OPEN ACCESS

Reconsidering biologic treatment recommendations for CRSwNP without asthma in EUFOREA guidelines

John Oppenheimer[1], G. Walter Canonica[2,3], Pascal Chanez[4], Juan Maza-Solano[5,6], Claire Tacon[7], Konstantina Kallinikou[8], Peter Howarth[7], Matteo Bonini[9,10], Ibon Eguiluz-Gracia[11], Arnaud Bourdin[12]

[1] Department of Internal Medicine, University of Medicine and Dentistry of New Jersey/Rutgers New Jersey Medical School, Newark, NJ, USA

[2] Personalized Medicine, Asthma and Allergy, Humanitas Clinical and Research Center IRCCS, Milan, Italy

[3] Department of Biomedical Sciences, Humanitas University, Milan, Italy

[4] Department of Respiratory Diseases, Aix-Marseille University, Marseille, France

[5] Rhinology and Skull Base Unit, Department of Otolaryngology, University Hospital Virgen del Rocío, Seville, Spain

[6] Department of Surgery, University of Seville, Seville, Spain

[7] Global Medical Affairs, GSK, London, UK

[8] Respiratory Biologics, GSK, Athens, Greece

[9] Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

[10] National Heart and Lung Institute (NHLI), Imperial College London, London, UK

[11] Allergy Unit. Hospital Regional Universitario de Malaga and IBIMA-Plataforma BIONAND. RICROS Inflammatory Diseases. Malaga, Spain

[12] Department of Respiratory Diseases, PhyMedExp, University of Montpellier, INSERM CNRS, Montpellier, France

Rhinology 64: 3, 430 - 432, 2026

https://doi.org/10.4193/Rhin25.359

Received for publication:

July 2, 2025

Accepted: February 24, 2026

Associate Editor:

Sietze Reitsma

Dear Editor:

The recently published EUFOREA pocket guide "Biologics in Upper and Lower Airway Diseases" summarises recommendations on the use of biologics in chronic rhinosinusitis with nasal polyps (CRSwNP) and asthma [(1)] and offers advice on biologic choice for practicing clinicians. The creation of this pocket guide, in the absence of any head-to-head studies at that time, drew on expert opinions and published indirect treatment comparison (ITC) approaches [(2,3)]. It makes a single recommendation for a preferred biologic, in patients affected by CRSwNP, without concomitant asthma (apart from specific cases such as pregnancy), whilst offering different options in asthma endotypes and phenotypes. We wish to draw the attention of the readership to some additional considerations relating to biologic choice for these diseases and how they are classified.

It is well recognised that network analysis, such as ITCs, inherently warrant some caution in interpretation [(4)], due to study differences in heterogeneity of patient populations and approaches to data handling. This has relevance to conclusions drawn regarding biologic use in CRSwNP. Mepolizumab in its registration randomised controlled trial (RCT) in CRSwNP (SYNAPSE study, NCT03085797), met all its primary and secondary endpoints, significantly reducing nasal polyp size and nasal blockage score, whilst improving quality of life (Sino-Nasal Outcome Test-22 score) and other patient-reported outcomes, such as sense of smell [(5)]. The SYNAPSE study is, however, recognised to focus on a patient population that has more severe, refractory disease than that in the dupilumab registration trials (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52) [(6)]. As such, the dupilumab versus mepolizumab ITC [(2)] or the extended network meta-analysis comparison [(3)] are not comparing like-for-like and these statistical approaches should not be considered reliable grounds for recommending one treatment over another. All current licensed biologic therapies demonstrate efficacy in clinical practice [(7)]; there remains a need to better understand outcome heterogeneity and predictive response determinants which will not be forthcoming if use is restricted. Additional comparator studies, such as the EVEREST trial of dupilumab versus omalizumab [(8)], are required.

Mepolizumab targets interleukin (IL)-5, a pivotal type 2 (T2) cytokine influencing not only eosinophils but also epithelial cells, plasma cells, fibroblasts and mast cells [(9)]. Classifying dupilumab and tezepelumab as 'anti-T2' while labelling mepolizumab as merely 'anti-eosinophil' oversimplifies established disease biology and misrepresents the interconnected role and co-existent presence of T2 cytokines. These are often co-elevated in disease, with serum IL-5 levels correlating with elevated levels of IL-4, IL-13 and thymic stromal lymphopoietin [(10)]. The central role of IL-5 in the exaggerated tissue damage/repair response in chronic T2

disease is also evidenced by the reversal of airway remodelling in asthma with mepolizumab [11]. There is also evidence from the reverse perspective, with mepolizumab having a persistent benefit in improving patient outcomes despite therapy discontinuation in the RCT follow-up analysis [12], consistent with it having modified a key underlying pathological process in CRSwNP. As such studies are needed to understand if treatment is optimally used to improve severe disease once established or potentially applicable as adjunctive therapy to prevent disease recurrence after surgery or to stop progression in those with early post-surgical recurrence.

In summary, restricting the advice to a single biologic, in the absence of appropriately conducted head-to-head studies or long-term real-world outcomes, may limit patient options, undermine the ability to personalise care and constrain advances in treatment understanding. Although the EUFOREA pocket guide provides a valuable resource for practicing clinicians and we understand that regular updates are expected to reflect the fast-evolving therapeutic landscape, we feel that it is premature at present to restrict the recommendations on biologic choice in CRSwNP.

Acknowledgments

Editorial support (in the form of collating and incorporating authors' comments for each draft, grammatical editing and referencing) was provided by Nathan Ley, PhD, at Fishawack Indicia Ltd, UK, part of Avalere Health, and was funded by GSK.

