Original Research

Radiologic Improvement in Eosinophilic Chronic Rhinosinusitis During Tezepelumab Therapy for Severe Asthma: A Case Series

Yosuke Okinaka, Kazuma Sugahara, Youhei Yamamoto, Yosuke Takemoto, Junko Tsuda, Mei Sakamoto, Tatsuya Masaki, Shogo Nishimura, Tomoyasu Yamagata, Satoshi Nomura and Makoto Hashimoto

Department of Otolaryngology, Yamaguchi University Graduate School of Medicine, 1-1-1 Minamikogushi, Ube, Yamaguchi 755-8505, Japan

Running title: **Radiologic Improvement of ECRS with Tezepelumab**

Correspondence to Kazuma Sugahara, MD, PhD. Email address: kazuma@yamaguchi-u.ac.jp

Address: 1-1-1 Minamikogushi, Ube, Yamaguchi, Japan 755-8505,

Tel: 0836-22-2281

Word count: 1845

Abstract

Background: Eosinophilic chronic rhinosinusitis (ECRS) is generally characterized by refractory type 2 inflammation along with severe asthma. Although tezepelumab, an anti-thymic stromal lymphopoietin (TSLP) monoclonal antibody, has broad efficacy in severe asthma, its effects on sinonasal inflammation in ECRS remain unclear. In this retrospective observational study, we investigated the radiological and clinical changes in patients with ECRS and severe asthma treated with tezepelumab. Methods: Clinical data, blood eosinophil counts, fractional exhaled nitric oxide (FeNO), total serum IgE levels, lung function, and paranasal sinus CT findings of seven patients with ECRS who received tezepelumab for comorbid severe asthma at a single tertiary care center between 2022 and 2024, were collected. Radiologic severity was assessed using the Lund–Mackay score (LMS) at baseline and ≥6 months after treatment initiation. Results: The median LMS showed a trend toward reduction from baseline to ≥6 months, although this difference did not reach statistical significance ($p = 0.051$). In contrast, blood eosinophil counts, serum IgE levels, FeNO levels, and the FEV_1/FVC ratio did not show statistically significant changes during the observation period. Conclusion: Tezepelumab therapy showed a trend toward reduction in the Lund–Mackay score in patients with ECRS and severe asthma, although statistical significance was not reached. Systemic biomarkers and lung function remained stable.

Keywords: tezepelumab; thymic stromal lymphopoietin (TSLP); eosinophilic chronic rhinosinusitis (ECRS); Lund–Mackay score; type 2 inflammation.

Introduction

Eosinophilic chronic rhinosinusitis (ECRS) is a refractory phenotype of chronic rhinosinusitis characterized by diffuse eosinophilic inflammation, nasal polyp formation, and a high recurrence rate despite medical and surgical therapy. The Japanese Epidemiological Survey of Refractory Eosinophilic Chronic Rhinosinusitis (JESREC) study established the diagnostic criteria and showed that ECRS has more severe clinical manifestations and is frequently comorbid with asthma compared to non-ECRS.[1] The one airway concept highlights that upper and lower airway diseases share common immunological mechanisms, particularly type 2–mediated inflammation, which underlies both ECRS and asthma.[2] The EPOS 2020 also emphasized that type 2 inflammation is the dominant endotype in many patients with chronic rhinosinusitis with nasal polyps.[3]

Thymic stromal lymphopoietin (TSLP) is an epithelial cell–derived cytokine that functions as a key upstream regulator of type 2 inflammation. TSLP activates dendritic cells, type 2 innate lymphoid cells, basophils, and other effector cells that drive eosinophilic inflammation.[4] TSLP expression is increased in nasal polyps and inflamed sinonasal mucosa of patients with chronic rhinosinusitis, suggesting its involvement in disease pathogenesis.[5]

Tezepelumab is a human IgG2 monoclonal antibody that inhibits TSLP–TSLP receptor interactions, thereby suppressing multiple downstream inflammatory pathways. Clinical trials

have demonstrated its broad efficacy in patients with severe asthma. The PATHWAY study demonstrated significantly reduced asthma exacerbations, regardless of baseline type 2 biomarkers,[6] and the NAVIGATOR trial confirmed these findings in a larger population with severe, uncontrolled asthma.[7] Moreover, the CASCADE study reported that tezepelumab therapy reduced airway inflammatory cells, indicating upstream modulation of inflammatory cascades beyond peripheral biomarkers.[8]

Although biologics, such as dupilumab and mepolizumab, have beneficial effects in chronic rhinosinusitis with nasal polyps, including improving symptoms, polyp burden, and radiologic disease,[9,10] evidence regarding the impact of tezepelumab on sinonasal inflammation, particularly in ECRS, remains limited.

In Japan, tezepelumab was only approved for severe asthma in 2022, and its effects on sinonasal diseases have not been systematically evaluated. Therefore, in this study, we aimed to address this gap and generate clinical evidence in Japanese patients with ECRS.

This study investigated the clinical course of seven patients with ECRS who received tezepelumab for comorbid severe asthma. By evaluating longitudinal changes in symptoms, blood biomarkers, and radiological findings, we sought to clarify the potential sinonasal effects of anti-TSLP therapy.

Materials and Methods

Study design and patients

This retrospective observational study was conducted in the Department of Otolaryngology, Yamaguchi University Hospital. We reviewed the medical records of patients diagnosed with ECRS (based on the JESREC criteria), who received tezepelumab for comorbid severe asthma between 2022 and 2024. A total of 11 patients received tezepelumab during the study period. Among them, seven patients had paranasal sinus CT scans available both before and after initiation of tezepelumab and were therefore included in the final analysis. Four patients were excluded due to the absence of follow-up CT imaging, which precluded radiologic evaluation.

Treatment protocol

Tezepelumab (210 mg) was administered subcutaneously every 4 weeks, according to the national and institutional guidelines for severe asthma management. Previous biologic therapies (such as dupilumab, benralizumab, and mepolizumab) and subsequent treatment modifications were documented, including discontinuation or switching owing to inadequate response or adverse events.

Clinical assessments

Clinical symptoms related to ECRS and asthma were extracted from chart records. Laboratory markers, including blood eosinophil count, fractional exhaled nitric oxide (FeNO), and total serum IgE, were obtained at baseline and at 2 and 6 months after tezepelumab initiation.

Radiologic evaluation

Paranasal sinus computed tomography (CT) scans were obtained at baseline and at multiple time points ≥ 6 months after treatment initiation. Because CT imaging was not performed at standardized intervals, all seven patients underwent more than one CT scan during the post-treatment period. To ensure consistent evaluation, the lowest Lund–Mackay score (LMS)[11] observed among the CT scans performed ≥ 6 months after treatment initiation was adopted as the post-treatment LMS value. This approach was chosen to minimize the influence of transient mucosal edema and to capture the maximal radiologic improvement achieved during follow-up.

