International Journal of Otorhinolaryngology and Head and Neck Surgery
Alali S et al. Int J Otorhinolaryngol Head Neck Surg. 2025 Oct;11(5):508-512
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937
DOI: https://dx.doi.org/10.18203/issn.2454-5929.ijohns20252981

Original Research Article

The effect of decreasing the frequency of dupilumab administration after the first year on the control of chronic rhinosinusitis

Saleh Alali[1], Lana M. Saleh[1], Mohammed G. Aly[1], Sundus AlMukhodher[1]*, Rabea Khougeer[2]

[1]Department of Otolaryngology, Head and Neck Surgery, Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia
[2]Department of Allergy and Immunology, Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia

Received: 02 July 2025
Revised: 05 September 2025
Accepted: 12 September 2025

***Correspondence:**
Dr. Sundus AlMukhodher,
E-mail: sundusalmukhodher@gmail.com

ABSTRACT

Background: Chronic rhinosinusitis with nasal polyposis (CRSwNP) significantly impacts quality of life. Many studies have shown the effectiveness of dupilumab in controlling CRSwNP using bi-weekly protocol over the first year. However, the effect of spacing the dose beyond the first year remains unclear. This study aims to assess the efficacy of the increasing the interval of dupilumab administration in maintaining the effect achieved in the first year.
Methods: This prospective study includes CRSwNP patients receiving dupilumab for over a year who transitioned from a bi-weekly to a four-weekly regimen. Clinical response was assessed using nasal polyp size (NPS), sino-nasal outcome test-22 (SNOT-22), Lund-Mackay score (LMKS), serum immunoglobulin E (IgE) levels, and eosinophilic count at three time points: pre-treatment, during bi-weekly dosing, and after switching to four-weekly administration.
Results: A sustained clinical improvement was observed across all time points. NPS showed significant difference $F(2, 30) = 85.97$, $p<0.0001$, generalized eta squared=0.73. similarly, SNOT-22 scores and LMKS exhibited significant differences $F(1.33, 19.95) = 58.55$, $p<0.0001$, generalized eta squared =0.69 and $F(1.29,19.4) = 69.41$, $p<0.0001$, generalized eta squared=0.59 respectively. IgE levels and eosinophilic count also showed significant variation $F(2, 30) = 101.5$, $p<0.0001$, generalized eta squared=0.6 and $F(2, 28)$ 9.37, $p<0.0001$, generalized eta squared=0.13.
Conclusion: Decreasing the frequency of administration of dupilumab after the first year is associated with a sustained disease control.

Keywords: Dupilumab, Chronic rhinosinusitis, CRSwNP, Nasal polyps, Biologics, Type-2 inflammation, Treatment interval, SNOT-22, IgE, Eosinophils

INTRODUCTION

Chronic rhinosinusitis with nasal polyposis (CRSwNP) is a disease that significantly affects the patient's quality of life. There are different endotypes of chronic rhinosinusitis based on the immune response, a subtype of which is based on type-2 inflammation which shares the same pathogenic mechanism with other diseases like bronchial asthma and atopic dermatitis. This disease is known to be more severe with higher recurrence rates compared to other types of chronic rhinosinusitis.[1]

Patients with CRSwNP in general and especially those with type-2 inflammation may require multiple sinus surgeries along with medical management with inappropriate symptomatic control. Proper understanding of the pathogenesis of type-2 inflammation has led to the development of new biologic therapy "Dupilumab" which is effective in controlling type-2 inflammatory diseases.[2] Dupilumab is a monoclonal antibody that exerts its effect by blocking the activity of interleukin (IL) -4 and IL-13, which play an important role in type-2 inflammation.[3]

Dupilumab was approved by the Food and Drug Administration (FDA) for treating CRSwNP in 2019, and

since then, many studies have confirmed its effectiveness.[2-6] In Johns Hopkins Aramco Healthcare Hospital- Dharan, dupilumab has been used for patients with CRSwNP who fulfills the criteria set by the European Position Paper on rhinosinusitis and nasal polyps 2020 (EPOs 2020) and these patients were followed up according to the EPOs 2020 guidelines.

Dupilumab is initially administered as a loading dose of 600 mg subcutaneously (SC) followed by 300 mg SC every two weeks for the first year; however, following that, there has been no consensus over the treatment protocol. The most widely used protocol is based on shifting patients to four weekly injections after the first year and this protocol has been applied in our institute.

