LETTER TO THE EDITOR

Increasing the dosing interval of dupilumab in patients with severe asthma and chronic rhinosinusitis with nasal polyps

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To the Editor,

we present a series of five patients with severe eosinophilic asthma and chronic rhinosinusitis with nasal polyps (CRSwNP) in whom the dosing interval of dupilumab was extended from every 2 weeks to every 4 weeks while maintaining clinical stability.

Severe eosinophilic asthma responds effectively to biologic therapies [1], with several options available. Although no specific studies have examined the gradual extension of dupilumab dosing intervals in patients with asthma and CRSwNP, the drug has demonstrated efficacy in reducing nasal polyposis [2], decreasing exacerbations [3], and improving lung function [4]. However, evidence regarding the extension of dosing intervals in patients with favorable clinical outcomes remains limited.

CRSwNP associated with severe asthma represents a clinical challenge. Dupilumab has proven effective for both conditions [5]. In patients with well-controlled disease, dose interval extension may be considered, as shown in studies on atopic dermatitis [6] and recent work in CRSwNP [7].

A study published in *Chest* [8] evaluated the change from biweekly to monthly dupilumab dosing in 20 patients, with 85% maintaining disease control. Three patients experienced exacerbations due to upper respiratory infections and reverted to the biweekly regimen. These findings suggest feasibility of interval extension in selected patients.

We aimed to assess the safety and feasibility of extending dupilumab dosing intervals in a real-life setting.

We included five patients (four men and one woman) aged 46 to 66 years, all diagnosed with severe eosinophilic asthma and CRSwNP. Prior to dupilumab initiation, all patients were receiving:

- ICS/LABA/LAMA (beclomethasone/formoterol/glycopyrronium) twice daily
- Montelukast 10 mg daily
- Cetirizine 10 mg daily
- Intranasal mometasone 50 mcg (two sprays BID)
- As-needed inhaled salbutamol
- Two patients also received prednisone 5 mg/day

The following parameters were measured at baseline, 1 year, 2 years, and 6 months after dosing interval extension:

- Peripheral blood eosinophil count (cells/μL) [9]
- FEV1 before bronchodilation
- Asthma Control Test (ACT) [10]

- Sino-Nasal Outcome Test-22 (SNOT-22) [11,12]

Dupilumab was administered as a 600 mg loading dose followed by 300 mg every 2 weeks for 2 years. The dosing interval was then extended to every 4 weeks, with follow-up at 6 months.

- Prednisone was discontinued in both relevant patients within 12 months, without clinical deterioration.
- No patient required systemic corticosteroids or emergency visits during the 2-year follow-up.
- Six months after interval extension, ACT and SNOT-22 scores continued to improve or remained stable.
- FEV1 and eosinophil levels showed sustained or improved results.
- No exacerbations were reported post-extension.

Table 1 presents detailed data per patient.
Figure 1 shows the evolution of FEV1, eosinophils, SNOT-22, and ACT scores across all time points.

This case series supports the potential feasibility and safety of extending dupilumab dosing intervals in patients with well-controlled severe eosinophilic asthma and CRSwNP.

Patients initially presented with elevated eosinophils, impaired lung function, and severe symptoms. After 2 years of standard biweekly therapy, all achieved significant clinical improvement, allowing the dosing interval to be increased to 4 weeks.

After 6 months:

- Asthma and CRSwNP control was maintained.
- ACT and SNOT-22 scores showed improvement or stabilization.
- Lung function improved or remained stable.
- No systemic corticosteroids were needed.
- Prednisone was successfully withdrawn in appropriate cases.

Risks of dosing interval extension should also be considered. These include the possibility of loss of disease control and the theoretical development of neutralizing antibodies to dupilumab, which may reduce its long-term efficacy. Although not observed in our patient series, such risks should be evaluated on a case-by-case basis.

