. Results from well-designed real-life studies are what one might expect to achieve in routine care. They also extend the evidence base upon which treatment decisions and guideline recommendations can be based.

Data collected during this study provide a snapshot of the poorly controlled AR landscape in Sweden, as evidenced by the high physician consultation rate due to AR in the last year, the frequency of comedication use and patients' high baseline VAS scores. These data suggest that other AR treatment options may not be sufficient to control some patients' AR symptoms.

Patients' mean VAS score at baseline was 67.9 mm, indicating they had bothersome AR symptoms despite a majority of patients receiving treatment and emphasising the need for new, more-effective treatment options for AR. Inadequacy of previously used AR treatment options was also evidenced by the fact that the most common reason for prescribing MP-AzeFlu was "other therapies were considered insufficient."

The need for multiple physician visits reported here is interesting and will inflate the already high costs (mostly indirect) associated with AR in Sweden [2]. MP-AzeFlu provided fast and effective symptom control for patients with previously uncontrolled disease, potentially reducing costs associated with repeat physician visits.

Similar to the results of other studies [4, 24], many patients included in this NIS used multiple therapies (e.g. INS + OAS) in an attempt to achieve rapid and complete symptom relief. However, these patients remained symptomatic, as evidenced by high VAS scores at baseline, higher than those observed for patients previously treated with monotherapy. Comedication (e.g. with an INS and OAH or leukotriene antagonists) is not supported by data from clinical studies [25, 26], nor recommended by ARIA (due to insufficient evidence) [27].

MP-AzeFlu provided rapid and sustained symptom control in patients previously treated with mono- and multiple AR therapies. Furthermore, as MP-AzeFlu incorporates an intranasal antihistamine, an INS and a novel formulation in a single spray, it benefits from a rapid onset of action and will most likely improve patient compliance with an AR treatment regimen and eliminate the perceived need for polypharmacy (leading to socioeconomic advantages).

The main limitations of this NIS were the lack of control group and random assignment. Furthermore, study data were derived from clinical records and patients themselves, so the accuracy and completeness of data relied on the quality of these records and the ability of patients to recall information. Missing data could be a potential source of bias in the study results. However, in this study, data were complete for most variables and the rates of missing data ranged from 6 to 14% for other variables, which is considered acceptable for observational studies.

The strength of this study was the inclusion of a large number

of patients, considered sufficient to draw general conclusions on use, effectiveness and safety of MP-AzeFlu in routine clinical practice in Sweden. The consistency of findings among other countries [28-32] provides confidence in the robustness of the data. Finally, the use of the VAS, incorporated into the MACVIA-ARIA AR treatment algorithm [8], is a further strength, enabling extrapolation of how Swedish patients with AR may respond to MP-AzeFlu in the context of this updated guideline.

## Conclusions

In conclusion, prior to MP-AzeFlu prescription, patients with AR had uncontrolled disease, with reported high rates of multi-therapy usage and multiple physician visits. MP-AzeFlu provided effective and rapid symptom control in a real-world setting in Swedish patients with AR assessed using a VAS, the MACVIA-ARIA–endorsed language of AR control. The results were consistent regardless of patient age class, disease severity, phenotype or AR treatment history. The responder rates observed in real life were higher than those observed in RCTs. These results support the effectiveness of MP-AzeFlu for the treatment of patients with moderate to severe AR in real life.

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## Authorship contribution

All authors contributed to interpretation of data, drafting of the article and revising it critically and provided final approval of the version to be published.

## Conflict of interest

PS and AE report personal fees from Meda outside the submitted work. VS and KT have nothing to disclose.

