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SPECIAL SUPPLEMENT

OVERVIEW OF THE 2019 ALLERGIC RHINITIS AND ITS IMPACT ON ASTHMA (ARIA) NEXT-GENERATION UPDATE

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OVERVIEW OF THE 2019 ALLERGIC RHINITIS AND ITS IMPACT ON ASTHMA (ARIA) NEXT-GENERATION UPDATE AND ITS COMPARABILITY TO THE 2016 ARIA UPDATE AND 2020 AAAAI (AMERICAN ACADEMY OF ALLERGY, ASTHMA, AND IMMUNOLOGY) RHINITIS PRACTICE PARAMETER

OBJECTIVE AND SYNOPSIS OF 2019 ARIA UPDATE

- In 2019 and 2020, two guidelines on the pharmacotherapeutic management of allergic rhinitis (AR) were updated using a Grading of Recommendations, Assessment, Development and Evaluation (GRADE)-based approach or a mixed GRADE and consensus-based approach.[1,2] This article will provide a synopsis of the 2019 ARIA (Allergic Rhinitis and Its Impact on Asthma) next-generation update,[1] including comparisons to relevant recommendations made by the 2016 ARIA revision and 2020 AAAAI (American Academy of Allergy, Asthma, and Immunology) Rhinitis Practice Parameter.[2,3]
- While GRADE methodologies are often limited to randomized controlled trials, increasing emphasis is being placed on the importance of real-world data in reflecting patient needs and guiding clinical practices.[1] The purpose of this next-generation 2019 ARIA guideline was to refine the algorithm for AR treatment using previous GRADE-based guidelines and to uniquely incorporate real-world evidence (RWE) (randomized controlled trials (RCT), real-world data collected from mobile technology, and chamber studies).[1]
- A consensus group designed the "Contre les Maladies Chroniques pour un Vieillissement Actif" (MACVIA) algorithm to guide the selection of pharmacotherapy for AR and step-up or step-down of treatment based on disease control.[1] Two treatment protocols – one for untreated symptomatic adolescent and adult patients and the other for treated symptomatic adolescent and adult patients – were proposed.[1] Step-up and step-down treatment modifications were made based on assessments using a visual analogue scale (VAS), which is an instrument used to measure the severity of AR symptoms. AR treatments were classified.[1]
- The ARIA 2016 revision and US Practice Parameters 2017 focused on the efficacy and speed of action of AR treatments, primarily reviewing evidence from randomized controlled trials. Both are consistent with the current MACVIA algorithms.[1]
- Allergen exposure chambers facilitate stable allergen exposure and can be used to evaluate the onset of action of medications, an important consideration for clinicians and patients.[1] Chamber studies confirmed the rapid onset of efficacy for azelastine and its combinations; lack of difference

between azelastine alone and its combinations; delayed onset of action of other intranasal H1-antihistamines (INAH); lack of efficacy of intranasal corticosteroids (INCSs) prior to 2 hours; and azelastine and levocabastine/fluticasone furoate as quicker acting medications when compared to oral H1-antihistamines (OAH).[1]

- Mobile Airways Sentinel Network (MASK), included in the most recent ARIA, is a patient-centered technology tool that guides patient decisions using a plan developed by healthcare professionals.[1] It can help elucidate real life information.[1] Results from two MASK studies (>9000 users) demonstrated: issues with patient adherence, similar issues with adherence among physicians with AR, lack of a treatment trajectory and most patients self-medicate, the use of on-demand or frequently changing medications in poorly controlled cases, worsening control with greater medication use, less or no medication use in well-controlled cases, worse control with OAH monotherapy versus INCS, and superior efficacy of azelastine–fluticasone propionate combination (MPAzeFlu) versus INCSs.[1] The data also suggest that despite the MPAzeFlu being more commonly administered than INCS, patients receiving monotherapy with INCS-containing medications have a similar level of control.[1]
- Some potential limitations of MASK include sampling bias, outcome misclassification, issues around generalizability of data, lack of physician-confirmed diagnosis, and differing degrees of patient comfort with technology.[1] However, it provides novel perspectives that can be used alongside randomized controlled trials.[1]