We acknowledge that structured shorter-term follow-up data is not available in this cohort, limiting more detailed assessment of earlier de-escalation opportunities

In selected patients with well-controlled disease, extending the dupilumab dosing interval from 2 to 4 weeks may be a viable and cost-effective strategy, without compromising disease control. Larger and longer-term studies are necessary to confirm these findings and define optimal patient selection criteria.

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Author Contributions

- ACM: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing
- JCZ: Formal Analysis, Visualization, Writing – original draft, Writing – review & editing

Conflict of Interest

The authors declare no conflict of interest.

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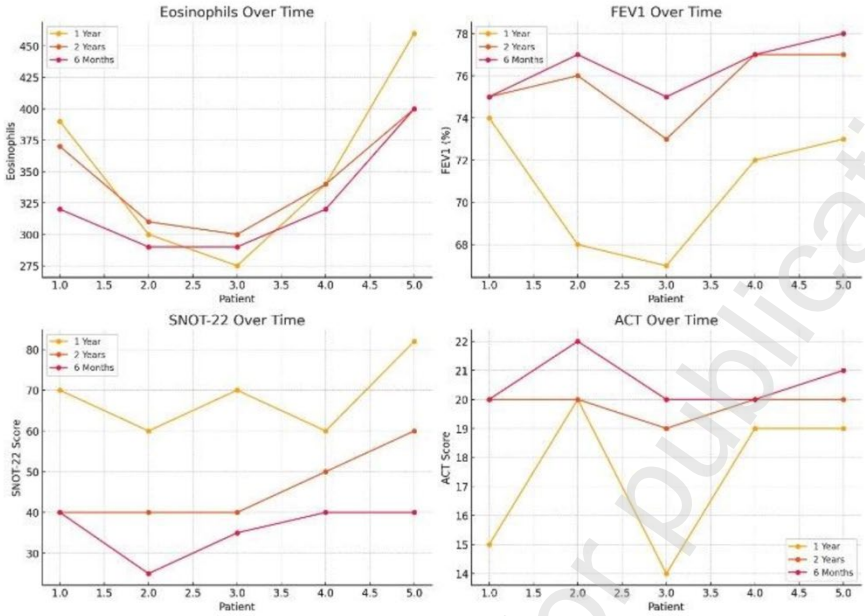
Patient	Sex	Age	Baseline Eosinophils	1-Year Eosinophils	2-Year Eosinophils	6-Months De-escalation Eosinophils	Baseline FEV1	1-Year FEV1	2-Year FEV1	6-Months De-escalation FEV1	Baseline SNOT-22	1-Year SNOT-22	2-Year SNOT-22	6-Months De-escalation SNOT-22	Baseline ACT	1-Year ACT	2-Year ACT	6-Months De-escalation ACT
1	M	60	430	390	370	320	71%	74%	75%	75%	74	70	40	40	11	15	20	20
2	M	54	360	300	310	290	68%	68%	76%	77%	80	60	40	25	18	20	20	22
3	M	66	270	275	300	290	65%	67%	73%	75%	90	70	40	35	9	14	19	20
4	F	46	360	340	340	320	68%	72%	77%	77%	81	60	50	40	15	19	20	20
5	M	56	500	460	400	400	65%	73%	77%	78%	90	82	60	40	13	19	20	21

Table 1. Data obteined from the study. Each patient was followed by **Eosinophil Levels** (Baseline, 1-Year, 2-Year, 6-Months Increasing the dosing interval of dupilumab), **FEV1 (%)** (Baseline, 1-Year, 2-Year, 6-Months Increasing the dosing interval of dupilumab), **SNOT-22 Scores** (Baseline, 1-Year, 2-Year, 6-Months Increasing the dosing interval of dupilumab) and **ACT Scores** (Baseline, 1-Year, 2-Year, 6-Months Increasing the dosing interval of dupilumab).



Here are the graphs showing the data for eosinophils, FEV1, SNOT-22, and ACT over the three time points: 1 year, 2 years, and 6 months after increasing dosing intervals Each graph compares how these measurements changed across patients at different stages of treatment.