



Editorial

Choosing biologics for uncontrolled asthma

A conundrum for clinicians



Like other areas of medicine, the field of allergy and immunology has undergone a large shift from a 1-size-fits-all mentality to that of personalized medicine. In fact, I believe allergy, of all fields of medicine, best depicts this shift, particularly within the management of allergic asthma and the emergence of endotypes and phenotypes. Creating a personalized asthma plan has truly become an art (and a science), with more options available to the clinician now than ever before to achieve asthma control for our patients. For example, 2020 brought an update to the National Heart, Lung, and Blood Institute guidelines that allows for more options regarding both intermittent inhaled corticosteroid and intermittent inhaled corticosteroid/long-acting beta agonist use.¹ But perhaps the best example of the shift toward precision medicine can be found within the world of biologics. Since the US Food and Drug Administration approval of Omalizumab in 2003 for the treatment of severe allergic asthma, 5 more agents were welcomed in the next decade, 4 of which were approved specifically for the treatment of eosinophilic asthma. The most recent addition to this group is Tezepelumab, which became the first agent with the US Food and Drug Administration approval for all types of severe asthma, including non-eosinophilic, and without the need for measuring biomarkers.² Treatment options continue to expand, with the reduction of approved ages to 6 years for several agents and expansion of treatment options to include devices for self- or home administration. With other agents currently being studied, we can only expect the list of medications to grow, further expanding our options as clinicians.

Although more available agents for asthma management have provided great benefit for our patients, at times, it can be a source of great confusion for providers. At the end of the day, or the end of the visit, we may find ourselves faced with the question, “Which biologic do I choose?” There is no simple algorithm or “recipe” to follow for every patient when it comes to choosing a biologic. Such is the beauty of precision medicine. The year of 2022 brought us several publications that have provided some much-needed clinical guidance in this matter. An article by Brusselle and Koppleman³ includes tables and algorithms that provide guidance on choosing an initial biologic therapy. The authors propose that biologic selection should be on the basis of the incorporation of clinical characteristics (age, onset, allergy status) with patient-specific biomarkers (total immunoglobulin E, blood eosinophil count, fractional exhaled nitric oxide) and the presence of coexisting conditions (allergic rhinitis, nasal polyposis, atopic dermatitis, chronic urticaria). Although this could certainly help to narrow the list of potential agents, it is not hard to imagine a scenario in which a provider may still be faced with more than 1 appropriate agent to initiate, especially with so much overlap

between agents in regard to the target population and outcome data. Although echoing the importance of precision medicine and shared decision making in the selection process, Wang and Wechsler⁴ take clinical guidance 1 step further by providing actual case examples. These cases allow clinicians to think through patient-specific comorbidities and various biomarker profiles to select the optimal biologic.

Despite the utilization of both biologic and clinical considerations, what remains lacking is actual head-to-head comparison data for the available biologic agents. Confusion exists specifically for patients who may seem to qualify equally for more than 1 agent. For example, what about our patients with allergic asthma, elevated immunoglobulin E levels, and high eosinophil counts? There is no good guidance for the selection of 1 agent over the other, nor does an algorithm exist that could guide the provider. To address this conundrum, Pitre et al,⁵ in this month's issue of *Annals*, present a systematic review and network meta-analysis comparing biologics for severe uncontrolled asthma. This improves on previous reviews by including the late trial data and taking into consideration how recommendations may vary by eosinophil level. Included in this review are adult patients with moderate, moderate-to-severe, or severe asthma. Using data from 63 different trials, the authors show that in patients with severe eosinophilic asthma, all available agents are effective at reducing exacerbations. This by itself is no surprise and is consistent with previous data. However, only 2 of these agents, Dupilumab and Tezepelumab, appeared to improve lung function. For patients with low eosinophil counts, however, biologics appeared to not prevent exacerbations or improve lung function. This is contrary to what one might expect for Tezepelumab, which has been approved for patients regardless of biomarkers. Thus, on the basis of this study, biologics appear to only be efficacious in those with elevated eosinophil counts. In addition, this review did not support the use of Omalizumab because it was less effective than the other agents. What does this mean for those of us in the trenches, trying to achieve control for our patients who are more difficult to treat? For starters eosinophil counts do matter—and they matter for all biologics. Perhaps low eosinophil counts should give us pause or at minimum lead us to proceed with more caution when deciding to prescribe a biologic.

Although the practical conundrum still exists, I am grateful for the more rational attempts that have been made to provide much-needed guidance to clinicians. Whether it be through algorithms, charts, or systematic reviews, the discussion is ongoing to provide clinicians with the necessary tools to provide optimal patient care. At the end of the day, and with the emergence of new agents and shifting recommendations, what has not changed is the role of shared decision making. Now, more than ever, the conversations we have with our patients are crucial for deciding the next steps. The conundrum remains, but perhaps the hurdle seems a bit easier to overcome in 2023.

Disclosures: The author has no conflicts of interest to report.

Funding: The author has no funding sources to report.

<https://doi.org/10.1016/j.anai.2023.01.030>

1081-1206/© 2023 American College of Allergy, Asthma & Immunology. Published by Elsevier Inc. All rights reserved.

Kasey Strothman, MD
Division of Allergy & Immunology
Department of Pediatrics
Nationwide Children's Hospital
The Ohio State University College of Medicine
Columbus, Ohio
Kasey.Strothman@Nationwidechildrens.org

Program Coordinating Committee (NAEPCC), Cloutier MM, Baptist AP, Blake KV, Brooks EG, Bryant-Stephens T, et al. Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. *J Allergy Clin Immunol*. 2020;146(6):1217–1270.

2. Zoumot Z, Al Busaidi N, Tashkandi W, Aljohaney AA, Isse S, Vidyasagar K, et al. Tezepelumab for patients with severe uncontrolled asthma: a systematic review and meta-analysis. *J Asthma Allergy*. 2022;15:1665–1679.
3. Brusselle GG, Koppelman GH. Biologic therapies for severe asthma. *N Engl J Med*. 2022;386(2):157–171.
4. Wang E, Wechsler ME. A rational approach to compare and select biologic therapeutics in asthma. *Ann Allergy Asthma Immunol*. 2022;128(4):379–389.
5. Pitre T, Jassal T, Angjeli A, Jarabana V, Nannapaneni S, Umair A, et al. A comparison of the effectiveness of biologic therapies for asthma: a systematic review and network meta-analysis. *Ann Allergy Asthma Immunol*. 2023;130(5):595–606.

References

1. Expert Panel Working Group of the National Heart, Lung, and Blood Institute (NHLBI) administered and coordinated National Asthma Education and Prevention