COMPARISONS OF THE 2019 ARIA UPDATE TO THE 2016 ARIA UPDATE AND 2020 AAAAI RHINITIS PRACTICE PARAMETER

- Most recommendations made in the 2016 ARIA update **(Table I)** were supported in the 2019 next-generation ARIA update, specifically the use of INCS rather than INAH, and similar efficacy profiles of INCSs/OAH combination treatment and INCSs alone.[1,3] However, while the 2019 ARIA update documented the superior efficacy of INCSs/INAH over INCSs alone, the 2016 update stated that either treatment option could be considered.[1,3]
- The use of the visual analog scale (VAS) as a tool to determine the need for treatment modification was not addressed in the 2016 ARIA guidelines.[3] However, VAS measurements are an important component of the 2019 next-generation ARIA treatment algorithm and 2020 AAAAI Rhinitis Practice Parameter, dictating treatment step-up/down modifications in both.[1-3]
- Similarly, most recommendations from the 2020 AAAAI Rhinitis Practice Parameter were consistent with evidence presented in the 2019 ARIA update **(Table I)**, specifically the similar efficacy profiles of INCSs/OAH combination and INCSs monotherapy, the efficacy of combination INCS/INAH treatment, and the superior potency of INCSs over leukotriene receptor antagonists (LTRAs).[1,2] However, while INCSs was supported as a first-line therapy for patients with moderate-to-severe rhinitis in the 2019 update, INAH was recommended as the first-line treatment for certain forms of AR in the 2020 AAAAI Rhinitis Practice Parameter.[1,2]

The 2019 ARIA next-generation update aimed to substantiate previous recommendations made in the 2016 ARIA, using RWE, and hence made no explicit new recommendations. It should be noted that no distinction was made between perennial allergic rhinitis (PAR) and seasonal allergic rhinitis (SAR) in the 2019 ARIA update. Significant recommendations and evidence-supported practices from the 2016 and 2019 ARIA guidelines are highlighted in the table below, and also compared to the 2020 AAAAI Rhinitis Practice Parameter.

TABLE I: COMPARISON OF EVIDENCE AND RECOMMENDATIONS FROM THE 2016 ARIA UPDATE, 2019 NEXT-GENERATION ARIA UPDATE, AND 2020 AAAAI RHINITIS PRACTICE PARAMETER.[1-3]

2016 ARIA UPDATE[3] WE RECOMMEND…	2019 ARIA NEXT-GENERATION UPDATE[1] THE EVIDENCE SHOWS THAT…	2020 AAAAI RHINITIS PRACTICE PARAMETER[2] WE RECOMMEND…
➢ The use of an INCS rather than an INAH in patients with SAR **(conditional recommendation; moderate certainty of evidence)**. ➢ The use of an INCS rather than an INAH in patients with PAR **(conditional recommendation; low certainty of evidence).**	➢ INAH are less effective than INCSs.	➢ No applicable recommendation was provided.
➢ No applicable recommendation was provided.	➢ INCSs should continue being prescribed as first-line therapy in patients with moderate-to-severe rhinitis.	➢ INAH should be offered as an initial treatment option for patients with SAR. **(Strength of recommendation: Strong; Certainty of evidence: High)** ➢ INAH should be offered as an initial treatment option for patients with intermittent AR. **(Strength of recommendation: Strong; Certainty of evidence: Ungraded)**
➢ The use of a combination of an INCS with an OAH or an INCS alone in patients with SAR **(conditional recommendation; low certainty of evidence).** ➢ The use of an INCS alone rather than a combination of an INCS with an OAH in patients with PAR **(conditional recommendation; very low certainty of evidence).**	➢ The combination of INCSs and OAH offers no advantage over INCSs.	➢ A combination of an OAH and an INCS should not be prescribed in preference to monotherapy with an INCS in patients >12 years of age with symptoms of SAR. **(Strength of the recommendation: Strong; Certainty of evidence: Moderate)** ➢ A combination of an OAH and an INCS should not be prescribed in preference to monotherapy with an INCS in all patients with SAR and PAR. **(Strength of recommendation: Conditional; Certainty of evidence: Very low)**
➢ The use of a combination of an INCS with an INAH or an INCS alone in patients with SAR **(conditional recommendation; moderate certainty of evidence).** ➢ The use of either a combination of an INCS with an INAH or an INCS alone in patients with PAR **(conditional recommendation; very low certainty of evidence).**	➢ The combination of INCSs and INAH is more effective than INCSs.	➢ A combination of an INCS and an INAH should be considered for the initial treatment of moderate/severe nasal symptoms of SAR in patients aged >12 years. **(Strength of the recommendation: Conditional; Certainty of evidence: High)** ➢ A combination of an INCS and an INAH should be considered for moderate/ severe SAR and PAR that is resistant to pharmacologic monotherapy. **(Strength of recommendation: Conditional; Certainty of evidence: Moderate)**
➢ No applicable recommendation was provided.	➢ LTRA are less potent than INCSs.	➢ The clinician should use an INCS over an LTRA for the initial treatment of moderate/severe SAR in patients 15 years of age and older. **(Strength of the recommendation: Strong; Certainty of evidence: High)**

