



Impact of biologics on treatment of CRSwNP

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Management of CRSwNP has changed extensively over the past 20 years¹⁻⁷

Diagnosis of CRSwNP was based solely on **patient symptoms**, with treatment focused on saline lavages, antibiotics, NCS and OCS^{1,2}

A wealth of new research on **diagnosis and treatment of CRSwNP** led to updates to the guidelines¹

Research continued to shed light on the pathophysiology of CRSwNP with guidance published for the **multidisciplinary team**, new **classifications of CRS**, further understanding into **epidemiology and future research needs**⁴

Following the approval of multiple biologics, guidelines were updated to reference **biologics** with suggestions on where these may fit into the **treatment paradigm**^{6,7}

A FOCUS ON DIAGNOSIS AND TREATMENT

ENTERING INTO THE BIOLOGIC ERA OF RESEARCH

Pre 2000s

2005

2007

2012

2017

2020

2021
onwards

The **first-ever EPOS position paper** was published, focusing on evidence regarding what was understood around CRSwNP¹

This included clearer guidelines on the **definition, diagnosis and treatment of CRSsNP and CRSwNP**, which included definitions for **difficult-to-treat rhinosinusitis, control and disease and rhinosinusitis in children**³

Research then focused on more **targeted treatments for CRSwNP** and the first biologic for CRSwNP was approved in 2019⁵

CRS, chronic rhinosinusitis; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; EPOS, European position paper on rhinosinusitis and nasal polyps; ICS, inhaled corticosteroids; NCS, nasal corticosteroids; OCS, oral corticosteroids.

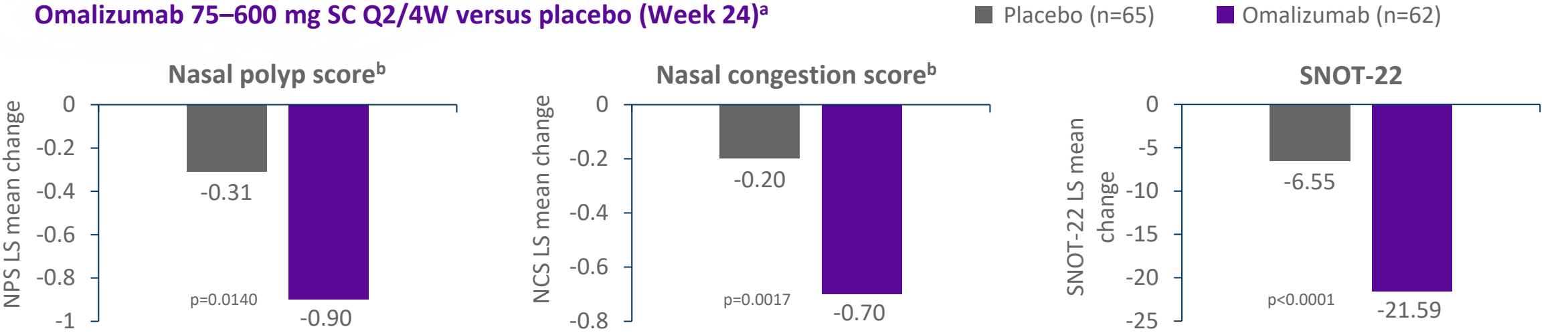
1. Fokkens W, et al. *Rhinol.* 2007;45:97–101; 2. Mullol J. *Otolaryngol Pol.* 2009;63(7):3–4; 3. Fokkens W, et al. *Rhinol.* 2012;50(1):1–12; 4. Fokkens W, et al. *Rhinol.* 2020;58(2):82–111; 5. Sanofi. Dupixent® (dupilumab). SmPC. https://www.ema.europa.eu/en/documents/product-information/dupixent-epar-product-information_en.pdf. Last updated 20 April 2026. Accessed 20 April 2026; 6. Fokkens W, et al. *Rhinol.* 2023;61(3):194–202; 7. Orlandi RR, et al. *Int Forum Allergy Rhinol.* 2021;11(3):213–739.

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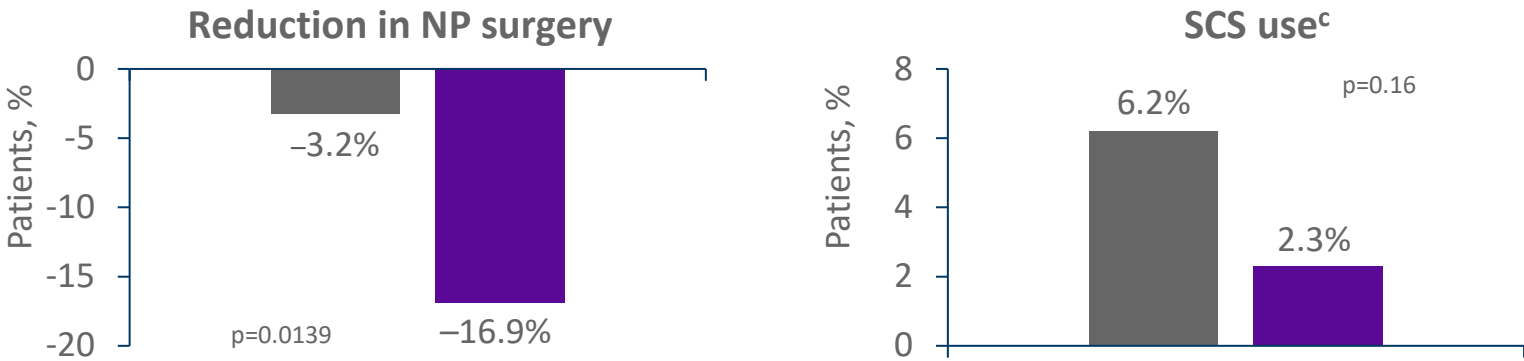
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Early biologic approaches targeting IgE addressed a single component of type 2 inflammation and offered effective clinical outcomes versus placebo¹

Omalizumab 75–600 mg SC Q2/4W versus placebo (Week 24)^a



Objective	To determine the efficacy and safety of omalizumab in CRSwNP in Phase 3 POLYP 1 (N=138) and POLYP 2 (N=127) trials
Trial design	Adults with CRSwNP with inadequate response to intranasal CS were randomised (1:1) to omalizumab or placebo and intranasal mometasone for 24 weeks
Co-primary endpoints	Change from BL to Week 24 in NPS and NCS
Secondary endpoints	Change from BL to Week 24 SNOT-22 score, UPSIT, sense of smell, postnasal drip, runny nose, AEs



Please note that as head-to-head studies were not conducted between biologics, it is inappropriate to draw any comparisons and/or make any conclusions as the study design, demographics and other criteria may be different.

^aSubcutaneous dosing according to body weight and pretreatment serum IgE. ^bCo-primary endpoints. ^cPooled data from POLYP-1 and POLYP-2; placebo, n=130; dupilumab, n=135.

