Clinical management of dupilumab-induced blood eosinophilia in CRSwNP: a practical algorithm*

Eugenio De Corso[1], Marco Caminati[2], Peter W. Hellings[3], Claudio Montuori[4], Sietze Reitsma[5], Vibeke Backer[6], Wytske J. Fokkens[5]

[1] Otolaryngology, Head and Neck Surgery, Rhinology, A. Gemelli Universitary Hospital Foundation, IRCSS, Rome, Italy
[2] Allergy Unit and Asthma Center, Verona Integrated University Hospital and Department of Medicine, University of Verona, Italy
[3] Department of Otorhinolaryngology, Head and Neck Surgery, UZ Leuven, Leuven, Belgium
[4] Department of Head-Neck and Sensory Organs, Catholic University of Sacred Heart, Rome, Italy
[5] Department of Otorhinolaryngology and Head/Neck surgery, Amsterdam University Medical Centre, University of Amsterdam, Amsterdam, The Netherlands
[6] Department of Otorhinolaryngology, Head & Neck surgery, and Audiology, Rigshospitalet, Copenhagen University, Copenhagen, Denmark

Rhinology 63: 6, 768 - 770, 2025
https://doi.org/10.4193/Rhin25.266

***Received for publication:**
May 21, 2025
Accepted: August 21, 2025

Associate Editor:
Ahmad Sedaghat

Dupilumab is widely recognised as a highly effective therapy for severe chronic rhinosinusitis with nasal polyps (CRSwNP). A rise in blood eosinophil count (BEC) might occur during treatment across all approved indications. In CRSwNP, dupilumab-induced blood eosinophilia (DIBE) is typically of early onset, transient, and asymptomatic without impairing the drug's efficacy. A review including data from 11 clinical trials on all approved dupilumab indications reported eosinophilia-related clinical manifestations in only 7 of 4,666 patients receiving dupilumab[(1)]. Real-world studies confirm DIBE is largely benign, with only rare AEs requiring dupilumab discontinuation [(2,3)] such as eosinophilic pneumonia, especially in eosinophilic granulomatosis with polyangiitis (EGPA) patients [(2)]. Such exceedingly rare events were mainly described within the first months of treatment [(4)], however late onset DIBE (after 6 months) has also been detected, especially in patients dependent on systemic corticosteroids [(5)].

DIBE is hypothesized to result primarily from interleukin (IL)-4/IL-13 pathway blockade, disrupting eosinophil trafficking into tissues in patients with a likely IL-5 induced production and leading to transient blood accumulation [(2)]. Accordingly, baseline BEC was found significantly higher for patients developing BEC>1500 and >3000 cells/mm^3 [(6)].

No reliable predictors or biomarkers have been identified to determine which patients may experience clinical consequences. Indeed, there is no consistent correlation between DIBE values prior to initiation, thus it happens more frequently in patients with BEC>1500 cells/mm^3 prior to drug initiation and manifestations of eosinophil-driven organ damage; patients with BEC exceeding 3000 cells/mm^3 may remain entirely asymptomatic [(7)], whereas AEs have been reported even in patients without DIBE [(7)].

To mitigate DIBE potential safety risks, the EPOS/EUFOREA 2023 guidelines recommend routinely evaluating eosinophilia-related symptoms, intensifying BEC monitoring when BEC>1500 cells/mm^3 and considering therapeutic adjustments when BEC>3000 cells/mm^3 [(8)]. Practical algorithms have also been published to assist clinicians in managing DIBE [(2,9)] suggesting monitoring primarily based on BEC threshold values and additional investigations or interventions according to clinical manifestations. These flowcharts represent valuable tools to support the decision-making process, but they don't account for DIBE temporal dynamics and the nature of AEs, which may occur independently from DIBE itself [(2)].

Here, we propose a novel algorithm for DIBE monitoring and management, integrating established BEC thresholds with the timing of eosinophilia, as well as the occurrence and severity of AEs, which should also guide clinical actions (Figure 1). AE severity was classified based on the "Common Terminology Criteria for Adverse Events" (CTCAE).

Once dupilumab is initiated, close monitoring (1, 3 and 6 months) is recommended to detect early BEC peaks; late onset DIBE is rare, and long-term measurements are advised only in patients that highly needed systemic steroids.

In cases of mild-to-moderate AEs, priority should be given to their diagnosis and management; dupilumab may be continued, and eosinophilia can be monitored at intervals considered appropriate by the clinician. Conversely, the emergence of severe AEs (SAEs) necessitates dupilumab discontinuation regardless of BEC levels. Dupilumab should also be stopped if patients have BEC≥5000 cells/mm^3, at least until BEC values decrease to <5000 cells/mm^3.

