

^cDepartment of Medicine, Division of Clinical Immunology and Allergy, Centre Hospitalier de l'Université de Montréal (CHUM), Montreal, QC, Canada

^dDepartment of Medicine, Division of Allergy and Clinical Immunology, McGill University Health Centre (MUHC), McGill University, Montreal, QC, Canada

^eDepartment of Internal Medicine, Security Forces Hospital Program, Riyadh, Saudi Arabia

^fThe Research Institute of the McGill University Health Centre, McGill University, Montreal, QC, Canada

^gDepartment of Infectious Diseases, Centre for Antibiotic Allergy and Research, Austin Health, Heidelberg, VIC, Australia

^hDepartment of Pediatrics, Division of Allergy and Clinical Immunology, Centre Hospitalier Universitaire de Sherbrooke (CHUS), Sherbrooke, QC, Canada

ⁱDepartment of Medicine, Division of Allergy and Clinical Immunology, Centre intégré de santé et services sociaux (CISSS) de Laval, Laval, QC, Canada.

No funding was received for this work.

Conflicts of interest: M. Blaquière has been on the advisory board of ALK and has received honorarium from Novartis, Medexus, ALK, and Stallergenes. M. Fein has been on advisory boards and/or received consulting fees from ALK, Stallergenes, Medexus, Novartis, and Bausch Health. M.-N. Primeau has been on speakers' bureau and/or advisory boards for ALK, Bausch Health, CSL Behring Canada, Mead Johnson, Medexus, Mylan, Novartis, Nutricia, Pediapharm, and Pfizer. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication April 3, 2022; accepted for publication April 4, 2022.

Corresponding author: Matthieu Picard, MD, FRCPC, Division of Clinical Immunology and Allergy, Hôpital Maisonneuve-Rosemont, 5415 boulevard de l'Assomption, Montréal, QC H1T 2M4, Canada. E-mail: matthieu.picard@umontreal.ca.

REFERENCES

- Mathes S, Eberlein B, Darsow U, Faihs V, Vitus M, Bent M, et al. Variability of eliciting thresholds in PEG allergy limits prediction of tolerance to PEG-containing mRNA COVID vaccines. *J Allergy Clin Immunol Pract* 2022;10:1931-3.
- Picard M, Drolet JP, Masse MS, Filion CA, AL-Muhizi F, Fein M, et al. Safety of COVID-19 vaccination in patients with polyethylene glycol allergy: a case series. *J Allergy Clin Immunol Pract* 2022;10:620-5.e1.
- Hennighausen I, Pickert J, Mühlenbein S, Möbs C, Pfützner W. Successful Covid-19 vaccination of a patient with hypersensitivity against polyethylene glycol and polysorbate. *J Investig Allergol Clin Immunol*. Published online March 1, 2022. <https://doi.org/10.18176/jiaci.0801>.
- Kelso JM. The adverse reactions to vaccines practice parameter 10 years on-what have we learned? *Ann Allergy Asthma Immunol*. Published online January 31, 2022. <https://doi.org/10.1016/j.anai.2022.01.026>.
- Macy E, Pandya S, Sheikh J, Burnette A, Shi JM, Chung J, et al. Population-based incidence, severity, and risk factors associated with treated acute-onset COVID-19 mRNA vaccination-associated hypersensitivity reactions. *J Allergy Clin Immunol Pract* 2022;10:827-36.
- Chu DK, Abrams EM, Golden DBK, Blumenthal KG, Wolfson AR, Stone CA Jr, et al. Risk of second allergic reaction to SARS-CoV-2 vaccines: a systematic review and meta-analysis. *JAMA Intern Med* 2022;182:376-85.
- Brockow K, Mathes S, Fischer J, Volc S, Darsow U, Eberlein B, et al. Experience with polyethylene glycol allergy-guided risk management for COVID-19 vaccine anaphylaxis. *Allergy*. Published online November 22, 2021. <https://doi.org/10.1111/all.15183>.

<https://doi.org/10.1016/j.jaip.2022.04.005>

Anti-IL5/IL5R switching between biologics in patients with severe eosinophilic asthma



To the Editor:

We read with great interest the original article titled as “Long-term therapy response to anti-IL-5 biologics in severe asthma—a real-life evaluation” by Eger et al.¹ We would like to share our opinions on this study.

There is a great need for such studies, and it is a study that will fill the gap in the literature. We would like to thank Eger et al for their contribution to the literature with such a valuable study. Some points mentioned in the article drew our attention. First of all, we think that the criteria for the definition of super-responder are debatable. For

example, when a patient with oral corticosteroid (OCS)-dependent asthma has the following criteria, this patient is not considered a super-responder according to the authors' definition:

- The patient's baseline forced expiratory volume in 1 second (FEV₁) is low before biological therapy (eg, FEV₁: 68%); although there is improvement in FEV₁ (eg, FEV₁: 78%) after biological therapy, the FEV₁ may not rise above 80%, but the need for OCS may disappear completely and Asthma Control Questionnaire (ACQ) <1.5.