AE, adverse event; BL, baseline; CRSwNP, chronic rhinosinusitis with nasal polyps; CS, corticosteroids; LS, least squares; NCS, nasal congestion score; NP, nasal polyp; NPS, nasal polyp score; Q2/4W, every 2/4 weeks; SC, subcutaneous; SCS, systemic corticosteroids; SNOT-22, Sinonasal Outcome Test-22; UPSIT, University of Pennsylvania Smell Identification Test

1. Gevaert P, et al. *J Allergy Clin Immunol.* 2020;146(3):595–605.

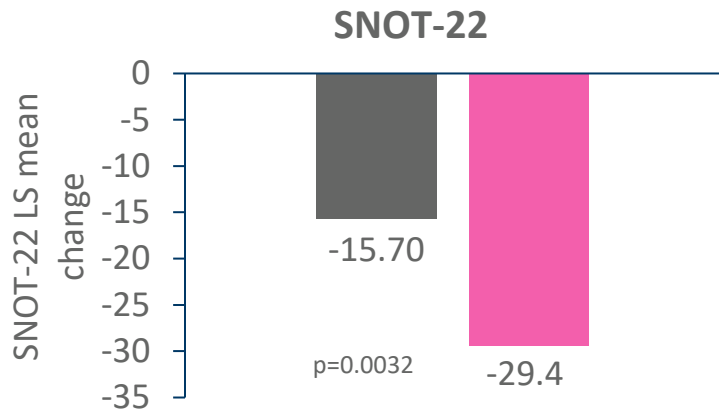
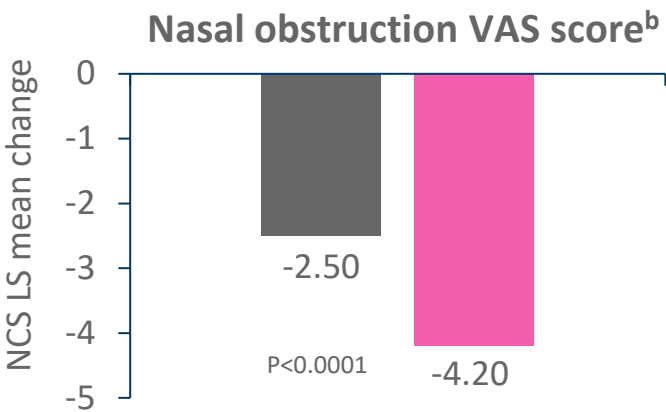
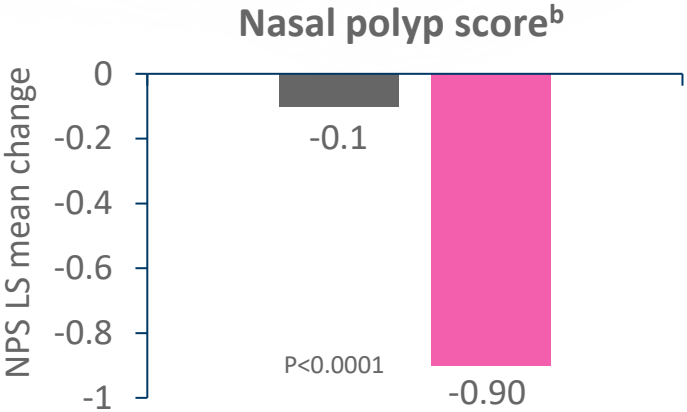
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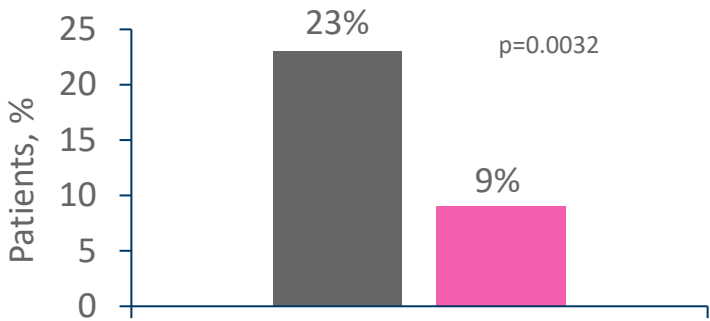
Subsequent targeting of IL-5 reduced eosinophilic inflammation and improved outcomes versus placebo¹

Mepolizumab 100 mg SC Q4W versus placebo (Week 52)^a

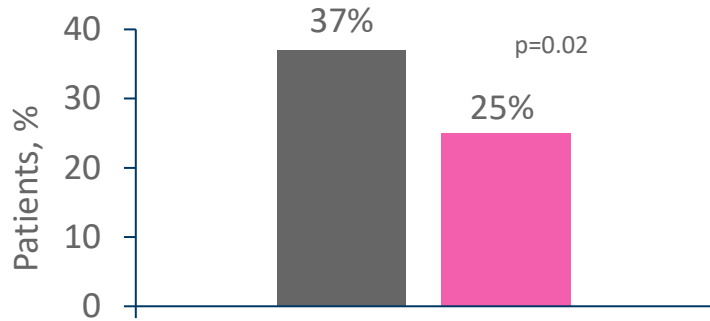
■ Placebo (n=201) ■ Mepolizumab (n=206)



Requirement for surgery



SCS use



Objective	To assess the efficacy and safety of mepolizumab in adults with recurrent, refractory, severe, bilateral CRSwNP
Trial design	Patients were randomised to mepolizumab 100 mg SC or placebo Q4W in addition to standard of care for 52 weeks
Co-primary endpoints	Change from BL in total endoscopic NPS at Week 52 and mean nasal obstruction VAS score (Weeks 49–52) in the ITT population
Secondary endpoints	Included: time to first nasal surgery until Week 52; proportion of patients requiring systemic CS for nasal polyps until Week 52 ^c

Please note that as head-to-head studies were not conducted between biologics, it is inappropriate to draw any comparisons and/or make any conclusions as the study design, demographics and other criteria may be different.

^aPatients received mepolizumab 100 mg SC Q4W or placebo in addition to standard of care for 52 weeks following a 4-week run-in period. ^bCo-primary endpoints. ^cAdditional secondary endpoints included: change from baseline in: mean overall VAS symptom score during weeks 49–52; SNOT-22 total score at week 52; mean composite VAS score (combining scores for nasal obstruction, nasal discharge, throat mucus, and loss of smell) during weeks 49–52; and mean VAS score for loss of smell during weeks 49–52. BL, baseline; CRSwNP, chronic rhinosinusitis with nasal polyps; ITT, intention-to-treat; LS, least squares; NPS, nasal polyp score; Q4W, every 4 weeks; SC, subcutaneous; SCS, systemic corticosteroids; VAS, visual analogue scale.

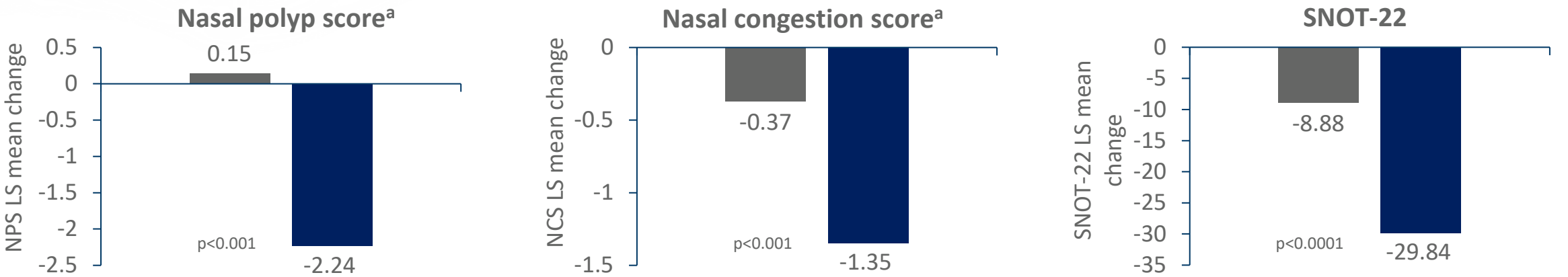
1. Han JK, et al. *Lancet Respir Med.* 2021;9(10):1141–1153.