AR (allergic rhinitis), INCS (intranasal corticosteroid), INAH (intranasal H1-antihistamines), LTRA (leukotriene antagonists), PAR (perennial allergic rhinitis), SAR (seasonal allergic rhinitis), OAH (oral H1-antihistamines)

CONCLUSIONS

The next-generation 2019 ARIA guidelines modified recommendations based on different forms of RWE, which are emerging as a promising adjunct to traditional forms of data collection such as RCTs.[1] Through RWE analysis, the majority of GRADE recommendations for AR were confirmed as was the AR treatment classification.[1] Additionally, while the overall ARIA algorithm and step-up/down approach have been confirmed, further testing with RWE is needed.[1] **(See Figure 1)**. This GRADE-based guideline is the first to incorporate different types of RWE.[1]

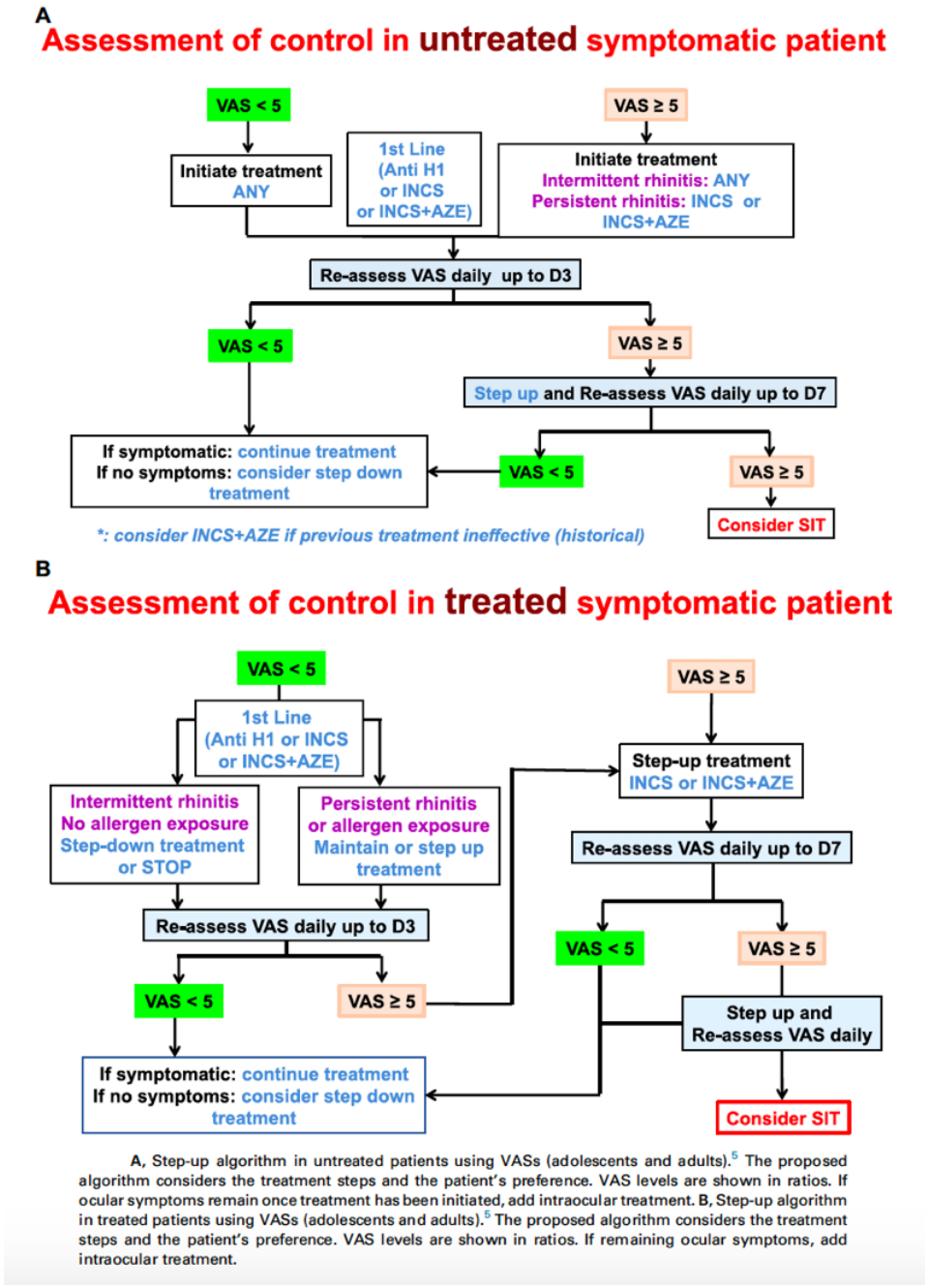

Figure 1. MACVIA treatment algorithm as presented in the 2019 ARIA update.

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