

Original Article



Impact of Biologics on Nasal Symptoms in Severe Asthmatics: Findings From the PRISM Study

Ji-Su Shim ,^{1†} Hyunkyoung Kim ,^{2†} Jae-Woo Kwon ,³ So-Young Park ,⁴ Sujeong Kim ,⁵ Byung-Keun Kim ,⁶ Young-Hee Nam ,⁷ Min-Suk Yang ,⁸ Mi-Ae Kim ,⁹ Sae-Hoon Kim ,¹⁰ Byung-Jae Lee ,¹¹ Taehoon Lee ,¹² Sang-Ha Kim ,¹³ Young-Joo Cho ,¹ Sang Min Lee ,¹⁴ Chan Sun Park ,¹⁵ Jae-Woo Jung ,¹⁶ Han-Ki Park ,^{5,17} Joo-Hee Kim ,¹⁸ Jeong-Hee Choi ,¹⁹ Ji-Yong Moon ,²⁰ Kyoung-Hee Sohn ,²¹ Gyu Young Hur ,²² Sang Hoon Kim ,²³ Hye-Kyung Park ,²⁴ Sunyoung Yoon ,²⁵ Hyun Jung Jin ,²⁶ Min-Hye Kim ,^{1*} Tae-Bum Kim ,^{2*} on behalf of the Precision Intervention in Severe Asthma (PRISM) Study Investigators

OPEN ACCESS

Received: Jan 8, 2025

Revised: Jul 4, 2025

Accepted: Sep 1, 2025

Published online: Oct 31, 2025

Correspondence to

Min-Hye Kim, MD, PhD

Department of Internal Medicine, Ewha Womans University College of Medicine, 260 Gonghang-daero, Gangseo-gu, Seoul 07804, Korea.

Tel: +82-2-6986-1642

Fax: +82-2-2655-2076

Email: mineyang81@ewha.ac.kr

Tae-Bum Kim, MD, PhD

Department of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea.

Tel: +82-2-3010-3280

Fax: +82-2-3010-6969

Email: tbkim@amc.seoul.kr

[†]Ji-Su Shim and Hyunkyoung Kim contributed equally to this work.

Copyright © 2025 The Korean Academy of Asthma, Allergy and Clinical Immunology · The Korean Academy of Pediatric Allergy and Respiratory Disease

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

¹Department of Internal Medicine, Ewha Womans University College of Medicine, Seoul, Korea

²Department of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

³Department of Allergy and Clinical Immunology, Kangwon National University School of Medicine, Chuncheon, Korea

⁴Division of Pulmonary, Allergy and Critical Care Medicine, Department of Internal Medicine, Chung-Ang University Gwangmyeong Hospital, Chung-Ang University College of Medicine, Seoul, Korea

⁵Department of Internal Medicine, School of Medicine, Kyungpook National University, Daegu, Korea

⁶Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

⁷Department of Internal Medicine, Dong-A University College of Medicine, Busan, Korea

⁸Department of Internal Medicine, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Seoul, Korea

⁹Department of Pulmonology, Allergy and Critical Care Medicine, CHA Bundang Medical Center, CHA University, Seongnam, Korea

¹⁰Division of Allergy and Clinical Immunology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

¹¹Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

¹²Department of Internal Medicine, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, Korea

¹³Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea

¹⁴Division of Respiratory Disease and Allergy, Department of Internal Medicine, Dankook University College of Medicine, Cheonan, Korea

¹⁵Department of Internal Medicine, Haeundae Paik Hospital, Inje University College of Medicine, Busan, Korea

¹⁶Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul, Korea

¹⁷Division of Allergy and Clinical Immunology, Department of Internal Medicine, Kyungpook National University Chilgok Hospital, Daegu, Korea

¹⁸Department of Internal Medicine, Hallym University Sacred Heart Hospital, Anyang, Korea

¹⁹Department of Pulmonology and Allergy, Hallym University Dongtan Sacred Heart Hospital, Hwaseong, Korea

²⁰Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea

²¹Department of Internal Medicine, Kyung Hee University Medical Center, Seoul, Korea

²²Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Korea

²³Department of Internal Medicine, Nowon Eulji Hospital, Eulji University School of Medicine, Seoul, Korea

²⁴Department of Internal Medicine, Pusan National University Hospital, Pusan National University College of Medicine, Busan, Korea