Abbreviations

CRSwNP, chronic rhinosinusitis with nasal polyps; IL, interleukin; ITC, indirect treatment comparison; RCT, randomised controlled trial; T2, type 2; TSLP, thymic stromal lymphopoietin.

Authorship contribution

All authors contributed to data interpretation, reviewed and revised the manuscript critically for important intellectual content, agreed to submit to Rhinology, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Conflict of interest

JO reports receiving consulting fees from Aquestive Therapeutics, ARS Pharmaceuticals and GSK; speaking honoraria from Sanofi-Regeneron; and advisory board honoraria from AstraZeneca, Amgen, Sanofi-Regeneron and GSK outside the submitted work. WC reports having received in the last 3 years research grants as well as lecture or advisory board fees from Alk-Abello, Allergy Therapeutics, Anallergo, Hal Allergy and Stallergenes Greer. PC has received consultancy fees from ALK, Almirall, AstraZeneca, Boehringer Ingelheim, Boston Scientific, Centocor, Chiesi, GSK, Johnson & Johnson, MSD, Novartis, Sanofi, SNCF and Teva Pharmaceuticals, has received industry-sponsored grants from ALK, AstraZeneca, Boehringer Ingelheim, Boston Scientific, Centocor, Chiesi, GSK, Novartis, Roche and Teva Pharmaceuticals, and is the president of the scientific committee for Fondation du Souffle

JM-S has received consultancy fees from AstraZeneca, GSK and Sanofi. CT, KK and PH are employed by GSK and hold financial equities in GSK. MB reports non-financial support for the conduct of the present work from GSK; has received research grants, consultancy and speaker fees from AstraZeneca, Chiesi, GSK, Lallemand, Lusofarmaco, Menarini, Niox, Omron and Sanofi. IEG has received honoraria for lectures and advisory activities from Chiesi, Gebro Pharma, Novartis, GSK, Sanofi, AstraZeneca, Abbvie, HAL Allergy, ALK, Diater, Leti Pharma, Allergopharma, Inmunotek and Viatris. AB reports non-financial support during the conduct of the study from GSK, consultancy fees from Acceleron Pharma, Actelion, Galapagos, MSD, Nuvaira, Pulmonx, United Therapeutics and Vertex Pharmaceuticals, grants and personal fees from Boehringer Ingelheim, and personal fees from AstraZeneca, Chiesi, GSK, Regeneron Pharmaceuticals and Sanofi

Funding

This article was funded by GSK. The sponsor was involved in reviewing the article. The sponsor did not place any restrictions on access to data or statements made in the manuscript. All authors had final responsibility for the decision to submit for publication.

References

1. Fokkens WJ, Backer V, Lund VJ, et al. Pocket guide: biologics in upper and lower airways in adults. Rhinology. 2025; 63(2): 242-244.
2. Hopkins C, Han JK, Fokkens W, et al. Dupilumab versus mepolizumab for chronic rhinosinusitis with nasal polyposis: an indirect treatment comparison. J Allergy Clin Immunol Pract. 2024; 12(12): 3393-3401.e15.
3. Oykhman P, Paramo FA, Bousquet J, Kennedy DW, Brignardello-Petersen R, Chu DK. Comparative efficacy and safety of monoclonal antibodies and aspirin desensitization for chronic rhinosinusitis with nasal polyposis: a systematic review and network meta-analysis. J Allergy Clin Immunol. 2022; 149(4): 1286-1295.
4. Guo JD, Gehchan A, Hartzema A. Selection of indirect treatment comparisons for health technology assessments: a practical guide for health economics and outcomes research scientists and clinicians. BMJ Open. 2025; 15(3):e091961.
5. Han JK, Bachert C, Fokkens W, et al. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Respir Med. 2021; 9(10):1141-1153.
6. Bachert C, Han JK, Desrosiers M, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials. Lancet. 2019;394(10209):1638-1650.

7. Cai S, Xu S, Zhao Y, Zhang L. Efficacy and safety of biologics for chronic rhinosinusitis with nasal polyps: a meta-analysis of real-world evidence. Allergy. 2025;80(5):1256-1270.
8. De Corso E, Canonica GW, Heffler E, et al. Dupilumab versus omalizumab in patients with chronic rhinosinusitis with nasal polyps and coexisting asthma (EVEREST): a multicentre, randomised, double-blind, head-to-head phase 4 trial. Lancet Respir Med 2025;13(12):1067-1077.
9. Buchheit KM, Shaw D, Chupp G, et al. Interleukin-5 as a pleiotropic cytokine orchestrating airway type 2 inflammation: effects on and beyond eosinophils. Allergy. 2024;79(10):2662-2679.
10. Bingham K, Zahrani YA, Stewart I, et al. Defining the blood cytokine profile in asthma to understand asthma heterogeneity. Immun Inflamm Dis. 2025;13(3):e70116.
11. Domvri K, Tsiouprou I, Bakakos P, et al. Effect of mepolizumab in airway remodelling in patients with late-onset severe asthma with an eosinophilic phenotype. J Allergy Clin Immunol. 2025;155(2):425-435.
12. Desrosiers M, Diamant Z, Castelnuovo P, et al. Sustained efficacy of mepolizumab in patients with severe chronic rhinosinusitis with nasal polyps: SYNAPSE 24-week treatment-free follow-up. Int Forum Allergy Rhinol. 2024;14(1):18-31.

John Oppenheimer
Department of Internal Medicine
University of Medicine and Dentistry of New Jersey
Rutgers New Jersey Medical School
Newark, NJ 07103
USA

E-mail: nallopp22@gmail.com