Radiological severity was quantified using the Lund–Mackay score (LMS) by two otolaryngologists blinded to clinical information, and longitudinal changes in LMS were recorded for each patient.

Two otolaryngologists independently scored all CT scans in a blinded manner. Inter-rater agreement was high, with discrepancies of no more than one point in any case.

When discrepancies occurred, the final LMS was determined by consensus between the two evaluators.

CT protocol

Paranasal sinus CT scans were performed using a multidetector CT system (Aquilion Precision, Canon Medical Systems, Otawara, Japan). Images were acquired with the patient in the supine position during quiet respiration. The scanning parameters were as follows: tube voltage 120 kV, noise index (SD) 11 HU, detector configuration 0.5 mm × 80 rows, gantry rotation time 0.5 s, pitch factor 0.637, and matrix size 512 × 512.

Axial images were reconstructed with a slice thickness of 0.5 mm and an interval of 0.5 mm. The display field of view (FOV) was 200 mm. Images were reconstructed using AiCE Body Standard for soft-tissue evaluation and AIDR 3D weak FC31 for bone evaluation. No contrast material was used for any scan.

Outcome measures

The primary outcome was change in LMS from baseline to ≥ 6 months after starting tezepelumab. Secondary outcomes included changes in the blood eosinophil count, FeNO, and

total serum IgE levels at baseline, 2 months, and 6 months. Adverse events and treatment discontinuations were also evaluated.

Statistical analysis

Continuous variables are expressed as medians and interquartile ranges. Because the sample size was small (n = 7), we did not assume normal distribution and therefore did not perform formal normality testing (e.g., Shapiro–Wilk test). Instead, comparisons between paired time points were conducted using the Wilcoxon signed-rank test, which does not require the assumption of normality. Statistical significance was defined as $p < 0.05$. All analyses and graph generation were performed using the KaleidaGraph software (Synergy).

Ethical considerations

This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Yamaguchi University Hospital (Approval No. 2025-150). Because this was a retrospective study using existing clinical data, obtaining written informed consent from all participants was not feasible. Therefore, the requirement for individual consent was waived, and an opt-out notice was posted on the institutional website in

accordance with institutional and national ethical guidelines. All data were anonymized prior to the analysis.

Results

Seven patients with ECRS and severe comorbid asthma were included in this study. The demographic and clinical characteristics of the patients are summarized in Table 1. The median age was 59 years (range, 40–77 years), and five patients were female. One patient (Case 1) had previously received dupilumab but was switched because of marked eosinophilia and subsequently continued tezepelumab treatment for 24 months. Four patients (Cases 4–7) were initiated and continuously received tezepelumab for 28–32 months. One patient (Case 2) discontinued tezepelumab after 25 months because of drug-induced urticaria. Another patient (Case 3) with a history of benralizumab use experienced asthma exacerbation 6 months after starting tezepelumab, and switched to dupilumab. Documented allergic sensitization varies among patients.

Radiological assessments were available for all seven patients. Frontal-plane sinus CT scans obtained at baseline and at ≥ 6 months demonstrated heterogeneous but generally favorable changes in sinus opacification (Fig. 1). Longitudinal trajectories of the LMS showed patient-specific fluctuations, with some patients exhibiting transient worsening; however, six of

the seven patients ultimately demonstrated a reduction in LMS compared to baseline, and the remaining patient showed minimal change (Fig. 2a). At ≥ 6 months, the median LMS tended to decrease compared with baseline; however, the difference did not reach statistical significance (Wilcoxon signed-rank test, $p = 0.051$) (Fig. 2b). Despite the lack of statistical significance, six of the seven patients demonstrated numerical reductions in LMS, indicating a consistent trend toward radiologic improvement.

Blood biomarkers showed heterogeneous patient-specific fluctuations without a consistent trend during the course of treatment. Blood eosinophil counts varied widely among the patients and did not show significant differences at baseline, 2 months, and 6 months (Fig. 3). Notably, Case 1 was switched to tezepelumab because of marked eosinophilia, and the patient's eosinophil count gradually decreased following treatment initiation. Serum total IgE levels also fluctuated in both directions, with increase in some cases and decrease in others; however, no statistically significant changes were observed across the three time points (Fig. 4). FeNO exhibited modest variability, generally trending downward in some patients, but without significant overall change (Fig. 5). The FEV_1/FVC ratio showed small fluctuations, but remained stable during treatment, with no significant temporal differences (Fig. 6).

Although systemic biomarkers and pulmonary function parameters did not significantly change during treatment, radiologic evaluation revealed a trend toward reduction in LMS,

suggesting improved sinonasal inflammatory burden in patients with ECRS receiving tezepelumab.

Discussion

In this case series of seven patients with ECRS and comorbid severe asthma treated with tezepelumab, we observed a trend toward reduction in LMS over a treatment period of ≥ 6 months. This finding suggests that TSLP blockade may be beneficial for sinonasal inflammation, extending beyond the established lower airway efficacy demonstrated in previous asthma trials.

ECRS is a subtype of chronic rhinosinusitis characterized by marked type 2 inflammation and frequently occurs with asthma, reflecting the one airway concept that links inflammatory processes across the upper and lower airways.[2,3] TSLP, an epithelial-derived cytokine, functions as an upstream regulator of type 2 immune response. It promotes the activation of dendritic cells and subsequent Th2-skewing, providing a mechanistic rationale for targeting this cytokine in disorders driven by type 2 inflammation.[4] TSLP activity is elevated in nasal polyps and inflamed sinonasal mucosa,[5] further implicating TSLP in the pathophysiology of CRS.

Tezepelumab, a monoclonal antibody that inhibits TSLP-mediated signaling, has demonstrated broad clinical efficacy in treating severe asthma. The PATHWAY and NAVIGATOR trials showed that tezepelumab significantly reduced asthma exacerbations across a wide range of baseline type 2 biomarker levels.[6,7] These results indicate that TSLP inhibition acts upstream of canonical type 2 cytokines and may modulate airway inflammation, even in patients without elevated eosinophil or IgE levels.