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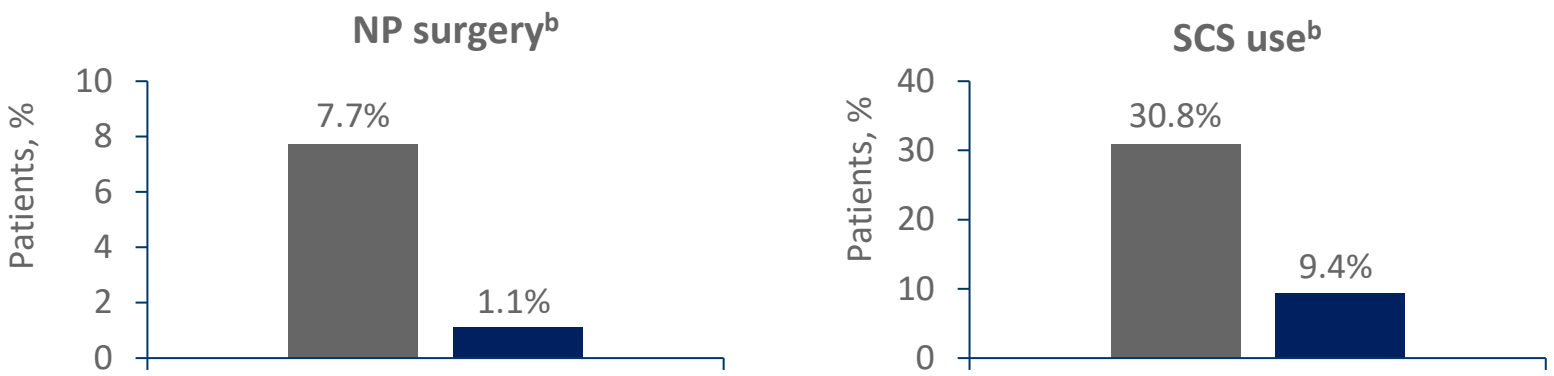
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Targeting IL-4 and IL-13 expanded the impact across type 2 inflammatory pathways and improved outcomes versus placebo^{1,2}

Dupilumab 300 mg SC Q2W vs placebo (Week 52)^{1,2}



Objective	To assess the efficacy and safety of dupilumab in adults with CRSwNP despite prior therapy with systemic CS, surgery, or both
Trial design	Patients with bilateral CRSwNP and symptoms despite SCS use or surgery, with or without comorbid asthma, were randomized in SINUS-24 and SINUS-52. SINUS-24: dupilumab 300 mg SC or placebo Q2W weeks for 24 weeks. SINUS-52: dupilumab 300 mg SC Q2W for 52 weeks, dupilumab Q2W for 24 weeks and then Q4W for 28 weeks, or placebo Q2W for 52 weeks
Co-primary endpoints	Change from BL in endoscopic NPS and nasal congestion severity ^b at week 24
Secondary endpoints	Included: Change from BL at week 24 in sinus opacification (Lund-Mackay CT ^c); patient-reported total symptom score ^d ; daily loss of smell/smell impairment; SNOT-22 score; UPSIT smell test



Please note that as head-to-head studies were not conducted between biologics, it is inappropriate to draw any comparisons and/or make any conclusions as the study design, demographics and other criteria may be different

^aCo-primary endpoints. ^bPooled data from SINUS-24 and SINUS-52; placebo, n=286; dupilumab, n=438; individual NP surgery or SCS use p-value was not reported; combined proportion of patients requiring SCS of NP surgery: placebo=33.9%, dupilumab=9.6%; p<0.0001.²

^bBased on monthly average of daily score recorded by patients. ^cLund-Mackay CT scores was the third coprimary endpoint in Japan. ^dComposite severity score consisting of the sum of daily symptoms of nasal congestion, loss of smell, and anterior or posterior rhinorrhoea.

CRSwNP, chronic rhinosinusitis with nasal polyps; LS, least squares; NCS, nasal congestion score; NP, nasal polyp; NPS, nasal polyp score; Q2W, every 2 weeks; SC, subcutaneous; SCS, systemic corticosteroid.

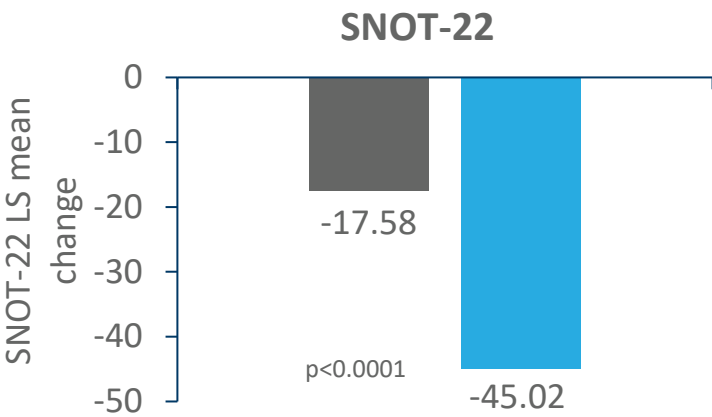
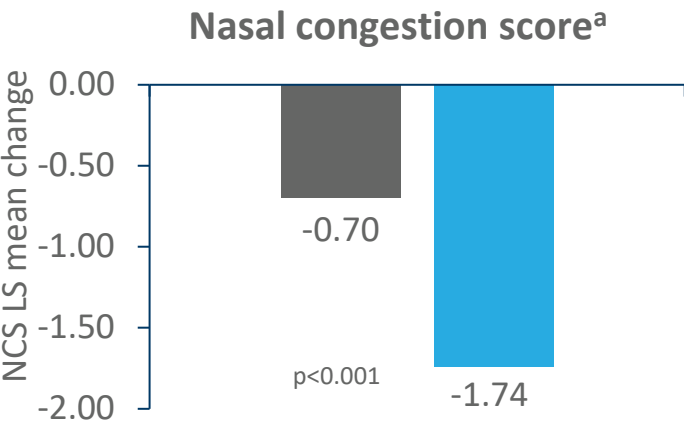
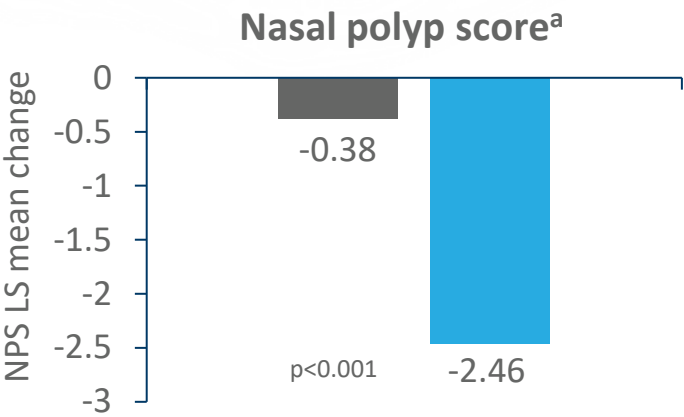
1. Sanofi. Dupixent® (dupilumab). SmPC. https://www.ema.europa.eu/en/documents/product-information/dupixent-epar-product-information_en.pdf. Last updated 20 April 2026. Accessed 20 April 2026; 2. Bachert C, et al. *Lancet*. 2019;394(10209):1638– 1650 and suppl app.. Z4-89222 | Date of preparation: September 2026. © 2026 AstraZeneca. All Rights Reserved. This information is intended for healthcare professionals only.

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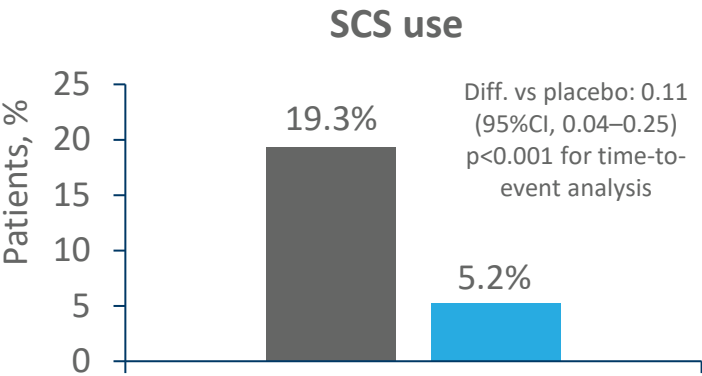
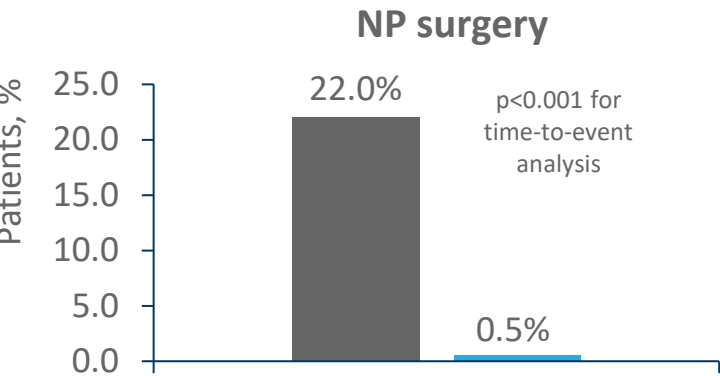
Targeting upstream TSLP expands the impact across multiple type 2 pathways (IL-4, IL-5, IL-13) and beyond to improve outcomes versus placebo¹