²⁵Department of Allergy and Pulmonology in Internal Medicine, Chungnam National University, Chungnam National University Sejong Hospital, Sejong, Korea

²⁶Division of Pulmonology and Allergy, Department of Internal Medicine, Yeungnam University Medical Center, College of Medicine, Yeungnam University, Daegu, Korea

ORCID iDs

Ji-Su Shim 
<https://orcid.org/0000-0002-8846-0364>
 Hyunkyoung Kim 
<https://orcid.org/0000-0002-0065-9214>
 Jae-Woo Kwon 
<https://orcid.org/0000-0003-1639-3606>
 So-Young Park 
<https://orcid.org/0000-0002-5224-3077>
 Sujeong Kim 
<https://orcid.org/0000-0002-2494-9216>
 Byung-Keun Kim 
<https://orcid.org/0000-0001-5147-6306>
 Young-Hee Nam 
<https://orcid.org/0000-0001-8759-2982>
 Min-Suk Yang 
<https://orcid.org/0000-0002-9861-0530>
 Mi-Ae Kim 
<https://orcid.org/0000-0003-1253-6075>
 Sae-Hoon Kim 
<https://orcid.org/0000-0002-2572-5302>
 Byung-Jae Lee 
<https://orcid.org/0000-0001-6940-0836>
 Taehoon Lee 
<https://orcid.org/0000-0002-9224-0866>
 Sang-Ha Kim 
<https://orcid.org/0000-0002-1763-5366>
 Young-Joo Cho 
<https://orcid.org/0000-0002-9414-5934>
 Sang Min Lee 
<https://orcid.org/0000-0002-9568-2096>
 Chan Sun Park 
<https://orcid.org/0000-0003-0113-8354>
 Jae-Woo Jung 
<https://orcid.org/0000-0002-3411-735X>
 Han-Ki Park 
<https://orcid.org/0000-0002-5460-9917>
 Joo-Hee Kim 
<https://orcid.org/0000-0002-1572-5149>
 Jeong-Hee Choi 
<https://orcid.org/0000-0002-0599-875X>
 Ji-Yong Moon 
<https://orcid.org/0000-0003-2459-3448>
 Kyoung-Hee Sohn 
<https://orcid.org/0000-0001-8407-8080>
 Gyu Young Hur 
<https://orcid.org/0000-0001-5039-0199>
 Sang Hoon Kim 
<https://orcid.org/0000-0002-4105-0552>
 Hye-Kyung Park 
<https://orcid.org/0000-0003-4065-2962>
 Sunyoung Yoon 
<https://orcid.org/0000-0002-4205-1434>
 Hyun Jung Jin 
<https://orcid.org/0000-0003-2888-420X>
 Min-Hye Kim 
<https://orcid.org/0000-0002-1775-3733>

ABSTRACT

Purpose: The sino-nasal outcome test (SNOT-22) is a patient-reported outcome measure for chronic rhinosinusitis (CRS), assessing treatment response after 6 months of biologic uses in patients with severe CRS. We investigated score changes in each domain of SNOT-22 with biologics in patients with severe asthma.

Methods: A total of 229 patients with severe asthma and nasal symptoms were enrolled from a prospective, observational, multicenter cohort study. After 6 months of treatment with biologics or conventional GINA Step 4–5 management, SNOT-22 changes were evaluated by analyzing total and rhinological, extranasal rhinological, ear/facial, psychological, and sleep domain scores.

Results: The adjusted odds ratio (OR) of being a responder was significantly higher for dupilumab in the total (OR, 2.29; 95% confidence interval [CI], 1.08–4.87), extranasal rhinological (OR, 2.80; 95% CI, 1.20–6.56), physiologic (OR, 2.23; 95% CI, 1.03–4.83), and sleep dysfunction (OR, 2.50; 95% CI, 1.14–5.47) domain scores of SNOT-22 than those for conventional or anti-interleukin (IL)-5 antibody treatment. After adjusting for the history of CRS diagnosis, dupilumab users had higher ORs for total SNOT-22 (OR, 2.20; 95% CI, 1.02–4.77) and extranasal rhinological (OR, 2.77; 95% CI, 1.16–6.60) scores. When SNOT-22 was plotted by the type of treatment at 0, 1, and 6 months, an overall trend of decreased total/domain scores of SNOT-22 was observed in the biologic-treated group compared to the conventional group, with the most pronounced decrease in dupilumab-treated group.