Certain studies have been conducted to assess the effect of increasing the interval of dupilumab administration in patients with atopic dermatitis, which resulted in decline in disease control.[7] Up to our knowledge, no previous study has evaluated the effect of dose adjustment after the first year on sustaining CRSwNP control. The aim of this study is to assess the efficacy of the increasing the interval of dupilumab administration in maintaining the effect achieved in the first year.

METHODS

Patients

This prospective case study included all patients with CRSwNP whom have been receiving dupilumab injection for more than a year and have been following up in the outpatient clinic of the Otorhinolaryngology Head and Neck Surgery Department of Johns Hopkins Aramco Healthcare Hospital-Dhahran from October 2020 to June 2023. Approval from the institutional review board of the hospital was obtained.

Inclusion criteria included patients older than 18 years and patients who were shifted to the four weekly injection protocol for at least four months. Patients who refused to be enrolled in the study or those with insufficient data were excluded. Informed consent was obtained from the patients prior to starting therapy with dupilumab and verbal consent was re-obtained during the follow up appointments.

Study protocol

All patients were evaluated prior to starting dupilumab, at least once during the first year and at four months after shifting them to the once four weekly protocol. The following parameters were assessed in each appointment to evaluate CRSwNP control: serum immunoglobulin E (IgE) levels, absolute eosinophilic count, nasal polyp size (NPS), sino-nasal outcome test-22 (SNOT-22) score using its validated Arabic form and the LMKS, calculated based on a thin cut (1 mm) computerized tomography of the nose and paranasal sinuses.[8] The treatment protocol followed the EPOS2020 guidelines. Participants were initially administered a 600 mg loading dose of dupilumab followed by 300 mg every two weeks for the first year, and then shifted to 300 mg every four weeks, alongside the use of a mometasone nasal spray (100 µg) in each nostril twice daily.[1]

The previously-mentioned parameters were compared at three time points, prior to starting dupilumab (point A), at least four months after starting twice monthly injections (point B) and at least four months after shifting to monthly injections (point C).

Statistical analysis

Descriptive data was summarized using frequencies and percentages for categorical data, while continuous data was summarized using mean, standard deviation, median, minimum, and maximum. A one-way repeated measures analysis of variance (ANOVA) was conducted to determine whether the mean clinical outcome values significantly differed between the three time points (point A, B and C). Post-hoc analysis was performed using Bonferroni adjustment. A p value less than 0.05 was considered statistically significant. Analysis was conducted using RStudio (2023.06.0+421).

RESULTS

Among the 35 patients receiving dupilumab treatment, 19 patients met the study inclusion criteria. Three of which were excluded due to insufficient data: two due to incomplete laboratory workup and one due to lack of clinical and radiological assessment prior to receiving dupilumab. A total of 16 patients were included in the study. Most of the included patients were males (69%).

The provided statistics in (Table 1) show a consistent decrease over time for bilateral endoscopic NPS, IgE levels, eosinophil count, SNOT-22 scores, and LMKS values, indicating sustained effect of dupilumab treatment after decreasing the frequency of its administration to four weeks.

Significant differences were observed across time points for various measures. Specifically, bilateral endoscopic NPS showed significant difference ($F(2,30) = 85.97$, $p<0.0001$, generalized eta squared=0.73) (Figure 1). The IgE levels showed significant variation ($F(2,30) = 101.5$, $p<0.0001$, generalized eta squared=0.6) (Figure 2).

Similarly, the Eosinophil count displayed significant differences ($F(2,28) = 9.37$, $p<0.0001$, generalized eta squared=0.13) (Figure 3). The SNOT-22 scores also exhibited significant differences ($F(1.33,19.95) = 58.55$, $p<0.0001$, generalized eta squared=0.69) (Figure 4). Lastly, the LMKS values demonstrated significant differences across time points ($F(1.29,19.4) = 69.41$, $p<0.0001$, generalized eta squared=0.59) (Figure 5).

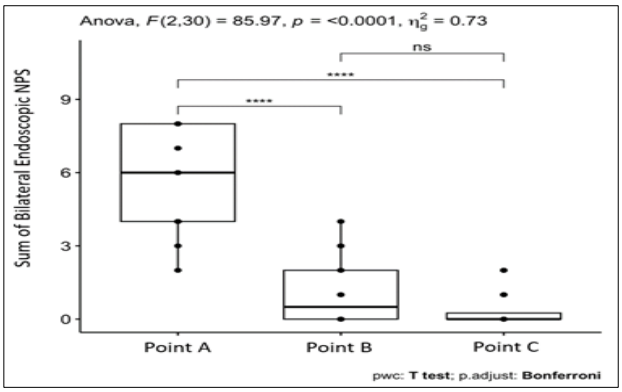

Figure 1: The difference between the mean score of the bilateral nasal polyp size at three time points.