In our study, although systemic biomarkers including blood eosinophils, serum IgE, and FeNO did not show significant changes, radiological evaluation demonstrated a trend toward improvement in the LMS, with six of seven patients exhibiting numerical reductions. This dissociation between systemic biomarkers and radiological outcomes may reflect the unique upstream mechanism of TSLP inhibition, which could alter local sinonasal inflammation without producing measurable changes in circulating markers. This dissociation between systemic biomarkers and radiological outcomes is consistent with previous findings showing that TSLP blockade exerts broad immunological effects, even in patients with low type 2 biomarker levels.[6,7] In the PATHWAY and NAVIGATOR trials, tezepelumab reduced asthma exacerbations irrespective of baseline eosinophil, IgE, or FeNO levels, suggesting that its upstream mechanism could modulate local airway inflammation without producing prominent changes in circulating markers.[6,7] Furthermore, the well-recognized heterogeneity of biomarker

expression in ECRS and CRSwNP, as highlighted in EPOS 2020,[3] supports the interpretation that blood biomarkers may not necessarily reflect sinonasal inflammatory activity. Nevertheless, given the small sample size of this study (n=7), the absence of statistically significant changes in systemic biomarkers may also reflect limited statistical power rather than a true lack of biological effect. Larger studies are needed to clarify whether systemic biomarkers change in response to TSLP inhibition.

Our findings add to the emerging clinical experience that supports the potential utility of tezepelumab in treating upper airway disease. Dupilumab, which inhibits interleukin (IL)-4 and IL-13 signaling, effectively reduces sinus opacification and polyp burden in CRSwNP.[9] Although data on TSLP inhibition in ECRS remain limited, our observations suggest that tezepelumab may also have therapeutic relevance for sinonasal diseases, particularly in patients with persistent inflammation, in addition to other biologics. Given the upstream position of TSLP in the inflammatory cascade, TSLP inhibition may enable broader modulation of airway inflammation than agents targeting downstream cytokines. However, this hypothesis requires confirmation in larger controlled studies.

This study had several limitations. Its retrospective design, small sample size, and the absence of a control group limit the generalizability of the results. The timing of CT imaging was not standardized and concomitant treatments, including intranasal corticosteroids and prior

sinus surgery, may have influenced the outcomes. Furthermore, biomarker variability and the heterogeneity of ECRS phenotypes complicate interpretation. In addition, changes in pulmonary function and systemic biomarkers may have been affected by patients' prior biologic treatments, the use of systemic corticosteroids, and seasonal variation, none of which could be fully controlled in this study. In Japan, tezepelumab was approved and launched in 2022, with indication limited to severe asthma; its use in chronic rhinosinusitis is not permitted. Consequently, the potential effects of tezepelumab on sinonasal diseases in the Japanese population have not been systematically evaluated and opportunities to acquire adequate clinical experience remain limited.

However, the present study provides preliminary evidence that tezepelumab ameliorates radiological inflammation in patients with ECRS and severe asthma. Prospective controlled studies are warranted to better define the role of TSLP inhibition in upper airway disease and to determine whether radiological improvement can be translated into long-term symptom control and reduced disease recurrence.

Conclusion

Tezepelumab treatment was associated with a trend toward reduced LMS in patients with eosinophilic chronic rhinosinusitis and severe comorbid asthma, although the change did

not reach statistical significance ($p = 0.051$). Systemic biomarkers and lung function remained stable overall, suggesting that TSLP inhibition may exert localized effects on sinonasal inflammation, independent of circulating markers. These preliminary findings indicate a potential role of tezepelumab in managing upper airway inflammation; however, confirmation in larger, prospective studies is essential.

Acknowledgments

We express our sincere gratitude to Professor Kazuto Matsunaga of the Department of Respiratory Medicine and Infectious Diseases, Yamaguchi University Graduate School of Medicine, for granting permission and providing valuable cooperation in the preparation of this case series.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Tokunaga T, Sakashita M, Haruna T, Asaka D, Takeno S, Ikeda H, Nakayama T, Seki N, Ito S, Murata J, Sakuma Y, Yoshida N, Terada T, Morikura I, Sakaida H, Kondo K, Teraguchi K, Okano M, Otori N, Yoshikawa M, Hirakawa K, Haruna S, Himi T, Ikeda K, Ishitoya J, Iino Y, Kawata R, Kawauchi H, Kobayashi M, Yamasoba T, Miwa T, Urashima M, Tamari M, Noguchi E, Ninomiya T, Imoto Y, Morikawa T, Tomita K, Takabayashi T, Fujieda S. Novel scoring system and algorithm for classifying chronic rhinosinusitis: the JESREC Study. Allergy. 2015 Aug;70(8):995-1003. doi: 10.1111/all.12644. Epub 2015 May 26.
2. Samitas K, Carter A, Kariyawasam HH, Xanthou G. Upper and lower airway remodelling mechanisms in asthma, allergic rhinitis and chronic rhinosinusitis: The one airway concept revisited. Allergy. 2018 May;73(5):993-1002. doi: 10.1111/all.13373. Epub 2017 Dec 22.
3. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, Toppila-Salmi S, Bernal-Sprekelsen M, Mullol J, Alobid I, Terezinha Anselmo-Lima W, Bachert C, Baroody F, von Buchwald C, Cervin A, Cohen N, Constantinidis J, De Gabory L, Desrosiers M, Diamant Z, Douglas RG, Gevaert PH, Hafner A, Harvey RJ, Joos GF, Kalogjera L, Knill A, Kocks JH, Landis BN, Limpens J, Lebeer S, Lourenco O, Meco C, Matricardi PM, O'Mahony L, Philpott CM, Ryan D, Schlosser R, Senior B, Smith TL, Teeling T, Tomazic

PV, Wang DY, Wang D, Zhang L, Agius AM, Ahlstrom-Emanuelsson C, Alabri R, Albu S, Alhabash S, Aleksic A, Aloulah M, Al-Qudah M, Alsaleh S, Baban MA, Baudoin T, Balvers T, Battaglia P, Bedoya JD, Beule A, Bofares KM, Braverman I, Brozek-Madry E, Richard B, Callejas C, Carrie S, Caulley L, Chussi D, de Corso E, Coste A, El Hadi U, Elfarouk A, Eloy PH, Farrokhi S, Felisati G, Ferrari MD, Fishchuk R, Grayson W, Goncalves PM, Grdinic B, Grgic V, Hamizan AW, Heinichen JV, Husain S, Ping TI, Ivaska J, Jakimovska F, Jovancevic L, Kakande E, Kamel R, Karpischenko S, Kariyawasam HH, Kawauchi H, Kjeldsen A, Klimek L, Krzeski A, Kopacheva Barsova G, Kim SW, Lal D, Letort JJ, Lopatin A, Mahdjoubi A, Mesbahi A, Netkovski J, Nyenbue Tshipukane D, Obando-Valverde A, Okano M, Onerci M, Ong YK, Orlandi R, Otori N, Ouennoughy K, Ozkan M, Peric A, Plzak J, Prokopakis E, Prepageran N, Psaltis A, Pugin B, Raftopulos M, Rombaux P, Riechelmann H, Sahtout S, Sarafoleanu CC, Searyoh K, Rhee CS, Shi J, Shkoukani M, Shukuryan AK, Sicak M, Smyth D, Sindvongs K, Soklic Kosak T, Stjarne P, Sutikno B, Steinsvag S, Tantilipikorn P, Thanaviratananich S, Tran T, Urbancic J, Valiulius A, Vasquez de Aparicio C, Vicheva D, Virkkula PM, Vicente G, Voegels R, Wagenmann MM, Wardani RS, Welge-Lussen A, Witterick I, Wright E, Zabolotniy D, Zsolt B, Zwetsloot CP. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology. 2020 Feb 20;58(Suppl S29):1-464. doi: 10.4193/Rhin20.600.