Conclusions: Dupilumab demonstrates a significant improvement not only in total SNOT-22 scores but also in the extranasal rhinological, physiologic, and sleep dysfunction domain scores compared to conventional or anti-IL-5 treatment in patients with severe asthma and nasal symptoms.

Keywords: Asthma; rhinosinusitis; monoclonal antibodies; sino-nasal outcome test-22; treatment outcome

INTRODUCTION

Chronic rhinosinusitis (CRS) is an inflammatory disease of the nose and paranasal sinuses lasting more than 12 weeks.¹ The diagnostic criteria include nasal symptoms such as nasal blockage, obstruction, congestion, or nasal discharge, in addition to either facial pain/pressure or reduction/loss of smell, showing either 1) characteristic nasal endoscopic findings such as nasal polyps (NPs), and/or mucopurulent discharge, or edematous mucosal changes leading to obstruction primarily in the middle meatus or 2) mucosal changes within the ostiomeatal complex and/or sinuses on computed tomography scans.¹ CRS affects 5%–12% of the general population and is generally divided into 2 phenotypes: with NPs (CRSwNP) or without NPs.^{1,2} Patients with CRSwNP have poorer quality of life (QoL) and more comorbidities such as asthma, bronchiectasis, and non-steroidal anti-inflammatory drug-exacerbated respiratory disease.³ Severe uncontrolled CRSwNP has been treated with a combination of medical therapy, surgical interventions, and, more recently, biologics.^{3,4}

According to the 2023 European Position Paper on Rhinosinusitis and NPs/European Forum for Research and Education in Allergy and Airway Diseases update, biologics such as omalizumab, dupilumab, and mepolizumab can be considered for patients with bilateral NPs and previous sinus surgery if they meet at least 3 out of the following 5 criteria: 1) evidence

Tae-Bum Kim 
<https://orcid.org/0000-0001-5663-0640>

Disclosure

There are no financial or other issues that might lead to conflict of interest.

of type 2 (T2) inflammation, represented by tissue eosinophils $\geq 10/\text{HPF}$, blood eosinophils $\geq 150/\mu\text{L}$, or total immunoglobulin E (IgE) $\geq 100 \text{ kU/mL}$; 2) requirement for systemic corticosteroids at least twice per year or long-term low-dose oral corticosteroids for ≥ 3 months; 3) severe QoL impairment with 22-item sino-nasal outcome test (SNOT-22) score ≥ 40 ; 4) loss of smell; and 5) concomitant asthma.^{4,5} The response should be evaluated after 6 months of biologics treatment, and the SNOT-22 is a key measure for assessing symptom changes before and after treatment due to its ease of use.⁴

The SNOT-22 is a widely used, validated questionnaire comprising 5 symptom domains for assessing disease-specific QoL in patients with CRS.⁶ It is also commonly used to monitor symptom progression over time, to evaluate response to medical treatments, and to support longitudinal assessment in both clinical and research settings.⁷ In this study, we investigated changes in SNOT-22 scores across the 5 domains in adult patients with asthma requiring GINA Step 4–5 treatment over 6 months of either conventional treatment or biologics. We compared the differences in treatment outcomes between conventional and biologic treatments, as well as among different types of biologics.

MATERIALS AND METHODS

Study protocols

We used data from the Precision Medicine Intervention in Severe Asthma (PRISM) study, which is an ongoing prospective study that began in May 2020 and is an observational, multicenter cohort study of patients with severe asthma from severe asthma clinics in South Korea (38 centers) and the United Kingdom (3 centers).⁸ The PRISM study enrolled adult patients with a diagnosis of asthma from an allergist or pulmonologist and classified as having severe asthma according to the European Respiratory Society/American Thoracic Society criteria published in 2014.⁹ Patients were included if they required GINA Step 4–5 treatment or systemic corticosteroid treatment for more than 50% of the past year, or if they remained uncontrolled despite such treatment.⁹ Subjects were then categorized as type 2 (T2)-high or T2-low asthma based on skin prick tests, blood eosinophils, sputum eosinophils on induced sputum analysis, and fractional exhaled nitric oxide (FeNO) levels. T2-high asthma was defined as meeting at least one of the following criteria: blood eosinophils $\geq 150/\mu\text{L}$, sputum eosinophils $\geq 2\%$, FeNO level $\geq 20 \text{ ppb}$, and suspected allergic asthma with sensitization to an inhalant allergen.^{8,10}