Or

- In a patient who initially received 20 mg maintenance prednisolone treatment and had an FEV₁ >80% and ACQ <1.5 in the second year of biological treatment, the maintenance prednisolone dose may be reduced to 4 mg but may not be completely discontinued. On the other hand, according to the authors' definition of super-responder, for example, a patient who was already on low-dose OCS (eg, 4 mg prednisolone) treatment at the beginning and whose prednisolone was discontinued at the end of 2 years after the addition of biological therapy and fulfilling the other super-responder criteria could be considered a super-responder. Considering all these, we think that the super-responder criteria should be more standardized and suitable for daily practice. Another point that draws our attention is that after 2 years of treatment in the super-responder group, it was stated in Table I that comorbidities of chronic rhinosinusitis, nasal polyposis (NP), chronic otitis, and allergic rhinoconjunctivitis were under control with these biologics; however, the control criteria were not defined in this article.

An important finding presented by the authors is that 31% of those with super-responders were shown to be super-responders when they switched from the first biological to another biological. How many of these transitions were partial responder or nonresponder before switch? If it is nonresponder with the first biological but becomes super-responder after switching to the second biological, this will be significant in emphasizing the importance of the transition between anti-IL5/IL5R biologics.

Another important result in this study is the demonstration that patients in the super-responder group were associated with the absence of NPs, although statistically insignificant. However, some studies have shown that the presence of comorbid NP predicts that severe asthma may respond well to anti-IL5/IL5R monoclonal antibodies.²⁻⁵ In addition, in the Global Initiative for Asthma report, NP is included in the criteria for good response to anti-IL5/IL5R in patients with eosinophilic severe asthma.⁶

Finally, the authors also stated that anti-IL5/IL5R was discontinued in 3 patients because of adverse effects. However, mentioning the adverse effects leading to discontinuation would have been very helpful to the readers.

İnsu Yılmaz, MD
Gülden Paçacı Çetin, MD
Bahar Arslan, MD

Division of Immunology and Allergy, Department of Chest Diseases, Erciyes University School of Medicine, Kayseri, Turkey.
No funding was received for this work.

Conflicts of interest: The authors declare that they have no relevant conflicts of interest. Received for publication March 18, 2022; accepted for publication April 12, 2022. Corresponding author: İnsu Yılmaz, MD, Division of Immunology and Allergy, Department of Chest Diseases, Erciyes University School of Medicine, Kayseri 38039, Turkey. E-mail: insu2004@yahoo.com.

REFERENCES

1. Eger K, Kroes JA, Ten Brinke A, Bel EH. Long-term therapy response to anti-IL-5 biologics in severe asthma—a real-life evaluation. *J Allergy Clin Immunol Pract* 2021;9:1194-200.
2. Wenzel SE. Severe adult asthma: integrating clinical features, biology, and therapeutics to improve outcomes. *Am J Respir Crit Care Med* 2021;203:809-21.
3. Bagnasco D, Milanese M, Rolla G, Lombardi C, Bucca C, Heffler E, et al. The North-Western Italian experience with anti IL-5 therapy and comparison with regulatory trials. *World Allergy Organ J* 2018;11:34.
4. Chapman KR, Albers FC, Chipps B, Munoz X, Devouassoux G, Bergna M, et al. The clinical benefit of mepolizumab replacing omalizumab in uncontrolled severe eosinophilic asthma. *Allergy* 2019;74:1716-26.
5. Bleecker ER, Wechsler ME, FitzGerald JM, Menzies-Gow A, Wu Y, Hirsch I, et al. Baseline patient factors impact on the clinical efficacy of benralizumab for severe asthma. *Eur Respir J* 2018;52:1800936.
6. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. <https://ginasthma.org/gina-reports/> 2021. Accessed March 18, 2022.

<https://doi.org/10.1016/j.jaip.2022.04.017>

Reply to “Anti-IL5/IL5R switching between biologics in patients with severe eosinophilic asthma”



To the Editor:

Yılmaz et al¹ are right that there is no consensus on the criteria for defining super-responders to biologics in asthma. We chose a super-response definition excluding any residual disease manifestation such as markers of inflammation (eg, chronic oral corticosteroid use and exacerbations), airflow limitation, or asthma symptoms, because this determines disease burden and prognosis. Our response definition therefore reflects complete remission under treatment, which we believe should be the ultimate treatment goal in all patients with severe asthma.² However, the examples the authors described aptly illustrate the shortcomings of the definition we used in our study.³ We fully agree that response criteria should be standardized once sufficient clinical experience with the asthma biologics has been obtained.