4. Ziegler SF, Liu YJ. Thymic stromal lymphopoietin in normal and pathogenic T cell development and function. Nat Immunol. 2006 Jul;7(7):709-14. doi: 10.1038/ni1360.

5. Nagarkar DR, Poposki JA, Tan BK, Comeau MR, Peters AT, Hulse KE, Suh LA, Norton J, Harris KE, Grammer LC, Chandra RK, Conley DB, Kern RC, Schleimer RP, Kato A. Thymic stromal lymphopoietin activity is increased in nasal polyps of patients with chronic rhinosinusitis. J Allergy Clin Immunol. 2013 Sep;132(3):593-600.e12. doi: 10.1016/j.jaci.2013.04.005. Epub 2013 May 17. PMID: 23688414

6. Corren J, Parnes JR, Wang L, Mo M, Roseti SL, Griffiths JM, van der Merwe R. Tezepelumab in Adults with Uncontrolled Asthma. N Engl J Med. 2017 Sep 7;377(10):936-946. doi: 10.1056/NEJMoa1704064. Erratum in: N Engl J Med. 2019 May 23;380(21):2082. doi: 10.1056/NEJMx180026.

7. Menzies-Gow A, Corren J, Bourdin A, Chupp G, Israel E, Wechsler ME, Brightling CE, Griffiths JM, Hellqvist Å, Bowen K, Kaur P, Almqvist G, Ponnarambil S, Colice G. Tezepelumab in Adults and Adolescents with Severe, Uncontrolled Asthma. N Engl J Med. 2021 May 13;384(19):1800-1809. doi: 10.1056/NEJMoa2034975.

8. Diver S, Khalfaoui L, Emson C, Wenzel SE, Menzies-Gow A, Wechsler ME, Johnston J, Molfino N, Parnes JR, Megally A, Colice G, Brightling CE; CASCADE study investigators. Effect of tezepelumab on airway inflammatory cells, remodelling, and hyperresponsiveness

in patients with moderate-to-severe uncontrolled asthma (CASCADE): a double-blind, randomised, placebo-controlled, phase 2 trial. Lancet Respir Med. 2021 Nov;9(11):1299-1312. doi: 10.1016/S2213-2600(21)00226-5. Epub 2021 Jul 10. Erratum in: Lancet Respir Med. 2021 Nov;9(11):e106. doi: 10.1016/S2213-2600(21)00446-X.

9. Bachert C, Han JK, Desrosiers M, Hellings PW, Amin N, Lee SE, Mullol J, Greos LS, Bosso JV, Laidlaw TM, Cervin AU, Maspero JF, Hopkins C, Olze H, Canonica GW, Paggiaro P, Cho SH, Fokkens WJ, Fujieda S, Zhang M, Lu X, Fan C, Draikiwicz S, Kamat SA, Khan A, Pirozzi G, Patel N, Graham NMH, Ruddy M, Staudinger H, Weinreich D, Stahl N, Yancopoulos GD, Mannent LP. 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 Nov 2;394(10209):1638-1650. doi: 10.1016/S0140-6736(19)31881-1. Epub 2019 Sep 19. Erratum in: Lancet. 2019 Nov 2;394(10209):1618. doi: 10.1016/S0140-6736(19)32218-4.

10. Han JK, Bachert C, Fokkens W, Desrosiers M, Wagenmann M, Lee SE, Smith SG, Martin N, Mayer B, Yancey SW, Sousa AR, Chan R, Hopkins C; SYNAPSE study investigators. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): a randomised,

double-blind, placebo-controlled, phase 3 trial. Lancet Respir Med. 2021 Oct;9(10):1141-1153. doi: 10.1016/S2213-2600(21)00097-7. Epub 2021 Apr 16.

11. Lund, VJ, Mackay, IS; Staging in rhinosinusitus. Rhinology. 1993 Dec;31(4):183–4.

Figure Legends

Table1 Baseline characteristics and treatment profiles of the seven patients.

This table summarizes the demographic and clinical characteristics of the seven patients, including age, sex, previously used biologics, duration of tezepelumab treatment, and documented allergic sensitization.

Fig.1 Serial paranasal sinus CT images of Cases 1–7 before and after treatment.

Frontal-plane CT scans obtained at baseline and at ≥ 6 months after initiating tezepelumab treatment are shown for each patient. Changes in sinus opacification varied across cases, with six patients demonstrating radiological improvement and one showing minimal or no radiological changes. The Lund–Mackay score (LMS) was calculated at each time point.

Fig.2 Changes in Lund–Mackay scores (LMS) before and after treatment.

(a) Longitudinal changes in LMS from baseline through follow-up in all seven cases. The vertical axis represents the LMS, and the horizontal axis shows months after treatment initiation. Patient-specific trajectories are illustrated as line plots.

(b) Box-and-whisker comparison of LMS at baseline and ≥ 6 months after treatment initiation. Boxes represent the interquartile range (IQR) with the median shown as a horizontal line;

whiskers indicate the range. Although the median LMS tended to be lower at ≥ 6 months, the difference did not reach statistical significance (*: Wilcoxon signed-rank test, p = 0.051).

Fig.3 Longitudinal changes in blood eosinophil counts before and after treatment.

Blood eosinophil counts at baseline and 2 and 6 months after tezepelumab initiation are shown. Individual patient trajectories are displayed as line plots. Box-and-whisker plots are overlaid, representing the median (center line), interquartile range (box), and range (whiskers) at each time point. No significant differences were observed among the three time points.

Fig.4 Longitudinal changes in serum IgE levels before and after treatment.

Serum IgE levels at baseline and 2 and 6 months after tezepelumab initiation are shown. Individual patient trajectories are presented as line plots. Box-and-whisker plots overlaid on the line plots indicate the median, interquartile range, and range at each time point. No significant differences were observed among the three time points.

Fig.5 Longitudinal changes in fractional exhaled nitric oxide (FeNO) levels before and after treatment.