We believe that multidisciplinary team (MDT) evaluation is essential to guide clinical decisions in the presence of SAEs, BEC ≥3000 cells/mm^3 irrespective of clinical symptoms, and persistent and/or late high BEC values with mild-to-moderate AEs

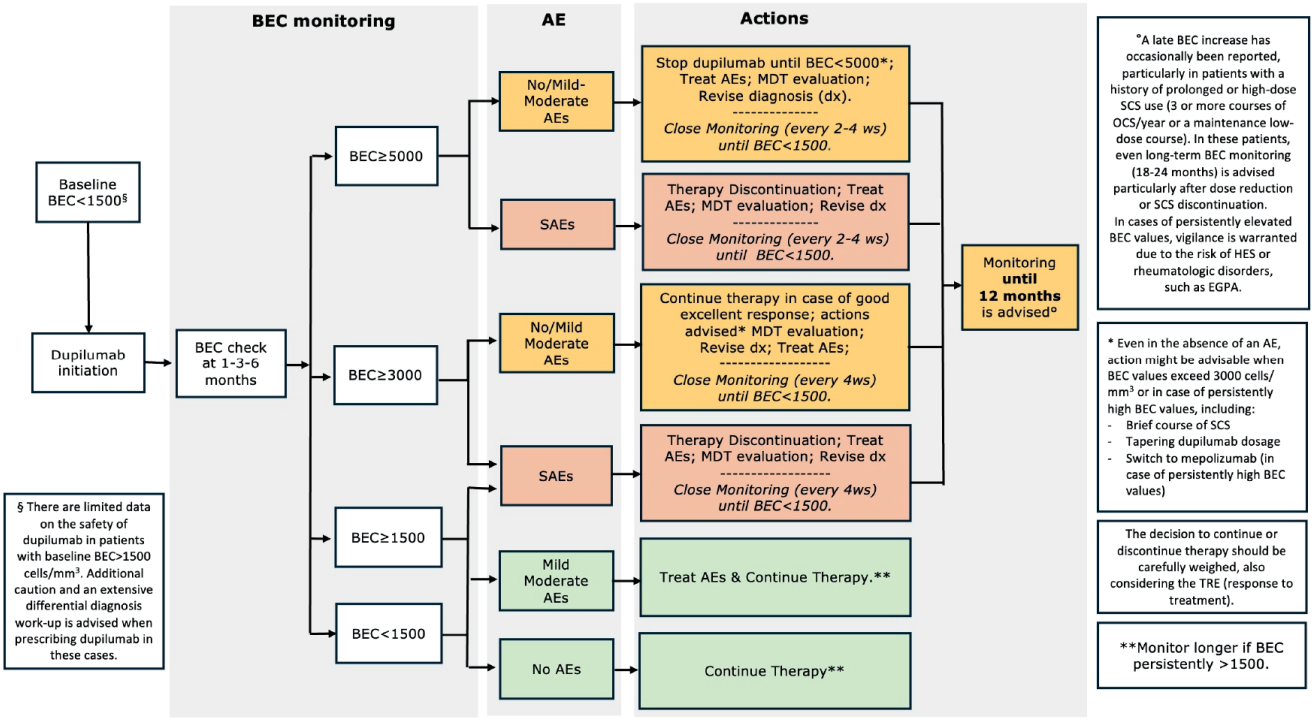

Figure 1. Clinical algorithm for monitoring and management of DIBE. AEs have been defined as: (1) mild: patient is asymptomatic or has mild symptoms, clinical or diagnostic observations only, intervention not indicated; (2) moderate: AEs may limit age-appropriate instrumental daily life activities, with minimal, local or non-invasive intervention indicated; (3) severe (medically significant but not immediately life-threatening): AEs may be disabling and limiting self-care daily life activities, with hospitalization or prolongation of hospitalization indicated. The proposed algorithm is intended for no-EGPA patients. EGPA patients should be managed in a MDT context guided by specialists of vasculitis. This algorithm should be applied to all patients who develop DIBE, irrespective of the timing of its onset.
Abbreviations: AE: adverse event; BEC: blood eosinophil count; dx: diagnosis; EGPA: eosinophilic granulomatosis with poliangitis; HES: hypereosinophilic syndrome; m(s): month(s); MDT: multidisciplinary team; SAE: severe adverse event; SCS: systemic corticosteroids; ws: weeks.

(Figure 1). Indeed, BEC fluctuations during any type of biologics may be indicative of coexisting autoimmune conditions, such as EGPA. For this reason, otolaryngologists should not only monitor eosinophil levels but also remain vigilant for clinical red flags [9] suggestive of this disease.