Study population

Based on phenotyping and discussions between physician and patient, each patient was treated with biologics or other conventional GINA Step 4–5 management. Biologics were administered upon registration following screening and adhering to the recommended dosing and treatment interval guidelines tailored to each pharmaceutical agent and FDA-approved indications in Korea, and study subjects were classified into two groups; subjects who had been treated with pharmacologic treatments without any biologics (conventional group) and those with additional uses of T2-biologics (mepolizumab/reslizumab/dupilumab-used ones; biologics-treated group). The decision to continue, modify, or discontinue biologics was made at the discretion of the treating physician based on asthma control status and individual clinical circumstances, reflecting routine real-world clinical practice rather than a predefined protocol. Follow-up assessments were conducted at baseline, 1, 6, and 12 months, collecting demographic details, comorbidities, asthma phenotype, lung function

tests, bronchodilator (BD) response, blood cell count, induced sputum analysis, FeNO levels, symptom scores, and exacerbation occurrences. All patients who presented with one or more nasal symptoms, such as rhinorrhea, post-nasal drip, nasal obstruction, facial pain or pressure, and hyposmia were enrolled. All participants completed 6 months of follow-up from the PRISM study. For the current analysis, we selected patients from the PRISM cohort who had completed both baseline and 6-month follow-up visits and had available SNOT-22 scores at both time points. Patients were included regardless of their history of CRS diagnosis. This study was approved by the Institutional Review Board of Ewha Womans University Medical Center (SEUMC 2020-04-014-023) and Asan Medical Center (2019-1676).

Variable definitions

The history of CRS diagnosis was defined as patients' self-report of whether they had ever been diagnosed by a doctor. Atopy was identified as positive for inhalant allergens by skin prick test or multiple allergen simultaneous test. Asthma exacerbation was defined as positive if subjects experienced at least one of the following: an unscheduled outpatient visit, an emergency department visit, a hospitalization, or a steroid burst identified through monthly telephone surveys. Steroid burst was defined as the use of a prednisolone dose greater than 30 mg/day or its equivalent for more than 3 consecutive days.

Definition of SNOT-22 responders at 6-month follow-up

Study participants were asked to complete the SNOT-22 every visit, which consists of 22 questions across 5 domains, each scored from 0 to 5, with a total score of 110; lower scores indicate better outcomes.^{6,11} The 22 items are categorized into 5 symptom domains: rhinological symptoms (range, 0–30), extranasal rhinological symptoms (range, 0–15), ear/facial symptoms (range, 0–25), psychological dysfunction (range, 0–35), and sleep dysfunction (range, 0–25; **Supplementary Table S1**).⁷ A secondary analysis of a prospective, multicenter, observational cohort study involving 276 patients with medically refractory CRS who underwent surgical management reported the mean minimal clinically important difference (MCID) for the SNOT-22 total score as 9.0.¹¹ The MCID is defined as the smallest change in an outcome that patients perceive as beneficial. It is a patient-centered metric that reflects both the magnitude of change and its perceived value from the patient's perspective.¹² The average MCID values for the rhinological, extranasal rhinological, ear/facial, psychological, and sleep domain scores were 3.8, 2.4, 3.2, 3.9, and 2.9, respectively.¹¹ We therefore defined SNOT-22 responders as those whose SNOT-22 scores decreased by at least the MCID values after a 6-month follow-up.

Statistical analyses

Descriptive statistics are presented as numbers (%) for categorical variables or mean $\pm$ standard deviation for continuous variables. General characteristics of the study population were assessed using Student's *t*-test for continuous variables and Pearson's χ^2 test for categorical variables. Univariate and multivariate logistic regression models were used to identify the predictive factors for a positive response in total and domain SNOT-22 scores according to the biologics used. To identify potential confounders, adjusted variables included age, sex, the forced expiratory volume in the first second (FEV1; %), and blood eosinophils (cells/ μ L) at baseline. Linear mixed models assessed changes in SNOT-22 scores from baseline to 1 and 6-month time points with age, sex, FEV1 (%), and blood eosinophil count as covariates. Statistically significant difference was defined as a *P* value < 0.05 . All statistical analyses were performed with the SAS (SAS Institute v.9.4, Cary, NC, USA) and the R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