With regard to control criteria of sinonasal comorbidities such as nasal polyps and chronic rhinosinusitis, we relied on the findings of nasal endoscopy in combination with the subjective absence of symptoms. We should have stated this more clearly in the article.

The comment by Yılmaz et al about an improved response after switching from one anti-IL-5 to another anti-IL-5 biological agent is important. Indeed, many partial responders (but none of the nonresponders) showed further improvement after switching to another anti-IL-5 biologic, and 4 patients subsequently became super-responders. We have written a separate article on outcomes after switching between asthma biologics that will be published shortly in this journal.⁴

Yılmaz et al rightly state that nasal polyposis is a predictor of a good response to anti-IL-5 with regard to asthma symptoms. However, regarding sinonasal manifestations, anti-IL-5 therapy failed to completely eliminate nasal polyps in our patients, so we could not label them as super-responders according to our definition.

Finally, regarding the adverse effects of anti-IL-5 biologics, 3 of our patients discontinued therapy because of migraine, severe dermatitis, and colon cancer, respectively.

Katrien Eger, MD^a

Johannes A. Kroes, MSc^b

Anneke ten Brinke, MD, PhD^c

Elisabeth H. Bel, MD, PhD^a

^aDepartment of Respiratory Medicine, Amsterdam University Medical Center, University of Amsterdam, Amsterdam, the Netherlands

^bDepartment of Clinical Pharmacy and Pharmacology, Medical Center Leeuwarden, Leeuwarden, the Netherlands

^cDepartment of Respiratory Medicine, Medical Center Leeuwarden, Leeuwarden, the Netherlands.

No funding was received for this work.

Conflicts of interest: A. ten Brinke reports institutional grants from GSK, TEVA, and AstraZeneca outside the submitted work and participated in advisory boards for AstraZeneca, TEVA, and Sanofi Regeneron. J. A. Kroes reports a grant from AstraZeneca. E. H. Bel reports institutional grants from GSK and TEVA; consulting fees from GSK, AstraZeneca, Sanofi, and Chiesi; honorarium for chairing a session from TEVA; and participation on an Advisory Board for AstraZeneca. K. Eger declares that she has no relevant conflicts of interest.

Received for publication April 11, 2022; accepted for publication April 12, 2022.

Corresponding author: Katrien Eger, MD, Department of Respiratory Medicine, Amsterdam UMC, University of Amsterdam, F5-260, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands. E-mail: k.a.eger@amsterdamumc.nl.

REFERENCES

1. Yılmaz I, Çetin G, Arslan B. Anti-IL5/IL5R switching between biologics in patients with severe eosinophilic asthma. *J Allergy Clin Immunol Pract* 2022;10:1935-6.
2. Menzies-Gow A, Bafadhel M, Busse WW, Casale TB, Kocks JWH, Pavord ID, et al. An expert consensus framework for asthma remission as a treatment goal. *J Allergy Clin Immunol* 2020;145:757-65.
3. Eger K, Kroes JA, Ten Brinke A, Bel EH. Long-term therapy response to anti-IL-5 biologics in severe asthma—a real-life evaluation. *J Allergy Clin Immunol Pract* 2021;9:1194-200.
4. Hashimoto S, Kroes JA, Eger K, Mau-Asam P, Hofstee HB, Bendien SA, et al. Real-world effectiveness of reslizumab in patients with severe eosinophilic asthma—“first initiators” and “switchers.” *J Allergy Clin Immunol Pract*. Published online April 26, 2022. <https://doi.org/10.1016/j.jaip.2022.04.014>.

<https://doi.org/10.1016/j.jaip.2022.04.018>

House dust mite liquid SLIT effective in atopic dermatitis even with suboptimal dosing



To the Editor:

We have read the article by Langer et al¹ on sublingual immunotherapy (SLIT) with a house dust mite (HDM) extract for atopic dermatitis (AD) with great interest and would like to congratulate our Brazilian colleagues for having been able to conduct a double-blind, placebo-controlled trial under the not always favorable local circumstances and with budget limitations. The study is of even greater importance because it managed to show statistically significant differences in favor of the active treatment group, even with a suboptimal SLIT administration schedule, as the investigators comment.

By taking a closer look at how the study was conducted, the patients characterized, and the liquid SLIT administered, we would like to make some comments, because we consider that the SLIT schedule could be improved and would like other readers to realize how an optimal liquid SLIT schedule with HDM allergen could look like.