## References

1. Eriksson J, Ekerljung L, Ronmark E, Dahlen B, Ahlstedt S, Dahlen SE, et al. Update of prevalence of self-reported allergic rhinitis and chronic nasal symptoms among adults in Sweden. Clin Respir J. 2012; 6: 159-168.
2. Cardell LO, Olsson P, Andersson M, Welin KO, Svensson J, Tennvall GR, et al. TOTALL: high cost of allergic rhinitis-a national Swedish population-based questionnaire study. NPJ Prim Care Respir Med. 2016; 26: 15082.
3. Bousquet PJ, Demoly P, Devillier P, Mesbah K, Bousquet J. Impact of allergic rhinitis symptoms on quality of life in primary care. Int Arch Allergy Immunol. 2013; 160: 393-400.
4. Price D, Scadding G, Ryan D, Bachert C, Canonica GW, Mullol J, et al. The hidden burden of adult allergic rhinitis: UK healthcare resource utilisation survey. Clin Transl Allergy. 2015; 5: 39.
5. Canonica GW, Bousquet J, Mullol J, Scadding GK, Virchow JC. A survey of the burden of allergic rhinitis in Europe. Allergy. 2007; 62 Suppl 85: 17-25.
6. Ciprandi G, Incorvaia C, Scurati S, Puccinelli P, Soffia S, Frati F, et al. Patient-related factors in rhinitis and asthma: the satisfaction with allergy treatment survey. Curr Med Res Opin. 2011; 27: 1005-1011.
7. Bousquet J, Malva J, Nogues M, Manas LR, Vellas B, Farrell J, et al. Operational Definition of Active and Healthy Aging (AHA): The European Innovation Partnership (EIP) on AHA Reference Site Questionnaire: Montpellier October 20-21, 2014, Lisbon July 2, 2015. J Am Med Dir Assoc. 2015; 16: 1020-1026.
8. Bousquet J, Schunemann HJ, Hellings PW, Arnavielhe S, Bachert C, Bedbrook A, et al. MACVIA clinical decision algorithm in adolescents and adults with allergic rhinitis. J Allergy Clin Immunol. 2016; 138: 367-374.
9. Bousquet J, Schunemann HJ, Fonseca J, Samolinski B, Bachert C, Canonica GW, et al. MACVIA-ARIA Sentinel NetworK for allergic rhinitis (MASK-rhinitis): the new generation guideline implementation. Allergy. 2015; 70: 1372-1392.
10. Bousquet PJ, Combescure C, Klossek JM, Daures JP, Bousquet J. Change in visual analog scale score in a pragmatic randomized cluster trial of allergic rhinitis. J Allergy Clin Immunol. 2009; 123: 1349-1354.
11. Demoly P, Bousquet PJ, Mesbah K, Bousquet J, Devillier P. Visual analogue scale in patients treated for allergic rhinitis: an observational prospective study in primary care: asthma and rhinitis. Clin Exp Allergy. 2013; 43: 881-888.
12. Bousquet PJ, Combescure C, Neukirch F, Klossek JM, Mechin H, Daures JP, et al. Visual analog scales can assess the severity of rhinitis graded according to ARIA guidelines. Allergy. 2007; 62: 367-372.
13. Del Cuvillo A, Santos V, Montoro J, Bartra J, Davila I, Ferrer M, et al. Allergic rhinitis severity can be assessed using a visual analogue scale in mild, moderate and severe. Rhinology. 2017; 55: 34-38.
14. Bousquet J, Bachert C, Canonica GW, Mullol J, Van Cauwenberge P, Bindslev Jensen C, et al. Efficacy of desloratadine in intermittent allergic rhinitis: a GA(2)LEN study. Allergy. 2009; 64: 1516-1523.
15. Price D, Smith P, Hellings P, Papadopoulos N, Fokkens W, Muraro A, et al. Current controversies and challenges in allergic rhinitis management. Expert Rev Clin Immunol. 2015; 11: 1205-1217.
16. Pilot of QA Tool Aimed at Objective Assessment of Real Life Research to be Launced at EAACI 2015; http://wwweffectivenessevaluation.org/pilot-qa-tool-aimed-objective-assessment-real-life-research-launched-eaaci20152015
17. Meltzer E, Ratner P, Bachert C, Carr W, Berger W, Canonica GW, et al. Clinically relevant effect of a new intranasal therapy (MP29-02) in allergic rhinitis assessed by responder analysis. Int Arch Allergy Immunol. 2013; 161: 369-377.
18. Price D, Shah S, Bhatia S, Bachert C, Berger W, Bousquet J, et al. A new therapy (MP29-02) is effective for the long-term treatment of chronic rhinitis. J Investig Allergol Clin Immunol. 2013; 23: 495-503.
19. Costa DJ, Amouyal M, Lambert P, Ryan D, Schunemann HJ, Daures JP, et al. How representative are clinical study patients with allergic rhinitis in primary care? J Allergy Clin Immunol. 2011; 127: 920-926 e1.
20. Lakemedelsverkets forfattningssamling LVFS 2003;6. Lakemedelsverkets foreskriffter och allmanna rad om klinisk provning av lakemedel for humant bruk, ISNN 1101-5225, 26 Juni 2003.
21. Lakemedelsingustriforeningen Lp21. Regler for icke-interventionsstudier och ekonomiskt stod till kvalitetsregister, Oktober 2010.