General characteristics

A total of 229 adult patients with severe asthma was enrolled, of which 183 were treated with biologics (30 for mepolizumab, 39 for reslizumab, and 114 for dupilumab) and 46 with conventional treatment. The mean age of the participants was 54.2 ± 10.9 years, the duration of asthma was 11.6 ± 8.7 years, and 49.3% of them had experienced acute asthma exacerbation in the previous 12 months. The prevalence of allergic rhinitis, CRS, and NPs was 71.6%, 47.6%, and 22.7%, respectively. The laboratory results were: eosinophil count of 567.7 ± 547.2 cells/ μ L, total IgE level of 403.3 ± 542.3 kU/L, induced sputum eosinophils of $18.1 \pm 26.1\%$, pre-BD FEV1 of $63.8 \pm 19.4\%$ predicted, and post-BD FEV1 of $67.4 \pm 19.6\%$ predicted (**Table 1**). When comparing responders and non-responders by each SNOT-22 domain score after 6 months of biologic or conventional treatment, self-medication of steroid bursts was significantly higher in extranasal rhinological responders (47.5% vs.

Table 1. Characteristics of the study subjects

Variables	Total (n = 229)
Age (yr)	54.2 ± 10.9
Male	107 (46.7)
BMI (kg/m ²)	25.0 ± 4.1
Smoking history	
Never-smoker	109 (47.6)
Ex-smoker	98 (42.8)
Current smoker	22 (9.6)
Asthma onset age (yr)	40.8 ± 14.0
Duration of asthma (yr)	11.6 ± 8.7
History of AE during last year	
Unscheduled visit to outpatient clinic	54 (23.6)
Unscheduled visit to ED	32 (14.0)
Hospitalization	30 (13.1)
ICU admission	1 (0.4)
Self-medication with steroid bursts	85 (37.1)
OCS maintenance	76 (33.2)
Previous use of biologics	74 (32.3)
Comorbidities	
Allergic rhinitis	164 (71.6)
Chronic rhinosinusitis	109 (47.6)
Nasal polyps	52 (22.7)
Asthma control status	
Partly controlled	94 (41.1)
Uncontrolled	96 (41.9)
Controlled	35 (15.3)
Atopy	95 (41.5)
Laboratory findings	
WBC ($10^3/\mu$ L)	8.0 ± 2.5
Eosinophils (cells/ μ L)	567.8 ± 547.2
Total IgE (kU/L)	403.3 ± 542.3
FeNO (ppb)	64.2 ± 52.2
Induced sputum eosinophil (%)	18.1 ± 26.1
Lung functions	
Pre-BD FEV1 (%)	63.8 ± 19.4
Pre-BD FEV1/FVC	0.65 ± 0.14
Post-BD FEV1 (%)	67.4 ± 19.6
Post-BD FEV1/FVC ratio	0.67 ± 0.14

Data are presented as number (%) or mean $\pm$ standard deviation.

BMI, body mass index; AE, acute exacerbation; ED, emergency department; ICU, intensive care unit; OCS, oral corticosteroids; WBC, white blood cell; IgE, immunoglobulin E; FeNO, fractional exhaled nitric oxide; BD, bronchodilator; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

31.3%, $P = 0.024$), and the proportion of uncontrolled asthma was significantly higher in rhinological, extranasal rhinological, ear/facial, and psychological responders. Ear/facial responders had a higher rate of atopy (53.0% vs. 36.8%, $P = 0.038$) and higher pre-BD FEV1% ($67.7\% \pm 19.2\%$ vs. $61.7\% \pm 19.3\%$, $P = 0.025$) and higher pre-BD FEV1/FVC (0.68 ± 0.13 vs. 0.63 ± 0.14 , $P = 0.016$). Sleep dysfunction responders also showed higher pre-BD FEV1% ($67.2\% \pm 17.9\%$ vs. $61.7\% \pm 20.1\%$, $P = 0.036$) and pre-BD FEV1/FVC (0.67 ± 0.13 vs. 0.63 ± 0.15 , $P = 0.033$; **Supplementary Table S2**).