FeNO levels measured at baseline, 2 months, and 6 months after tezepelumab initiation. Individual patient trajectories are shown as line plots. Box-and-whisker plots overlaid on the line plots represent the median, interquartile range, and range at each time point. No significant differences were observed among the three time points.

Fig.6 Longitudinal changes in FEV_1/FVC ratio before and after treatment.

The FEV_1/FVC ratios at baseline, 2 months, and 6 months after tezepelumab initiation are shown. Individual patient trajectories are depicted as line plots. Box-and-whisker plots overlaid on the line plots indicate the median, interquartile range, and range at each time point. No significant differences were observed among the three time points.

Table.1

Case	Age	Sex	Clinical Course	Allergies
1	59	Female	Dupilumab → eosinophilia → currently continuing for 24 months	None
2	67	Female	Tezepelumab → discontinued after 25 months due to urticaria	None
3	40	Female	Benralizumab → tezepelumab → asthma exacerbation at 6 months → switched to dupilumab	Dust mites, house dust
4	57	Male	Continuing tezepelumab for 32 months	Japanese cedar, Japanese cypress, grasses
5	64	Female	Continuing tezepelumab for 28 months	Dust mites, house dust, Japanese cedar, Japanese cypress
6	59	Female	Continuing tezepelumab for 30 months	Dust mites, house dust, Japanese cedar, animal dander
7	77	Male	Continuing tezepelumab for 29 months	Moth

Fig. 1

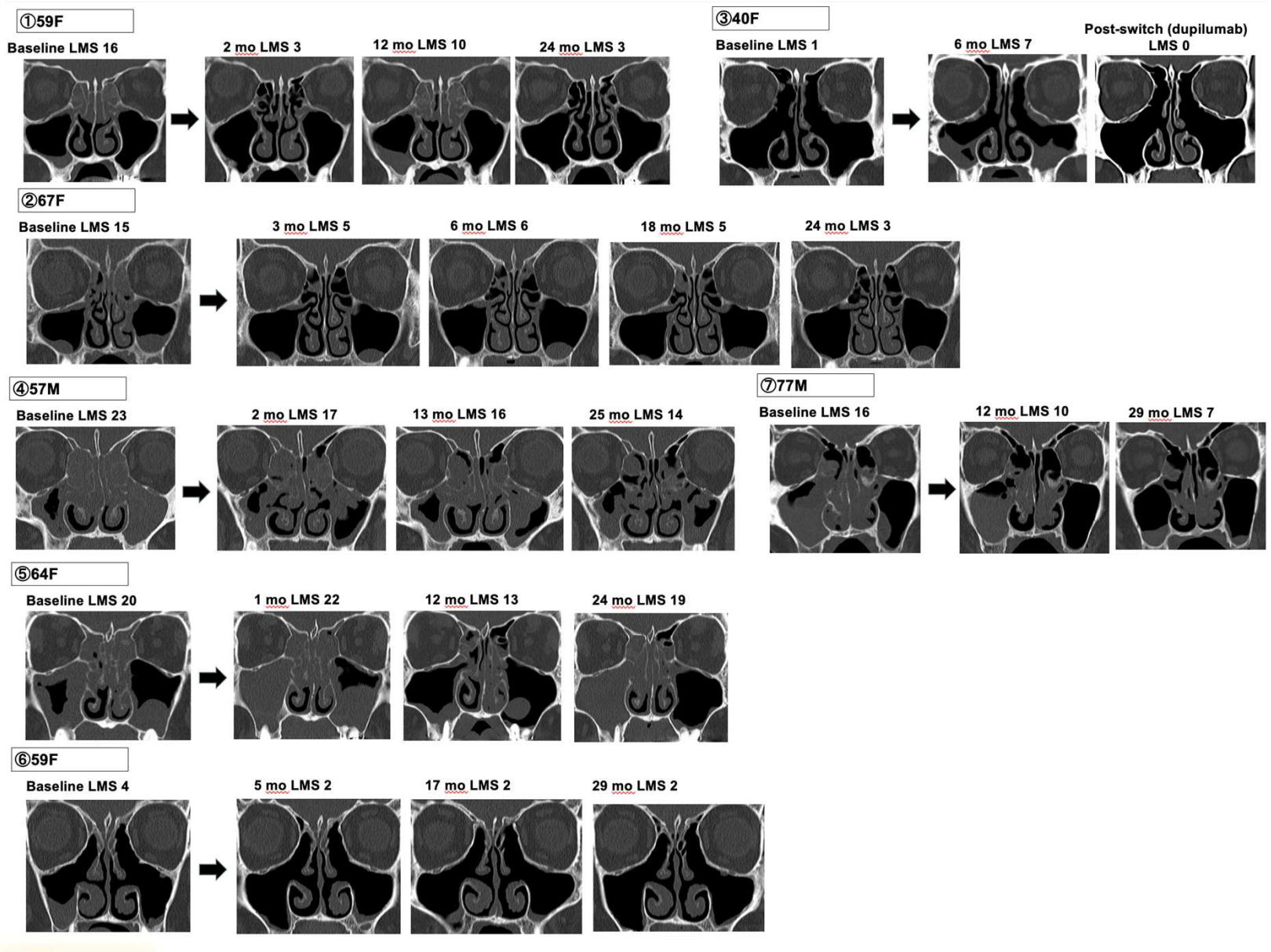

①59F
Baseline LMS 16
2 mo LMS 3
12 mo LMS 10
24 mo LMS 3
③40F
Baseline LMS 1
6 mo LMS 7
Post-switch (dupilumab)
LMS 0
②67F
Baseline LMS 15
3 mo LMS 5
6 mo LMS 6
18 mo LMS 5
24 mo LMS 3
④57M
Baseline LMS 23
2 mo LMS 17
13 mo LMS 16
25 mo LMS 14
⑦77M
Baseline LMS 16
12 mo LMS 10
29 mo LMS 7
⑤64F
Baseline LMS 20
1 mo LMS 22
12 mo LMS 13
24 mo LMS 19
⑥59F
Baseline LMS 4
5 mo LMS 2
17 mo LMS 2
29 mo LMS 2