22. Klimek L, Bachert C, Stjarne P, Dollner R, Larsen P, Haahr P, et al. MP-AzeFlu provides rapid and effective allergic rhinitis control in real-life: a pan-European study. Allergy Asthma Proc. 2016; 37: 376-386.
23. Berger W, Bousquet J, Fox AT, Juste J, Muraro A, Nieto A, et al. MP-AzeFlu is more effective than fluticasone propionate for the treatment of allergic rhinitis in children. Allergy. 2016; 71: 1219-1222.
24. Navarro A, Valero A, Rosales MJ, Mullol J. Clinical use of oral antihistamines and intranasal corticosteroids in patients with allergic rhinitis. J Investig Allergol Clin Immunol. 2011; 21: 363-369.
25. Anolik R. Mometasone Furoate Nasal Spray With Loratadine Study Group. Clinical benefits of combination treatment with mometasone furoate nasal spray and loratadine vs monotherapy with mometasone furoate in the treatment of seasonal allergic rhinitis. Ann Allergy Asthma Immunol. 2008; 100: 264-271.
26. Esteitie R, deTineo M, Naclerio RM, Baroody FM. Effect of the addition of montelukast to fluticasone propionate for the treatment of perennial allergic rhinitis. Ann Allergy Asthma Immunol. 2010; 105: 155-161.
27. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and Its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008;63 Suppl 86:8-160.
28. Klimek L, Bachert C, Mosges R, Munzel U, Price D, Virchow JC, et al. Effectiveness of MP29-02 for the treatment of allergic rhinitis in real-life: results from a noninterventional study. Allergy Asthma Proc. 2015; 36: 40-47.
29. Dollner R, Lorentz Larsen P, Sheyauldeen S, Kuhl H, Steinsvag S. Real-life effectiveness of a new allergic rhinitis therapy (MP29-02) in Norway. Allergy. 2015; 70: 486.
30. Agache I, Sarafoleanu C, Leur P, Bucur I, Doros I-C, Poenaru M. Real-life effectiveness of a new allergic rhinitis therapy (MP-AzeFlu*) in Romania. Allergy 2016;71:386.
31. Haahr P, Jacobsen C, Blegvad S, Christensen M, Kuhl H, Nielsen K. Real life effectiveness of a new allergic rhinitis therapy (MP29-02) in Denmark. Allergy. 2015; 70: 484-485.
32. Agache I, Doros IC, Leru PM, Bucur I, Poenaru M, Sarafoleanu C. MP-AzeFlu provides rapid and effective allergic rhinitis control: results of a non-interventional study in Romania. Rhinology. 2018; 56: 33-41.

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S Table 1. AR treatments since the last year (N = 431).

| AR treatment (multiple entries possible) | n (%) |
|---|---|
| Intranasal corticosteroid | 318 (73.8) |
| Oral antihistamine | 294 (68.2) |
| Intranasal decongestant | 104 (24.1) |
| Ocular antihistamine | 83 (19.3) |
| Oral leukotriene antagonist | 68 (15.8) |
| Intranasal antihistamine | 55 (12.8) |
| Systemic corticosteroid | 53 (12.3) |
| Ocular mast cell stabiliser | 26 (6.0) |
| Oral decongestant | 15 (3.5) |
| Intranasal mast cell stabiliser | 8 (1.9) |
| Other | 21 (4.9) |
| None | 37 (8.6) |
| Unknown | 3 (0.7) |
| Immunotherapy (in past or ongoing) | 71 (16.5) |
| Number of treatments listed above (excluding immunotherapy) | |
| 1 | 113 (26.2) |
| 2 | 126 (29.2) |
| 3 | 98 (22.7) |
| 4 | 55 (12.8) |
| 5 | 29 (6.7) |
| 6 | 9 (2.1) |
| 7 | 1 (0.2) |

AR = allergic rhinitis.