Clinical characteristics according to the biologics used

In 69 mepolizumab/reslizumab users, rhinological responders had a higher body mass index (26.3 ± 4.1 vs. 24.2 ± 3.1 kg/m², $P = 0.016$), and higher rates of uncontrolled asthma (65.4% vs. 41.9%, $P = 0.037$) and atopy (57.7% vs. 48.8%, $P = 0.032$). Ear/facial responders had a higher rate of uncontrolled asthma (80% vs. 38.8%, $P = 0.005$) and higher total IgE levels (452.1 ± 535.3 vs. 232.3 ± 199.2 kU/L, $P = 0.035$). Psychological responders had higher rates of uncontrolled asthma (69.3% vs. 39.5%, $P = 0.038$) and atopy (57.7% vs. 48.8%, $P = 0.032$). In sleep dysfunction responders, the onset of asthma symptoms occurred later (44.8 ± 13.1 vs. 37.8 ± 13.6 years, $P = 0.046$; **Table 2**).

In 114 dupilumab users, rhinological responders had higher pre-BD FEV1 ($69.0\% \pm 19.3\%$ vs. $60.4\% \pm 19.9\%$, $P = 0.022$) and post-BD FEV1 ($72.4\% \pm 18.0\%$ vs. $64.2\% \pm 20.3\%$, $P = 0.032$) values. Extranasal rhinological responders had a higher rate of atopy (53.2% vs. 29.9%, $P = 0.017$), higher pre- and post-FEV1 ($69.6\% \pm 17.79\%$ vs. $60.12\% \pm 20.65\%$, $P = 0.012$; $73.04\% \pm 17.02\%$ vs. $63.65\% \pm 20.68\%$, $P = 0.013$) and pre-/ post-BD FEV1/FVC (0.68 ± 0.13 vs. 0.61 ± 0.16 , $P = 0.017$; 0.71 ± 0.13 vs. 0.63 ± 0.15 , $P = 0.005$) values. The rate of uncontrolled asthma was higher in psychological responders (57.7% vs. 29.0%, $P = 0.014$) and sleep dysfunction responders (50.9% vs. 34.4%, $P = 0.045$). Sleep dysfunction responders had higher pre-/post FEV1 ($69.23\% \pm 17.46\%$ vs. $59.51\% \pm 21.08\%$, $P = 0.009$; $71.88\% \pm 17.2\%$ vs. $63.85\% \pm 21.08\%$, $P = 0.032$) and FEV1/FVC (0.68 ± 0.14 vs. 0.60 ± 0.15 , $P = 0.011$; 0.70 ± 0.14 vs. 0.63 ± 0.15 , $P = 0.010$; **Table 3**) values.

Odds ratios (ORs) for achieving MCID response in total and domain scores of SNOT-22

Responders whose asthmatic symptoms improved after a 6-month treatment did not differ from non-responders in the ORs who become responders for each domain of SNOT-22 in both the anti-interleukin (IL)-5 (mepolizumab and reslizumab)- and anti-IL-4 receptor alpha (anti-IL-4R α ; dupilumab)-treated groups (**Supplementary Table S3**).

When investigated SNOT-22 responses according to each biologic use while adjusting for age, sex, FEV1 (%), and eosinophil count, the dupilumab-treated group showed significantly increased OR for positive responses in total SNOT-22 (OR, 2.29; 95% confidence interval [CI], 1.08–4.87), extranasal rhinological (OR, 2.80; 95% CI, 1.20–6.56), psychological (OR, 2.23; 95% CI, 1.03–4.83), and sleep dysfunction (OR, 2.50; 95% CI, 1.14–5.47) scores than the conventional group (**Fig. 1A**). When adjusting for the history of CRS diagnosis, the dupilumab-treated group still showed significant benefits in total SNOT-22 (OR, 2.20; 95% CI, 1.02–4.77) and extranasal rhinological (OR, 2.77; 95% CI, 1.16–6.60; **Fig. 1B**) scores. There were no significant differences among mepolizumab/reslizumab users (**Tables 4 and 5**) or combined anti-IL-5 antibody-treated ones (**Supplementary Tables S4 and S5**).