Fig. 2

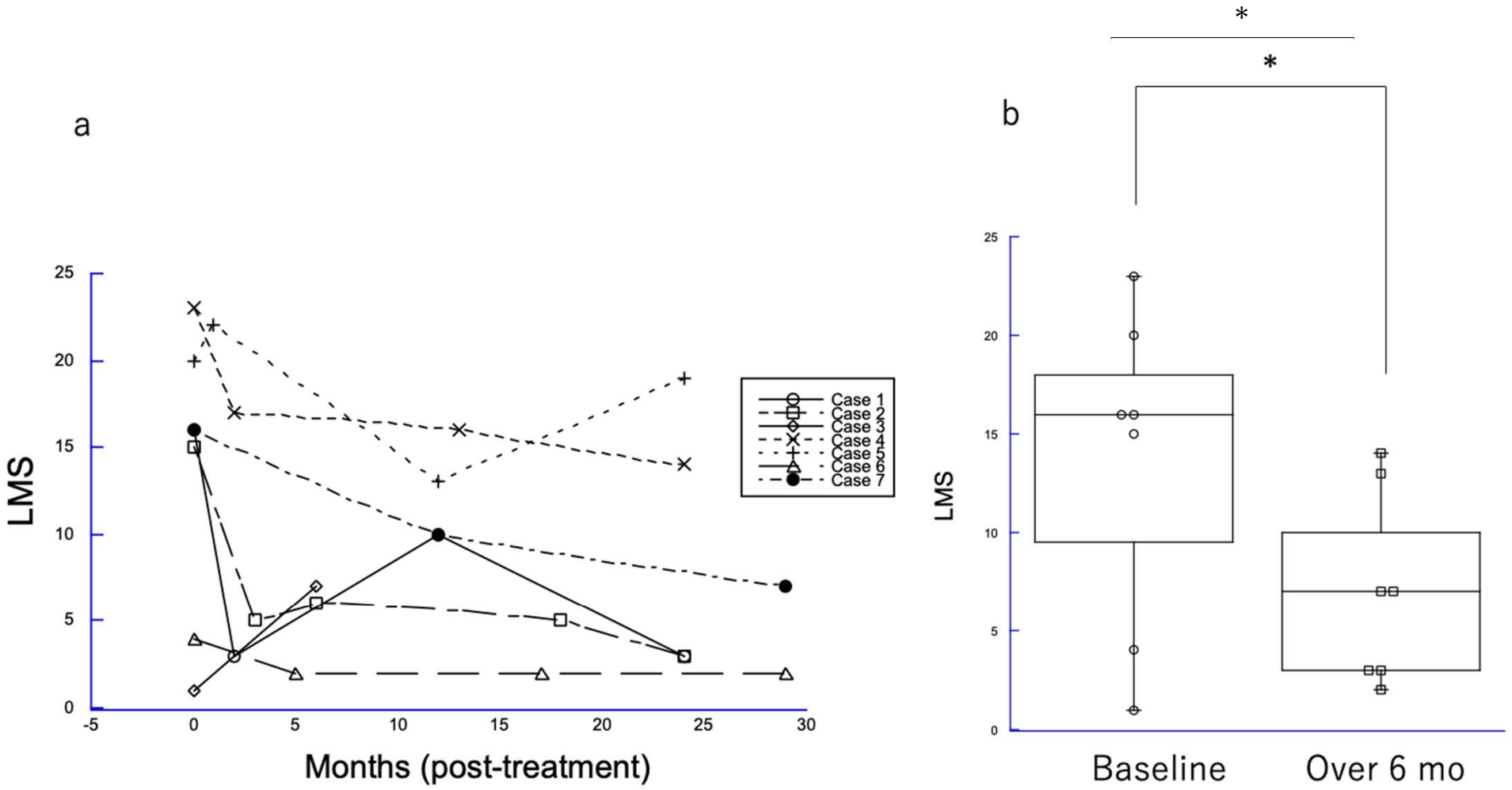

a
LMS
25
20
15
10
5
0
-5
0
5
10
15
20
25
30
Months (post-treatment)
Case 1
Case 2
Case 3
Case 4
Case 5
Case 6
Case 7
b
*
*
LMS
25
20
15
10
5
0
Baseline
Over 6 mo