Tezepelumab 210 mg SC Q4W vs placebo (Week 52)¹

■ Placebo (n=203) ■ Tezepelumab (n=205)



Objective	To assess the efficacy and safety of tezepelumab in patients with severe, uncontrolled CRSwNP
Trial design	Patients were randomized (1:1) to tezepelumab 210 mg or placebo SC Q4W for 52 weeks. Patients who completed treatment entered a 12- or 24-week FU to assess the durability of efficacy and safety.
Co-primary endpoints	Change from BL in total NPS and mean NCS at week 52
Secondary endpoints	Included: Change from BL at week 52 in mean loss-of-smell score; SNOT-22 total score; Lund–Mackay score; first decision to treat with surgery or use of systemic glucocorticoids (or both) over 52 weeks; and total symptom score



Please note that as head-to-head studies were not conducted between biologics, it is inappropriate to draw any comparisons and/or make any conclusions as the study design, demographics and other criteria may be different. Tezepelumab is not a Co-primary endpoints. indicated for the treatment of CRSwNP.

CRSwNP, chronic rhinosinusitis with nasal polyps; LS, least squares; NCS, nasal congestion score; NP, nasal polyp; NPS, nasal polyp score; Q4W, every 4 weeks; SC, subcutaneous; SCS, systemic corticosteroids; SNOT-22, Sino-Nasal Outcome Test-22.

1. Lipworth BJ, et al. *N Engl J Med*. 2025;392:1178–1188.

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Emerging evidence from key clinical trials

Emerging evidence has uncovered how epithelial cytokines act directly back on the epithelium, thereby creating a cycle of damage¹⁻³

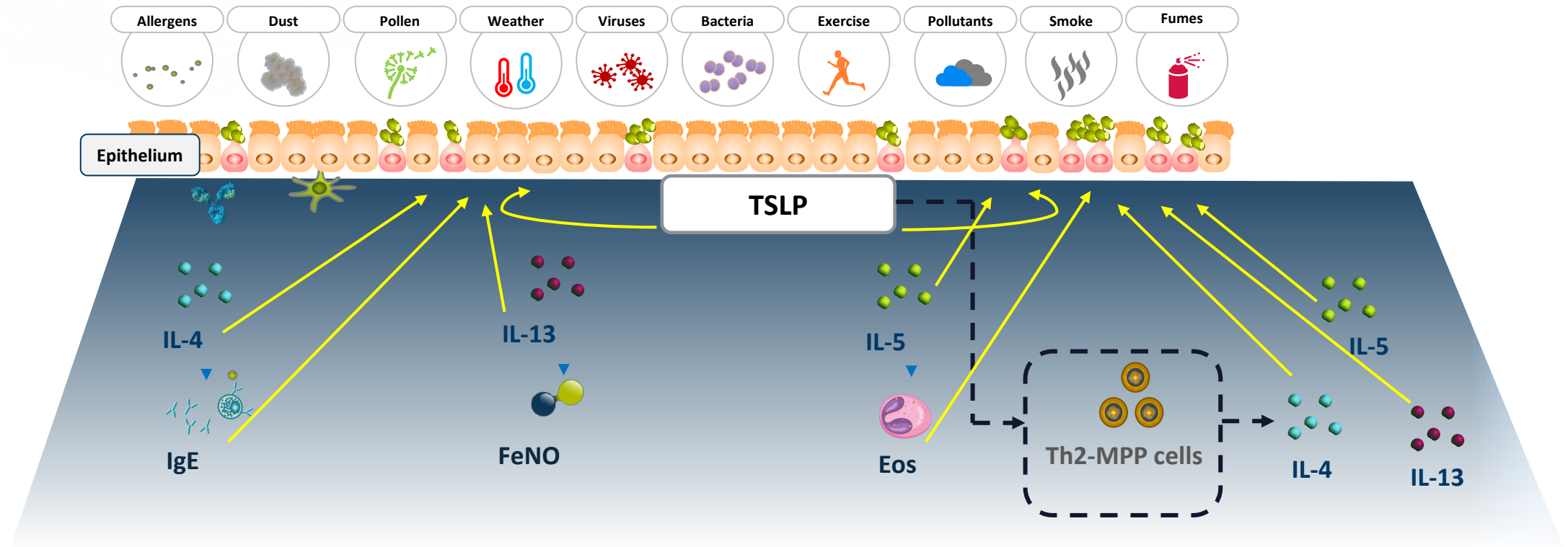


Figure adapted from Caminati M, et al. *Allergy*. 2024;79:1134–1145; and Merrill T and Kanaan A. *Clin Interv Aging*. 2022;17:685–698.

CRSwNP, chronic rhinosinusitis with nasal polyps; Eos, eosinophils; FeNO, fractional exhaled nitric oxide; IgE, immunoglobulin E; IL, interleukin; Th2-MPP, T helper 2-multipotent progenitor; TSLP, thymic stromal lymphopoietin.

1. Merrill T and Kanaan A. *Clin Interv Aging*. 2022;17:685–698; 2. Han J, et al. *J Allergy Clin Immunol*. 2025;155(2):AB442; 3. Kratchmarov R, et al. *Nat Immunol*. 2024;25(5):902–915.

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Targeting TSLP may help restore epithelial health by addressing multiple downstream pathways (IL-5, IL-4, IL-13)¹

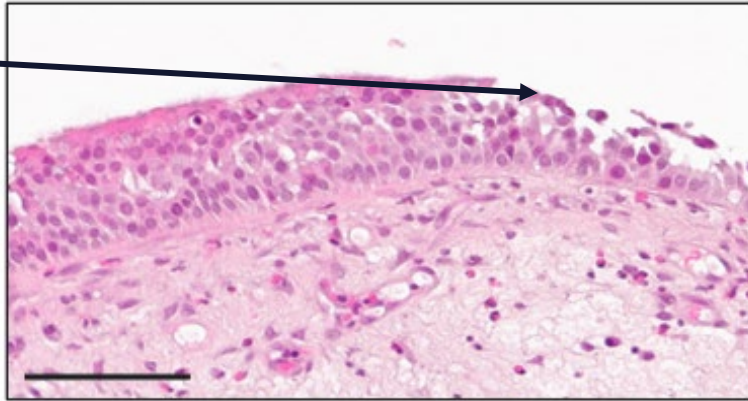
Blocking TSLP has been found to reduce eosinophils, FeNO and IgE versus placebo

Baseline

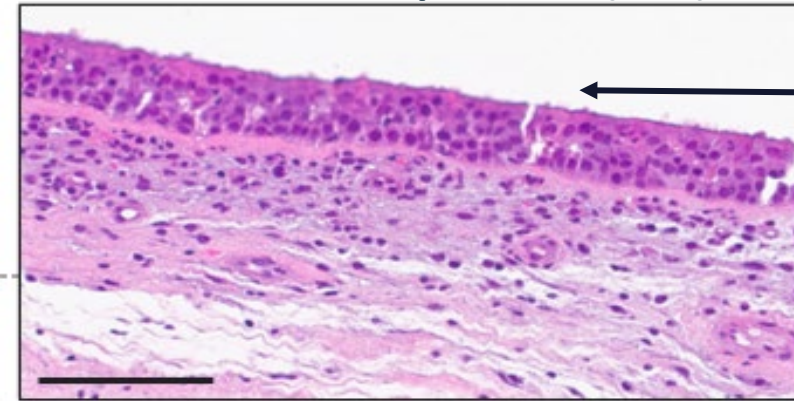
Week 52 of Tezepelumab (EOT)