Point A: prior to starting Dupilumab, point B: at least four months after starting Dupilumab every two weeks, point C: at least four months after shifting to monthly Dupilumab injections

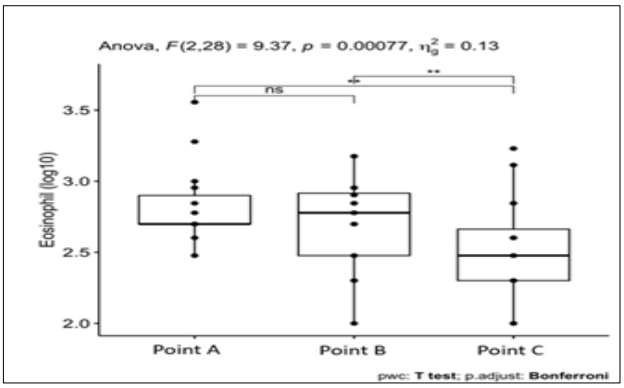

Figure 3: The mean eosinophilic count level at three time points.

Point A: prior to starting Dupilumab, point B: at least four months after starting Dupilumab every two weeks, point C: at least four months after shifting to monthly Dupilumab injections

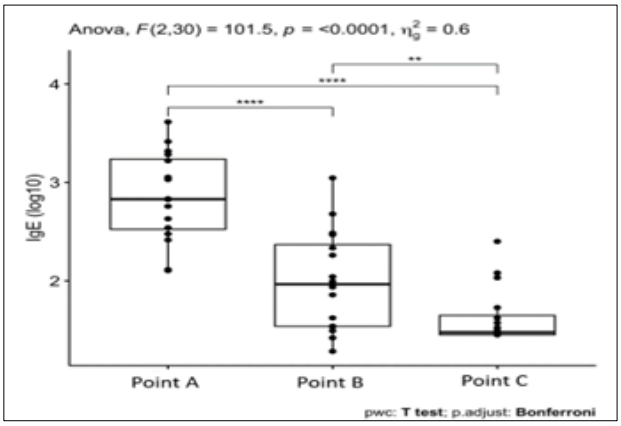

Figure 2: The difference between the mean serum IgE level at three time points.

Point A: prior to starting Dupilumab, point B: at least four months after starting Dupilumab every two weeks, point C: at least four months after shifting to monthly Dupilumab injections

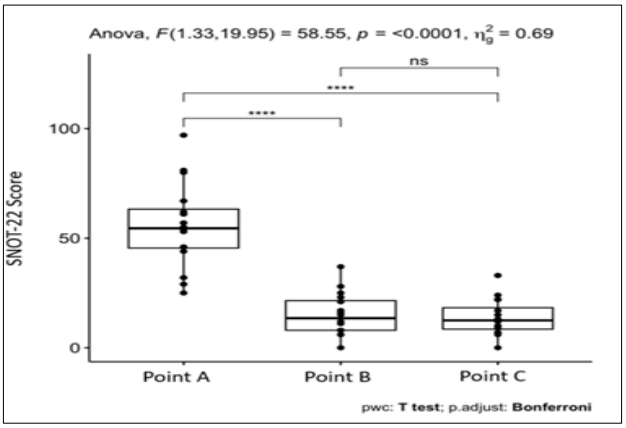

Figure 4: The mean SNOT-22 score at three time points.

Point A: prior to starting Dupilumab, point B: at least four months after starting Dupilumab every two weeks, point C: at least four months after shifting to monthly Dupilumab injections

Table 1: Clinical outcome characteristics (n=6).

Variable and interval	Mean	SD	Median	Minimum	Maximum
Sum of bilateral endoscopic NPS					
Point A	5.625	2.06	6	2	8
Point B	1.06	1.34	0.5	0	4
Point C	0.38	0.72	0	0	2
Serum IgE level					
Point A	1130.88	1101.41	676.0	127.0	4120.0
Point B	196.18	276.20	92.40	19.20	1110.0
Point C	56.44	59.27	30.0	28.3	251.30
Eosinophil count					
Point A	793.75	855.94	500.0	0.0	3600.0
Point B	643.75	416.28	600.0	100.0	1500.0
Point C	462.50	450.0	300.0	100.0	1700.0
SNOT-22 score					
Point A	55.56	19.47	54.5	25.0	97.0
Point B	15.06	9.72	13.5	0.0	37.0
Point C	13.75	8.24	12.5	0.0	33.0

Continued.