Fig. 3

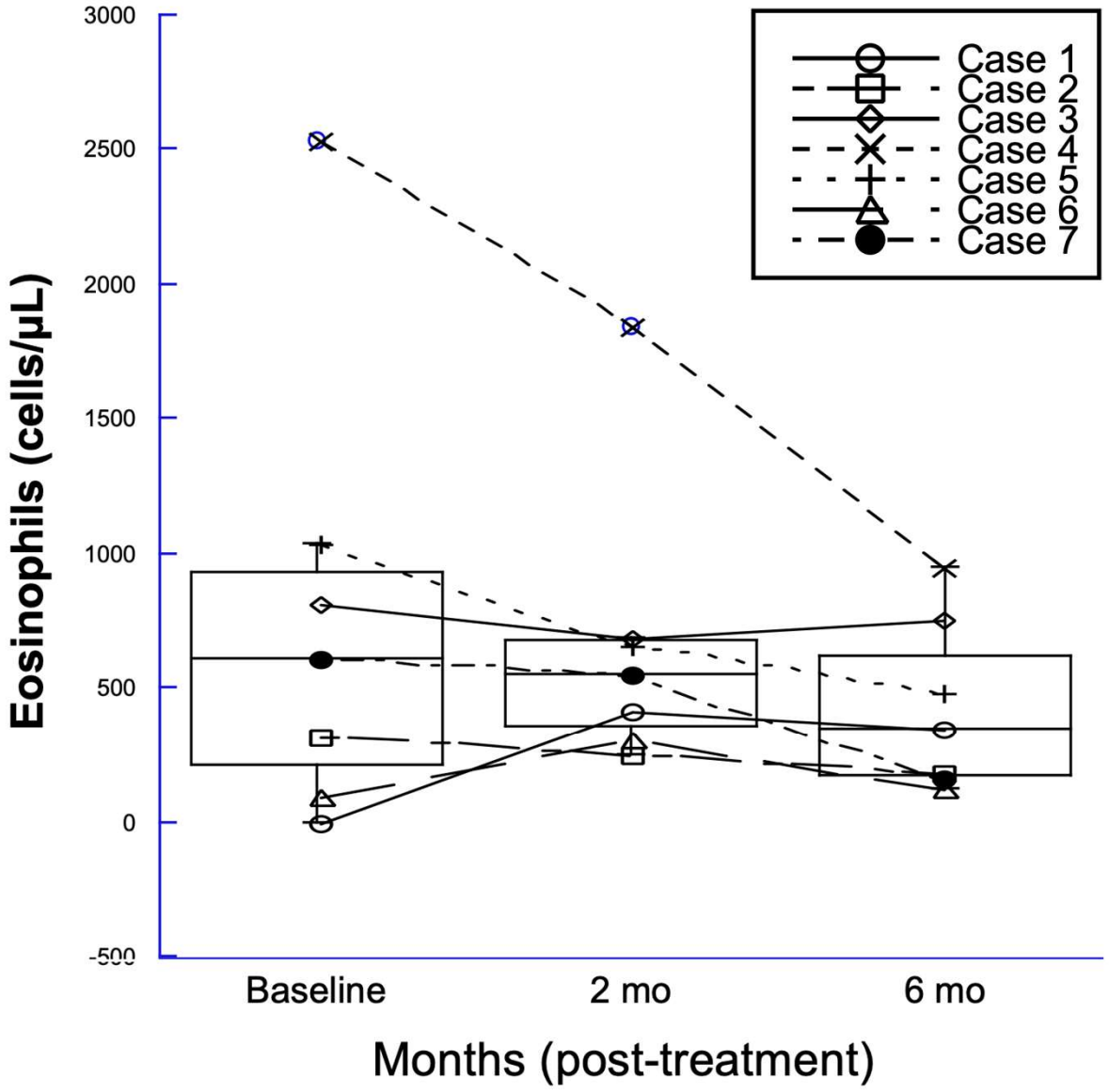

Case 1
Case 2
Case 3
Case 4
Case 5
Case 6
Case 7
3000
2500
2000
1500
1000
500
0
-500
Eosinophils (cells/μL)
Baseline
2 mo
6 mo
Months (post-treatment)

Fig. 4

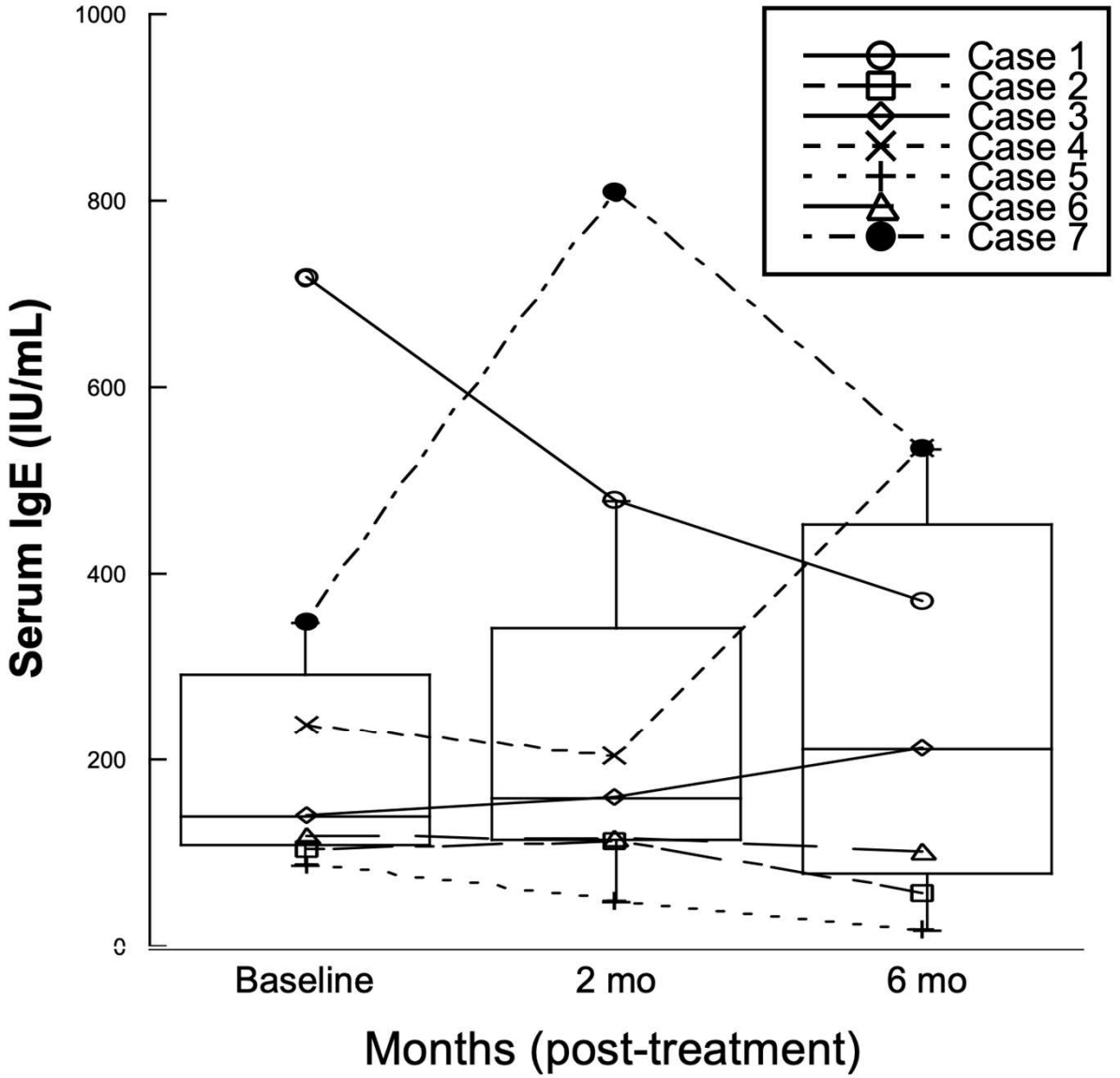

1000
800
600
400
200
0
Serum IgE (IU/mL)
Case 1
Case 2
Case 3
Case 4
Case 5
Case 6
Case 7
Baseline
2 mo
6 mo
Months (post-treatment)