Patchy AW
epithelial
damage

H&E

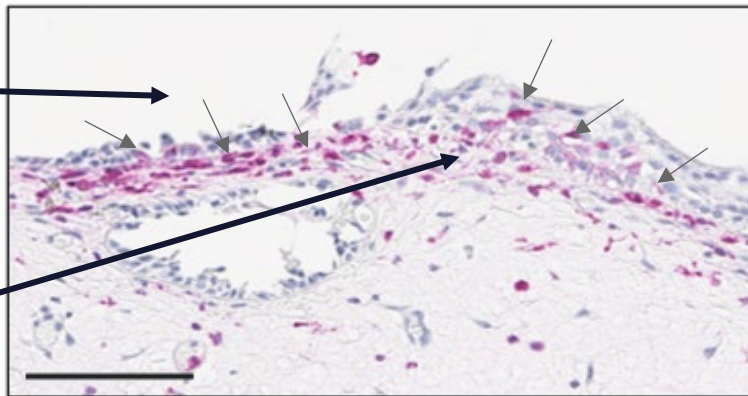


Lack of patchy
epithelium and
denudation

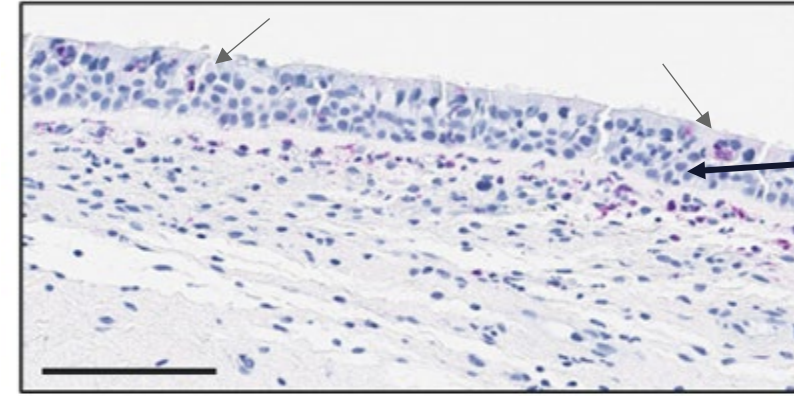


Large area of
epithelial
denudation

NP EDN



Improved
epithelial
integrity



Small arrows point to EDN

Representative images from one tezepelumab-treated patient at baseline and at EOT; the bar in the lower left of the images is equal to 100 μ m.

AW, airway; CRSwNP, chronic rhinosinusitis with nasal polyps; EDN, eosinophil-derived neurotoxin; EOT, end of treatment; H&E, haematoxylin and eosin; NP, nasal polyp; TSLP, thymic stromal lymphopoietin.

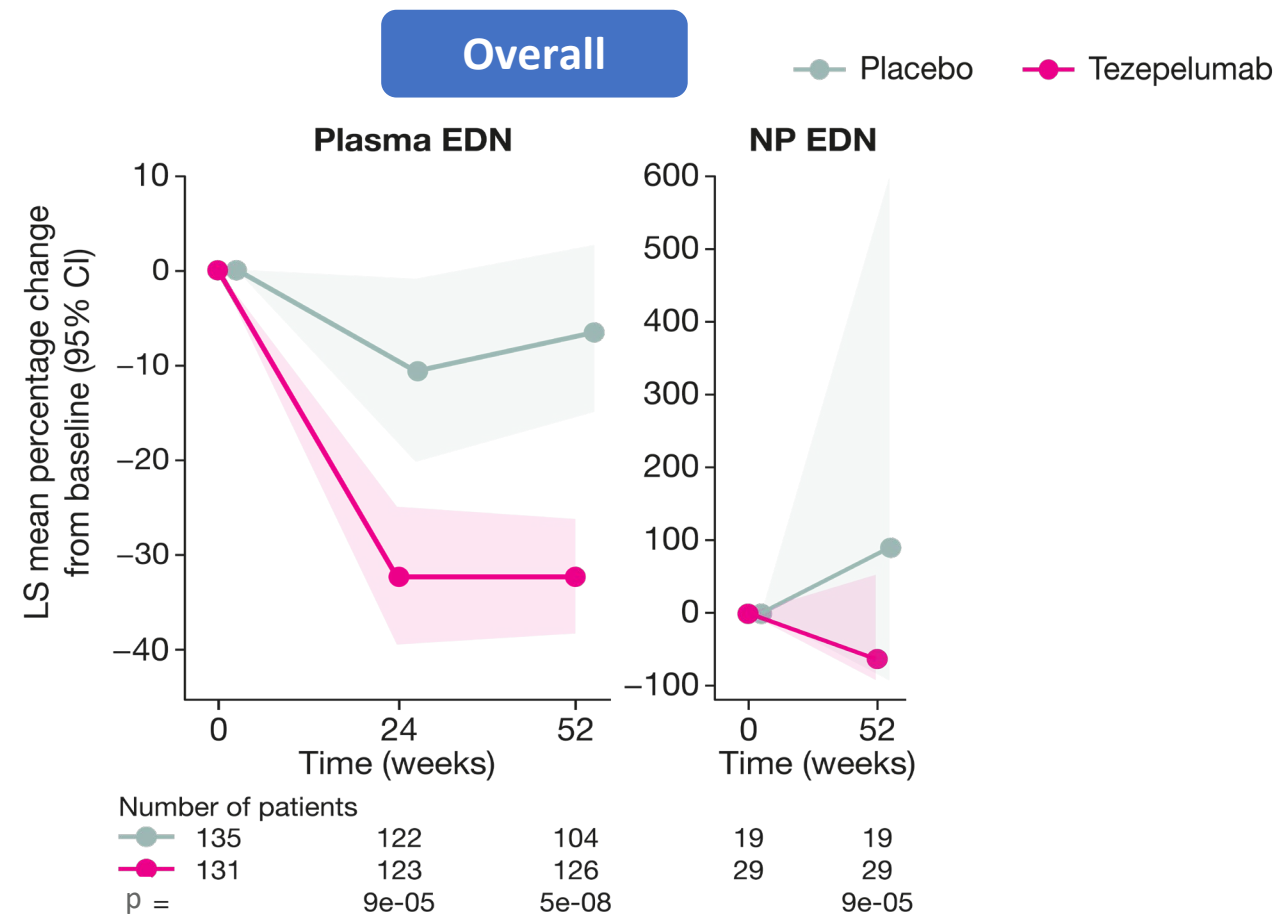
1. Lipworth BJ, et al. ERS Congress, Amsterdam, 27 September–1 October 2025. OA2336.

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Consistent with this, tezepelumab reduces systemic and tissue biomarkers of inflammation in CRSwNP¹

NP



The ‘comorbid asthma’ subpopulation also includes patients with non-steroidal anti-inflammatory-drug-exacerbated respiratory disease. Geometric LS mean change from baseline in IHC-positive cells/mm² between treatment arms was analysed using a Gaussian (parametric) linear regression model, with region, history of NP surgery and comorbidity status as covariates. P-values refer to the test of systematic difference between treatment arms in terms of change from baseline. CI, confidence interval; CRSwNP; chronic rhinosinusitis with nasal polyps; EDN, eosinophil-derived neurotoxin; IHC, immunohistochemistry; LS, least squares; NP, nasal polyp.