Variable and interval	Mean	SD	Median	Minimum	Maximum
LMKS					
Point A	19.75	3.57	20.0	14.0	24.0
Point B	11.19	4.87	12.0	2.0	20.0
Point C	8.81	3.66	7.50	3.0	15.0

Point A: prior to starting dupilumab, point B: at least four months after starting dupilumab every two weeks, point C: at least four months after shifting to monthly dupilumab injections, NPS: nasal polyp size, IgE: immunoglobulin E, SNOT-22: sino-nasal outcome test-22, LMKS: Lund-Mackay score

Post-hoc analyses with a Bonferroni adjustment revealed that all the pairwise differences, between time points, were statistically significantly different ($p \leq 0.05$), except for bilateral endoscopic NPS between point B and C, Eosinophil count between point A and B, and SNOT-22 score between point B and C (Figure 1-5).

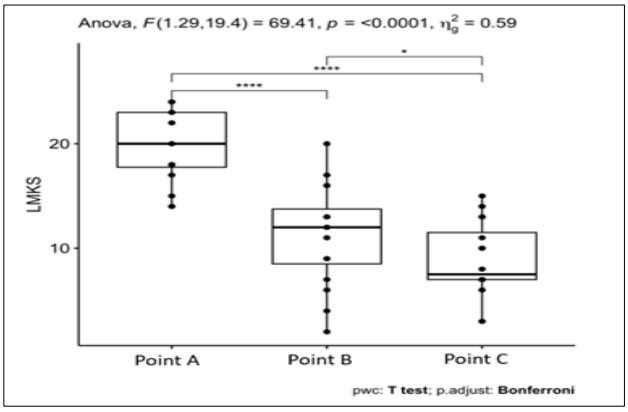

Figure 5: The mean LMKS at three time points.
Point A: prior to starting Dupilumab, point B: at least four months after starting Dupilumab every two weeks, point C: at least four months after shifting to monthly Dupilumab injections

DISCUSSION

Patients with CRSwNP can present with variable clinical symptoms including nasal obstruction/congestion, nasal discharge, post-nasal drip, facial pressure and hyposmia/anosmia, all of which can greatly affect the patient's quality of life. Some patients with CRSwNP respond well to medical and surgical treatment without recurrence. However, this is not the case in all patients. It was found that there are three different types of chronic rhinosinusitis based on the body's adaptive immune response.[1] Patients with type-2 inflammation were found to have more severe and resistant disease, with higher recurrence rates and associated with asthma. Type-2 inflammation is based on the activation of T helper 2 immune cells, which results in the production of IL-4, IL-5 and IL-13 cytokines and activation of eosinophils, mast cells and B helper cells that secret IgE antibodies.[1]

Patients with type-2 CRSwNP with recurrent disease require multiple courses of oral glucocorticoid to control symptoms. However, this increases the risk of encountering glucocorticoid adverse effects.[3] Therefore, it is essential to investigate other modalities of treatment. The recent growth in understanding the pathogenesis of CRSwNP, resulted in the expansion in the use of biologic therapies in the form of monoclonal antibodies. In July 2019, dupilumab became the first monoclonal antibody to be approved by FDA for treatment of CRSwNP.[3] Dupilumab targets cytokines involved in type-2 inflammation and its efficacy in other type-2 diseases including atopic dermatitis and asthma has been proven previously.[9,10]

In our study, we found that spacing dupilumab administration to once four-weekly after the first year was associated with sustained control of type-2 CRSwNP. Looking at each parameter, starting with the nasal polyp size, it was noticed that the study population continued to have reduction in the polyp size even after starting the new regimen for administration. Even though the difference in mean endoscopic NPS during the first year (while patients were on a 2-weekly administration regimen) and after shifting to the new regimen was statistically insignificant, the difference between the lateral and the patients' baseline was still found to be significant, indicating that these patients have at least continued to sustain the results that were achieved in the first year. Bachert et al has also noted a continued reduction in nasal polyp size in patients receiving a 4-weekly dupilumab injection when compared to placebo, even though the magnitude of reduction was less than the group on a 2-weekly injection.[11]