In the context of dupilumab therapy, increases in BEC are likely to be related to the drug's mechanism of action. Therefore, to discern when multidisciplinary evaluation and intervention are genuinely warranted, a structured algorithm is essential to guide clinical decision-making. Our algorithm refines previously proposed frameworks for DIBE management by integrating eosinophilia temporal dynamics and the severity of AEs. This algorithm offers a pragmatic tool that ensures patient safety and avoids unnecessary dupilumab discontinuation, especially in patients with sustained disease control. Further studies are required to elucidate the variability and clinical significance of DIBE temporal patterns and the factors that may predict DIBE clinical manifestations.

List of abbreviations

AE: adverse event; BEC: blood eosinophil count; CRSwNP: chronic rhinosinusitis with nasal polyps; DIBE: dupilumab-induced blood eosinophilia; EGPA: eosinophilic granulomatosis with polyangiitis; HES: Hypereosinophilic syndrome; IL: interleukin; MDT: multidisciplinary team; SAE: severe adverse event.

Authorship contribution

EDC: Conception and design. EDC, CM: Writing of manuscript. MC, PWH, SR, VB, WJF: Revision and editing of the manuscript. All authors approved final version of the manuscript.

Conflict of interest

EDC received speaker's honorarium and participated to advisory board for Novartis, Astrazeneca, Sanofi, Regeneron, GSK. MC has received advisory board and speaker fees from GSK, Chiesi, AstraZeneca, Sanofi and grant funding to his institution from AZ, GSK and Sanofi. CM has no conflict of interest. SR: Acted as consultant for and have received research funding from GSK, Sanofi, and Novartis. PWH: Consultant and recipient of lecture fees and/

or research grants from Sanofi, Regeneron, Novartis, GSK, ALK and Viatris. WJF: received grants for research in Rhinology from: ALK, AllergyTherapeutics, Chordate, Novartis, EU, GSK, MYLAN, Sanofi-Aventis, and Zon-MW. Prof. dr. Wytske Fokkens received consultation and/or speaker fees from Bioinspire, GSK, Novartis and Sanofi-Aventis/ Regeneron. VB: worked as advisor, supervisor, investigator of pharmaceutical studies, unrestricted grants, and others with: AstraZeneca, GSK, MSD & Shering Plough, ALK-Abello; Chiesi, Novartis, Pharmaxis, Pfizer, Boehringer Ingelheim, Aerocrine, Teva, Sanofi, Birk NPC.

Funding

None.

References

1. Wechsler ME, Klion AD, Paggiaro P, et al. Effect of dupilumab on blood eosinophil counts in patients with asthma, chronic rhinosinusitis with nasal polyps, atopic dermatitis, or eosinophilic esophagitis. J Allergy Clin Immunol Pract. 2022;10(10):2695–709.
2. Caminati M, Olivieri B, Dama A, et al. Dupilumab-induced hypereosinophilia: review of the literature and algorithm proposal for clinical management. Expert Rev Respir Med. 2022;16(7):713–21.
3. Li SH, Nehme KF, Moshkovich A, et al. Eosinophilia and adverse effects of dupilumab for respiratory indications: a real-world setting. J Allergy Clin Immunol Pract. 2025;13(1):121–31.
4. Lazzeroni M, Kemp P, Fokkens WJ, Reitsma S. Eosinophilic complications during dupilumab therapy for type 2 diseases: a systematic review. Rhinology. 2025;63(4):386-396.
5. De Corso E, Montuori C, Baroni S, et al. Temporal trends of blood eosinophilia in severe uncontrolled CRSwNP treated with dupilumab: a real-life study. Eur Arch Otorhinolaryngol. 2024;281(5):2429-2440.
6. Kemp P, van der Lans RJL, Otten JJ, et al. Hypereosinophilia during dupilumab treatment in patients with chronic rhinosinusitis with nasal polyps. Rhinology. 2024;62(2):202-207.
7. Caminati M, Maule M, Bagnasco D, et al. Profiling Blood hypereosinophilia in patients on dupilumab treatment for respiratory conditions: a real-life snapshot. J Allergy Clin Immunol Pract. 2025;13(6):1367-1374.e4.
8. Fokkens WJ, Viskens AS, Backer V, et al. EPOS/EUFOREA update on indication and evaluation of biologics in chronic rhinosinusitis with nasal polyps 2023. Rhinology. 2023;61(3):194-202.
9. Matucci A, Micheletto C, Vultaggio A. Severe asthma and biologics: managing complex patients. J Investig Allergol Clin. 2023;33(3):168–78.

Eugenio De Corso
Otolaryngology,
Head and Neck Surgery
Rhinology
A. Gemelli Universitary Hospital
Foundation
IRCSS
Rome
Italy

E-mail: eugenio.decorso@gmail.com