1. Lipworth BJ, et al. ERS Congress, Amsterdam, 27 September–1 October 2025. OA2336.

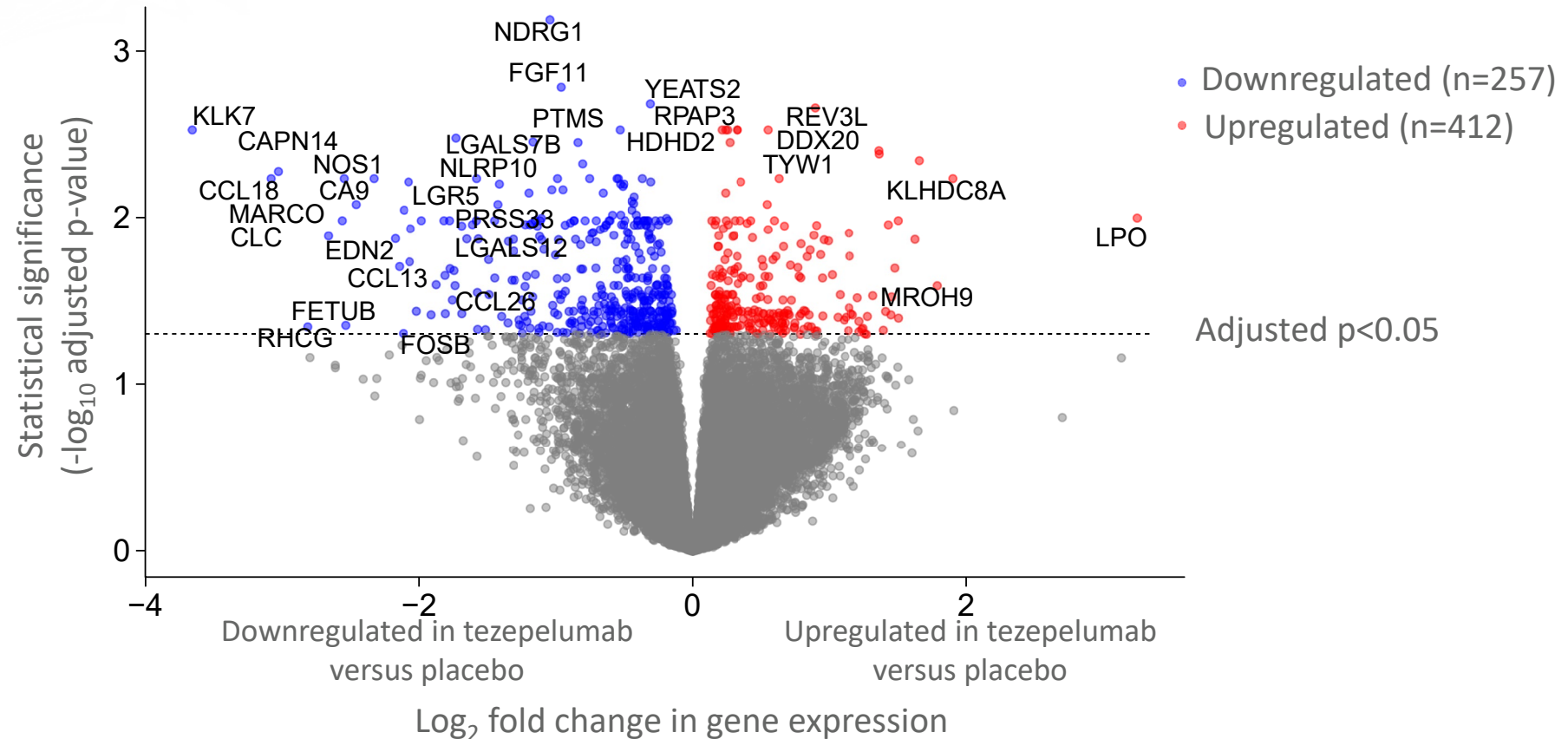
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Further analysis shows that targeting TSLP impacts broad gene expression pathways in nasal polyp tissue¹

- In WAYPOINT, adults with uncontrolled CRSwNP were randomized 1:1 to receive tezepelumab 210 mg or placebo SC Q4W for 52 weeks¹
- RNA sequencing was performed on 198 NP tissue samples obtained from 134 patients at baseline and week 52¹

Tezepelumab significantly altered expression of **669 genes** versus placebo¹



These data suggest that targeting TSLP influences multiple biological pathways at the tissue level

CRSwNP, chronic rhinosinusitis with nasal polyps; Q4W, every 4 weeks; RNA, ribonucleic acid; SC, subcutaneous; TSLP, thymic stromal lymphopoietin.

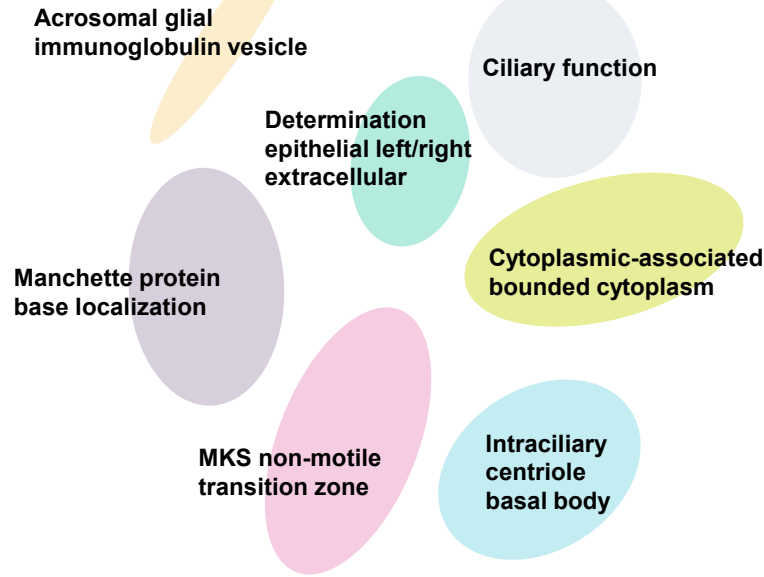
1. Lipworth BJ, et al. AAAAI Annual Scientific Meeting, Philadelphia, 27 February–2 March 2026. Poster 255.

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Indeed, these gene expression changes indicate modulation of multiple biological pathways associated with nasal polyp pathophysiology and epithelial health¹

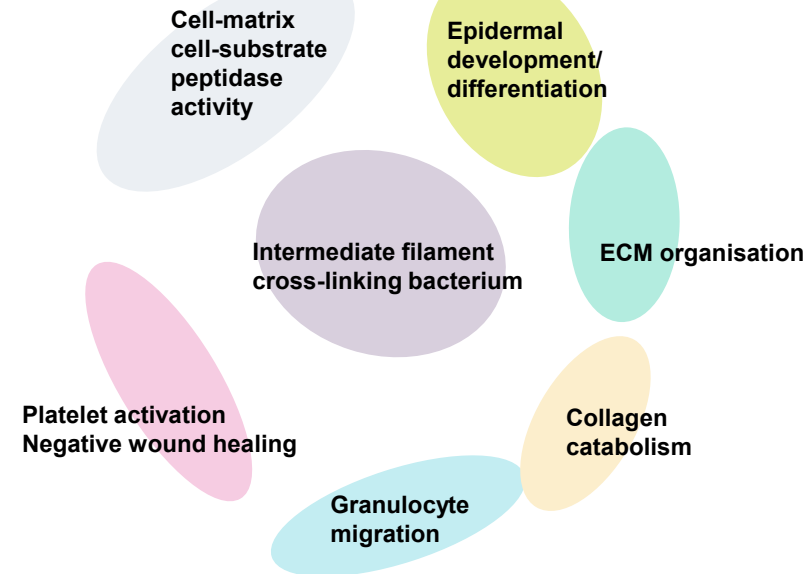
Pathways upregulated in tezepelumab versus placebo



Upregulated pathways¹

- Ciliary structure and function
- Epithelial differentiation and barrier-related processes
- Tissue remodelling and extracellular matrix organisation
- Immune cell migration and inflammatory responses
- Wound healing and repair mechanisms

Pathways downregulated in tezepelumab versus placebo



Downregulated pathways¹

- Microtubule and axoneme organisation
- Epithelial motility processes

TSLP, thymic stromal lymphopoietin.