In addition, a similar finding was noted when the SNOT-22 score was compared at the three time points (the overall difference in score after shifting to the 4-weekly regimen was significant when compared to the patients' baseline, but not when compared to the initial 2-weekly regimen). This may be because the patients' scores were very high prior to starting the medication. However, after the first year, their overall clinical scores, including the SNOT-22 score, was already low, making any further reduction less likely to be statistically significant, despite the fact of persistent minor improvement. When comparing the IgE levels and the eosinophilic count, it was noticed that there has been a continuous decline in their levels over time. A slight increase in eosinophil count was initially noted in some patients after starting dupilumab. However, this increase was transient. A similar finding was noted by Wechsler et al. when using dupilumab for various clinical conditions.[12]

Limitations

The study is based on a single center with a small sample size, which may limit the generalizability of these findings.

Moreover, the follow-up period was limited to a minimum of four months after shifting to the new protocol, which may not be sufficient to fully assess the long-term effects and sustainability of these results. Hence, future studies with larger sample sizes, longer follow-up periods, and multi-center designs are needed to provide more comprehensive data of the optimal dosing regimen for dupilumab in CRSwNP.

CONCLUSION

The results in our study showed that decreasing the frequency of dupilumab administration after the first year is associated with sustained clinical improvement. In addition, it can aid in improving patients' compliance and enhance cost-effectiveness. At this point, changing the patients' regimen should be thought of as a way of persevering the previously achieved outcome and hence it may be wise to delay the change in patients who are still not fully satisfied with their clinical status by the end of the first year. However, further studies are needed to assess the long-term effect of this protocol.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Fokkens WJ. EPOS2020: a major step forward. Rhinology. 2020;58(1):1.
2. Busse WW, Pavord ID, Siddiqui S, Khan AH, Praestgaard A, Nash S, et al. Dupilumab Improves Outcomes in Patients with Chronic Rhinosinusitis with Nasal Polyps and Coexisting Asthma Irrespective of Baseline Asthma Characteristics. J Asthma Allergy. 2023;16:411-9.
3. Kim J, Naclerio R. Therapeutic Potential of Dupilumab in the Treatment of Chronic Rhinosinusitis with Nasal Polyps: Evidence to Date. Ther Clin Risk Manag. 2020;16:31-7.
4. Albrecht T, Sailer MM, Capitani F, van Schaik C, Löwenheim H, Becker S. Real-world evidence for the effectiveness and safety of dupilumab in patients with CRSwNP after 1 year of therapy. World Allergy Organ J. 2023;16(5):100780.
5. De Corso E, Pasquini E, Trimarchi M, La Mantia I, Pagella F, Ottaviano G, et al. Dupilumab in the treatment of severe uncontrolled chronic rhinosinusitis with nasal polyps (CRSwNP): A multicentric observational Phase IV real-life study (DUPIREAL). Allergy. 2023;78(10):2669-83.
6. Galletti C, Barbieri MA, Ciodaro F, Freni F, Galletti F, Spina E, et al. Effectiveness and Safety Profile of Dupilumab in Chronic Rhinosinusitis with Nasal Polyps: Real-Life Data in Tertiary Care. Pharmaceuticals (Basel). 2023;16(4):630.
7. Worm M, Simpson EL, Thaçi D, Bissonnette R, Lacour JP, Beissert S, et al. Efficacy and Safety of Multiple Dupilumab Dose Regimens After Initial Successful Treatment in Patients With Atopic Dermatitis: A Randomized Clinical Trial. JAMA Dermatol. 2020;156(2):131-43.
8. Elwany S, Atef A, Ibrahim AA, Ismail AS, Hussein WK, Youssef AS, et al. Arabic translation and validation of SNOT-22. Egypt J Otolaryngol. 2017;33:611-5.
9. Blauvelt A, de Bruin-Weller M, Gooderham M, Cather JC, Weisman J, Pariser D, et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. Lancet. 2017;389(10086):2287-303.
10. Rabe KF, Nair P, Brusselle G, Maspero JF, Castro M, Sher L, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. N Engl J Med. 2018;378(26):2475-85.
11. Bachert C, Han JK, Desrosiers M, Hellings PW, Amin N, Lee SE, 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):1638-50.
12. Wechsler ME, Klion AD, Paggiaro P, Nair P, Staumont-Salle D, Radwan A, 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.

Cite this article as: Alali S, Saleh LM, Aly MG, AlMukhodher S, Khougeer R. The effect of decreasing the frequency of dupilumab administration after the first year on the control of chronic rhinosinusitis. Int J Otorhinolaryngol Head Neck Surg 2025;11:508-12.