Fig. 5

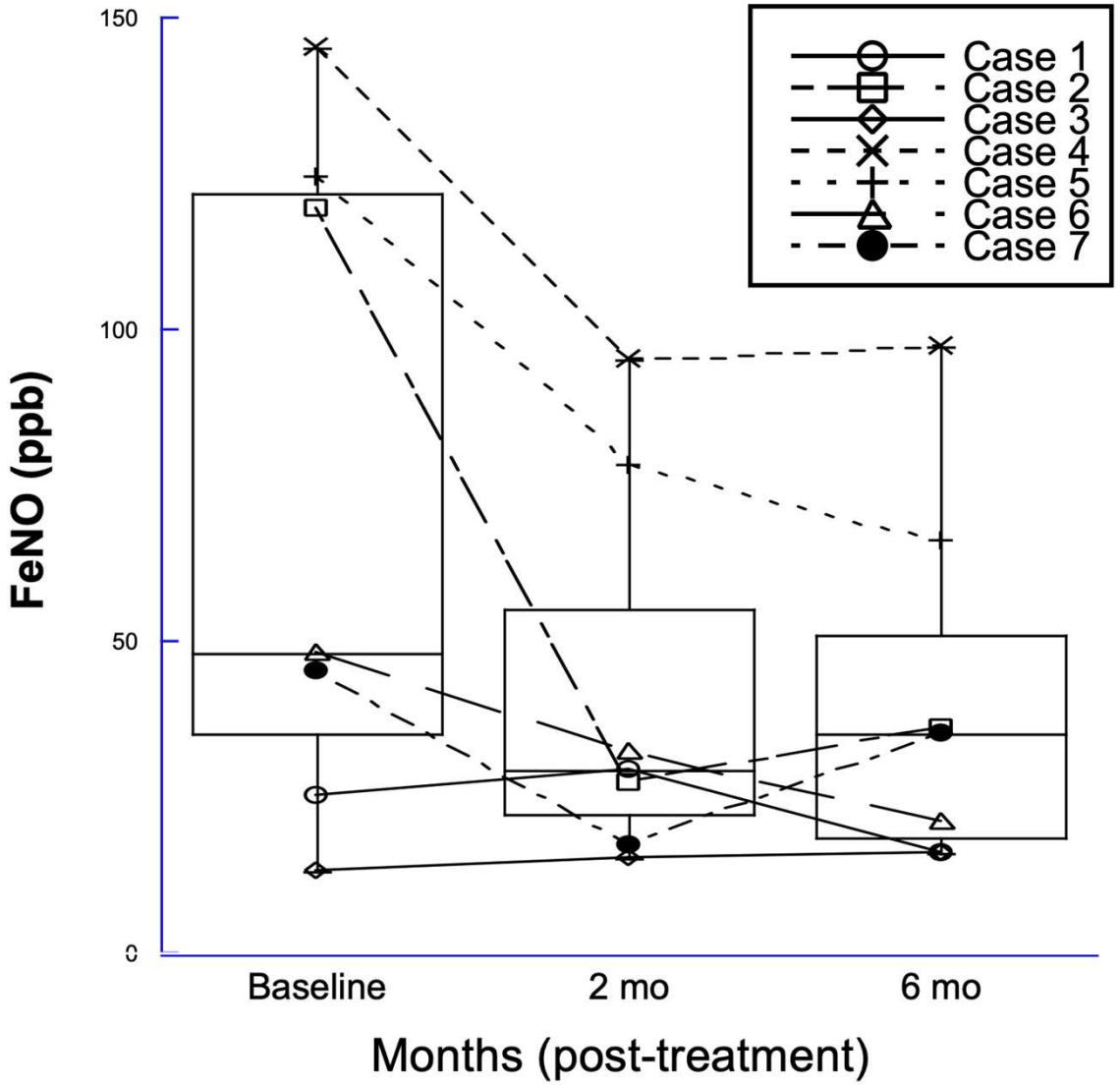
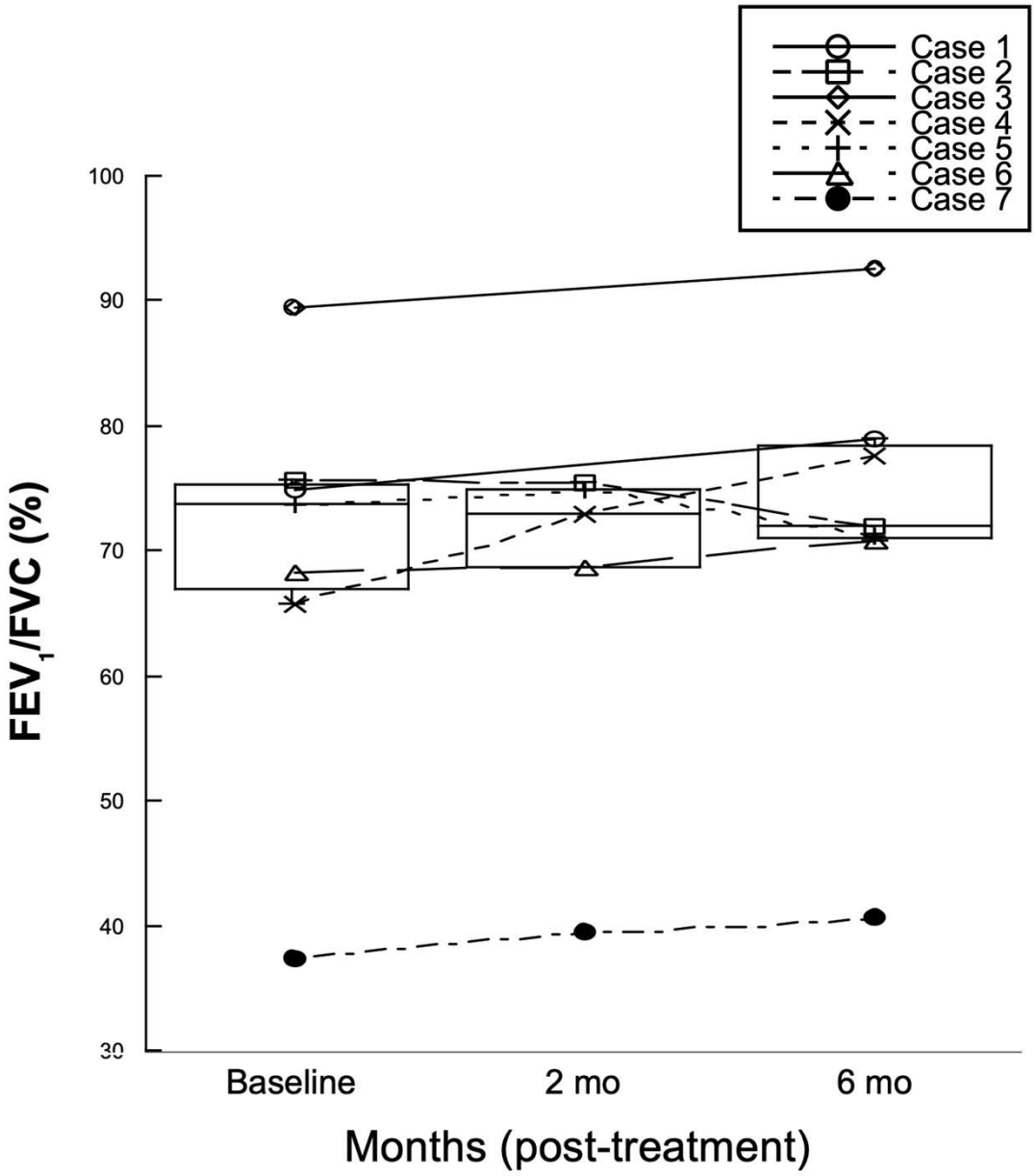

150
100
50
0
FeNO (ppb)
Case 1
Case 2
Case 3
Case 4
Case 5
Case 6
Case 7
Baseline
2 mo
6 mo
Months (post-treatment)

Fig. 6


Case 1
Case 2
Case 3
Case 4
Case 5
Case 6
Case 7
100
90
80
70
60
50
40
30
FEV1/FVC (%)
Baseline
2 mo
6 mo
Months (post-treatment)