1. Lipworth BJ, et al. AAAAI Annual Scientific Meeting, Philadelphia, 27 February–2 March 2026. Poster 255.

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With this in mind, what does epithelial health mean for patients with CRSwNP?

Translating epithelial dysfunction into patient impact



Healthy epithelium¹

- Intact barrier function
- Effective mucociliary clearance
- Regulated innate and adaptive immune signalling
- Balanced tissue repair and regeneration

Epithelial dysfunction in CRSwNP²

- Barrier disruption and increased permeability
- Impaired mucociliary clearance and increased exposure to environmental triggers
- Dysregulated T2 inflammation driven by epithelial cytokines
- Persistent inflammation with aberrant tissue repair and remodelling

Patient impact³

- Chronic inflammation and polyp formation
 - Nasal obstruction and congestion
- Recurrent symptoms and exacerbations
 - Olfactory dysfunction and reduced quality of life

Epithelial dysfunction doesn't just initiate disease, it drives ongoing cycles of damage and exacerbation⁴

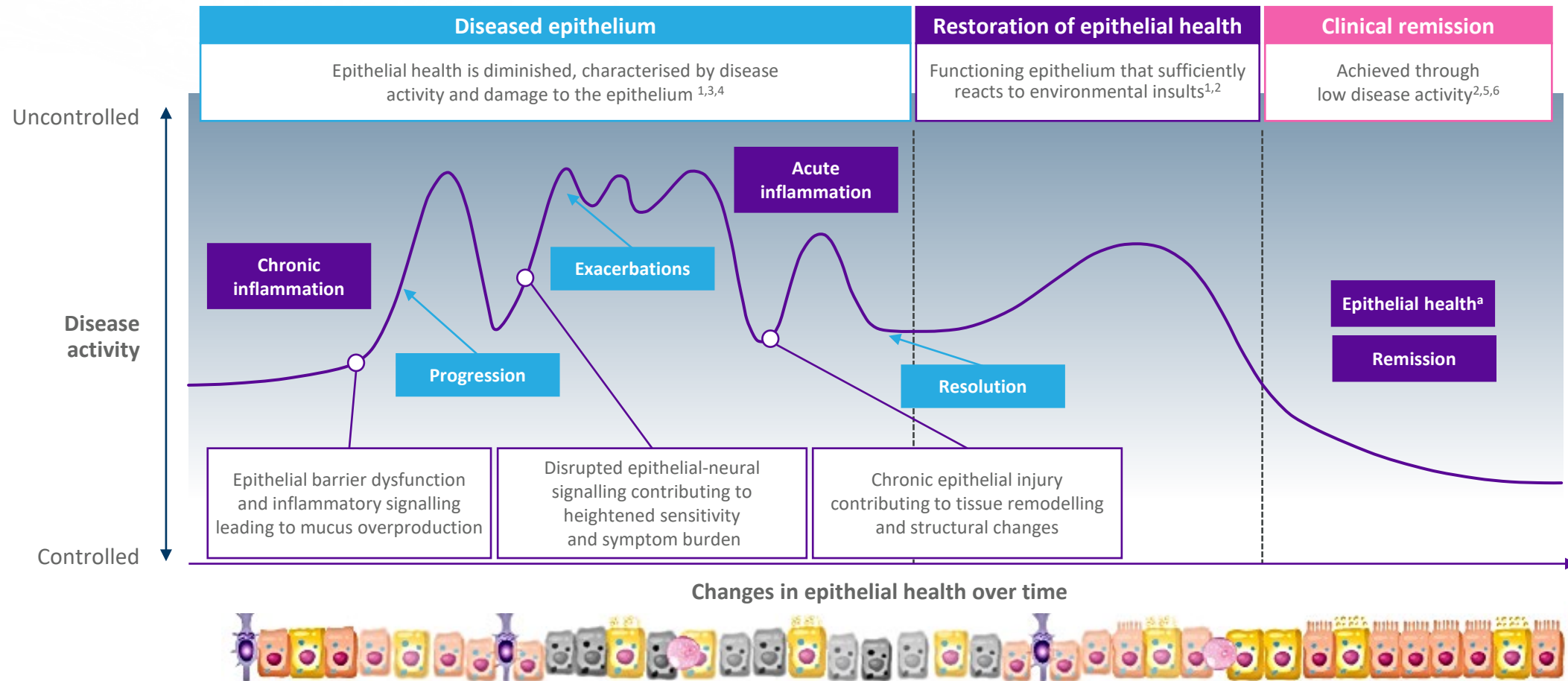
CRSwNP, chronic rhinosinusitis with nasal polyps; T2, type 2.

1. Ha J and Cho H. *Int J Mol Sci.* 2023;24(18):14229; 2. Kato A, et al. *J Allergy Clin Immunol.* 2022;149:1491–1503; 3. Claes N, et al. *Front Allergy.* 2021;2:761388; 4. Hellings PW and Steelant B. *J Allergy Clin Immunol.* 2020;145:1499–1509.

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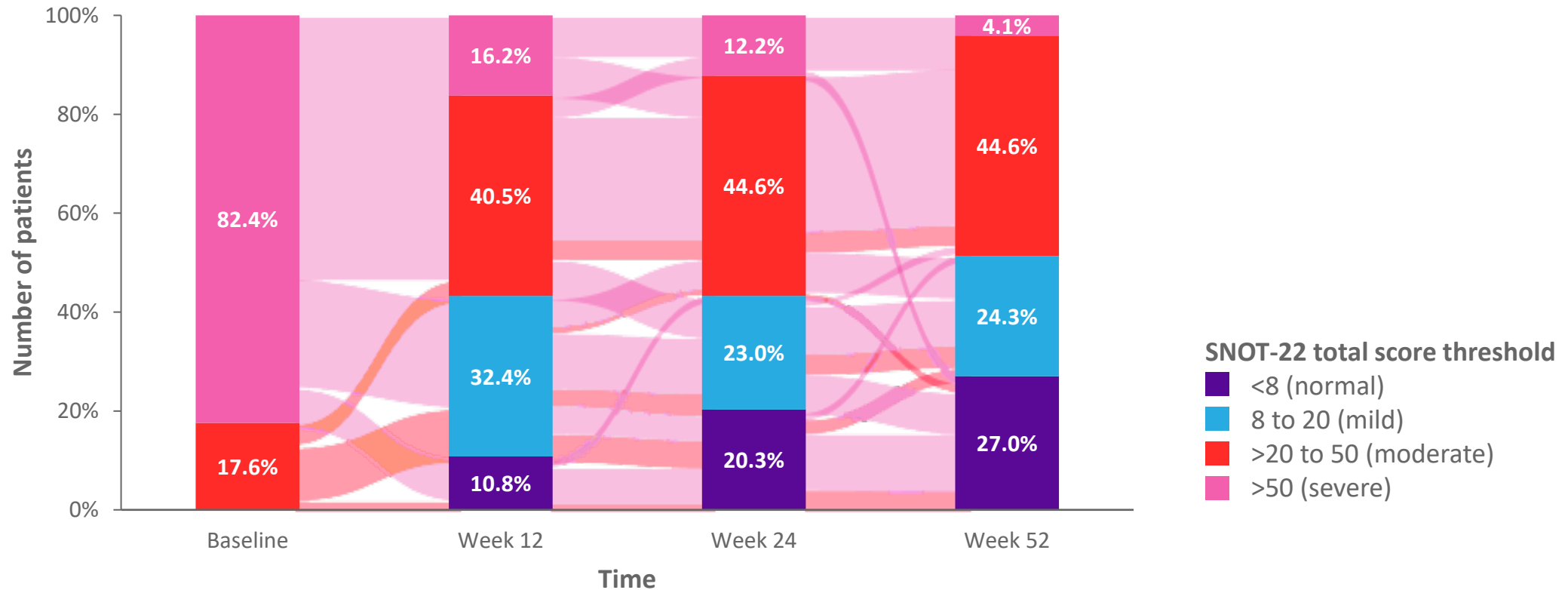
Restoring epithelial health by reducing epithelial-driven inflammation and cycles of epithelial damage could lead to clinical remission^{1,2}



^aThe extent to which epithelial health is restored in remission is still to be fully elucidated;^{2,7} however, it has been proposed that normalisation of underlying pathology, including epithelial function, is essential for complete remission.^{2,8}
1. Russell RJ, et al. *Eur Respir J.* 2024;63:2301397; 2. Brightling CE, et al. *Eur Respir Rev.* 2024;33:240221; 3. Heijink IH, et al. *Allergy.* 2020;75:1902–1917; 4. Porsbjerg C, et al. *Lancet.* 2023;401:858–873; 5. Vatrella A, Maglio A. *Expert Rev Respir Med.* 2025;19:1–5; 6. Fokkens WJ, et al. *Rhinol.* 2024;62:287–298; 7. Carpaij OA, et al. *Pharmacol Ther.* 2019;201:8–24; 8. Thomas D, et al. *Eur Respir J.* 2022;60:2102583.

Targeting epithelial-driven inflammation minimises disease activity and normalises symptom burden in CRSwNP¹

Proportion of patients with CRSwNP treated with tezepelumab with SNOT-22 total scores within the thresholds of normal, mild, moderate or severe at baseline, Weeks 12, 24 and 52 of treatment



CRSwNP, chronic rhinosinusitis with nasal polyps; SNOT-22, sino-nasal outcome test-22 questionnaire.

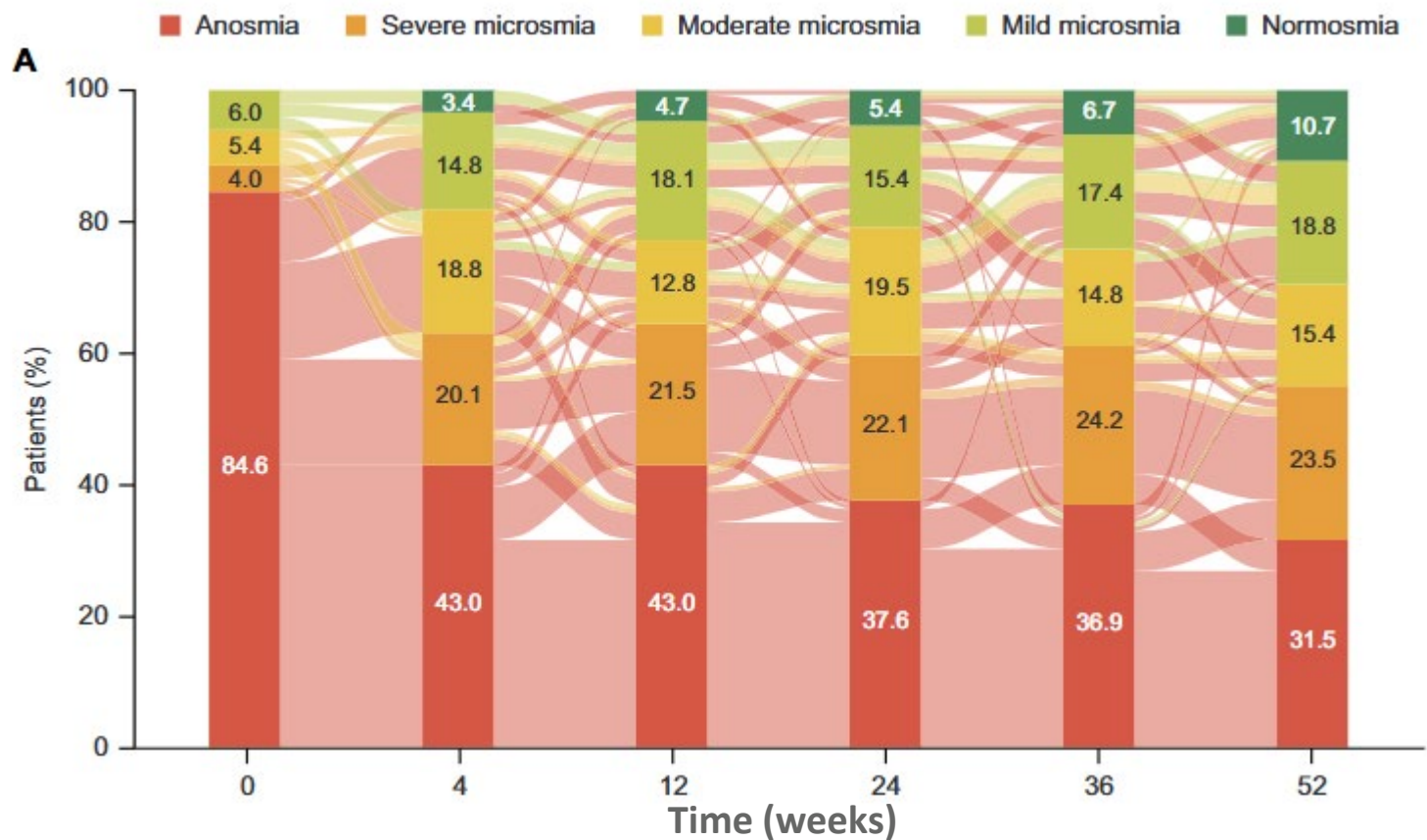
1. Han JK, et al. AAAAI Annual Scientific Meeting, Philadelphia, 27 February–2 March 2026. Poster 240.

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This, in turn, is associated with improvements in olfactory function which may indicate restoration of epithelial health¹

Proportion of patients with CRSwNP treated with tezepelumab (n=149) in each UPSIT olfactory diagnosis category in the overall population over time (in patients with complete data at all time points)



CRSwNP, chronic rhinosinusitis with nasal polyps; SNOT-22, sino-nasal outcome test-22 questionnaire; UPSIT, University of Pennsylvania Smell Identification Test.
1. Mullol J, et al. *Int forum Allergy Rhinol*. 2026. doi: 10.1002/alr.70090. Epub ahead of print.
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Summary

- Despite medical and surgical advances, CRSwNP is a chronic disease that remains difficult to treat^{1–3}
- CRSwNP is characterised by increased epithelial cytokine expression,⁴ with multiple heterogeneous and overlapping inflammatory pathways driven by upstream mediators^{5–9}
- Efficacy and safety data from Phase 3 trials of downstream pathway blockers have demonstrated meaningful improvements in CRSwNP symptoms, polyp size, QoL and progression-related outcomes, with broadly comparable safety^{10,11}

CRSwNP, chronic rhinosinusitis with nasal polyps; QoL, quality of life.

1. Chen S, et al. *Curr Med Res Opin.* 2020;36:1897–1911; 2. Starry A, et al. *Allergy.* 2022;77:2725–2736; 3. De Corso E, et al. *J Pers Med.* 2022;12:897; 4. Chiarella E, et al. *Int J Mol Sci.* 2020;21:6878; 5. Fokkens WJ, et al. *Rhinol.* 2020;58(Suppl S29):1–464; 6. Staudacher AG, et al. *Ann Allergy Asthma Immunol.* 2020;124(4):318–325; 7. Yli ACA, et al. *Allergy.* 2018;73(10):1964–1978; 8. Fokkens W, Reitsma S. *Otolaryngol Clin North Am.* 2023;56(1):1–10; 9. Kato A, et al. *J Allergy Clin Immunol.* 2022;149:1491–1503; 10. Bachert C, et al. *J Allergy Clin Immunol.* 2022;149:1309–1317.e12; 11. Gevaert P, et al. *Lancet.* 2025;405(10482):911–926.

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