Table 2. Baseline characteristics according to SNOT domain responders in 69 mepolizumab/reslizumab-treated subjects

Variables	SNOT-22															
	Total score (n = 69)	Domain 1: rhinologic symptoms		P value	Domain 2: extranasal rhinologic symptoms		P value	Domain 3: ear/facial symptoms		P value	Domain 4: psychological dysfunction		P value	Domain 5: sleep dysfunction		P value
		Non- responder (n = 43)	Responder (n = 26)		Non- responder (n = 26)	Responder (n = 26)		Non- responder (n = 49)	Responder (n = 20)		Non- responder (n = 43)	Responder (n = 26)		Non- responder (n = 46)	Responder (n = 23)	
Age (yr)	51.5 ± 11.2	51.9 ± 10.3	50.9 ± 12.7	0.722	51.3 ± 12.3	51.9 ± 9.3	0.812	51.0 ± 12.7	52.7 ± 6.3	0.486	51.2 ± 12.5	52.1 ± 8.9	0.745	50.8 ± 10.1	52.9 ± 13.2	0.465
Male	29 (42.0)	19 (44.2)	10 (38.5)	0.641	21 (48.8)	8 (30.8)	0.141	23 (46.9)	6 (30)	0.196	21 (48.8)	8 (30.8)	0.141	23 (50)	6 (26.1)	0.058
BMI (kg/m ²)	25.0 ± 3.6	24.2 ± 3.1	26.3 ± 4.1	0.016	24.7 ± 3.4	25.5 ± 4.0	0.399	25.2 ± 3.6	24.5 ± 3.7	0.476	25.3 ± 3.9	24.4 ± 3.3	0.336	24.8 ± 3.8	25.3 ± 3.4	0.579
Asthma onset age (yr)	40.3 ± 13.8	39.4 ± 14.6	41.7 ± 12.5	0.504	39.2 ± 14.5	42.0 ± 12.5	0.441	39.5 ± 15.0	42.1 ± 10.4	0.481	38.4 ± 15.2	43.2 ± 10.8	0.172	37.8 ± 13.6	44.9 ± 13.1	0.046
History of AE during last year																
Unscheduled visit of outpatient	24 (34.8)	13 (30.2)	11 (42.3)	0.308	14 (32.6)	10 (38.5)	0.618	16 (32.7)	8 (40)	0.561	16 (37.2)	8 (30.8)	0.586	16 (34.8)	8 (34.8)	0.379
Unscheduled visit to ED	13 (18.8)	7 (16.3)	6 (23.1)	0.535	11 (25.6)	2 (7.7)	0.110	9 (18.4)	4 (20)	1	10 (23.3)	3 (11.5)	0.343	8 (17.4)	5 (21.7)	0.748
Hospitalization	12 (17.4)	6 (14.0)	6 (23.1)	0.347	9 (20.9)	3 (11.5)	0.514	10 (20.4)	2 (10)	0.486	9 (20.9)	3 (11.5)	0.514	8 (17.4)	4 (17.4)	1
ICU admission	0 (0)	0 (0)	0 (0)	N/A	0 (0)	0 (0)	N/A	0 (0)	0 (0)	N/A	0 (0)	0 (0)	N/A	0 (0)	0 (0)	N/A
Self-medication with steroid bursts	31 (44.9)	19 (44.2)	12 (46.2)	1	16 (37.2)	15 (57.7)	0.167	20 (40.8)	11 (55)	0.591	20 (46.5)	11 (42.3)	0.877	22 (47.8)	9 (39.1)	0.738
OCS maintenance	19 (27.5)	13 (30.2)	6 (23.1)	0.519	14 (32.6)	5 (19.2)	0.230	16 (32.7)	3 (15)	0.136	14 (32.6)	5 (19.2)	0.230	13 (28.3)	6 (26.1)	0.849
Previous use of biologics	22 (31.9)	15 (34.9)	7 (26.9)	0.492	14 (32.6)	8 (30.8)	0.877	15 (30.6)	7 (35)	0.723	14 (32.6)	8 (30.8)	0.877	16 (34.8)	6 (26.1)	0.465
Comorbidities																
Allergic rhinitis	52 (75.4)	33 (76.7)	19 (73.1)	0.732	31 (72.1)	21 (80.8)	0.418	35 (71.4)	17 (85)	0.358	30 (69.8)	22 (84.6)	0.165	35 (76.1)	17 (73.9)	0.843
Chronic rhinosinusitis	36 (52.2)	25 (58.1)	11 (42.3)	0.202	23 (53.5)	13 (50)	0.779	26 (53.1)	10 (50)	0.817	22 (51.2)	14 (53.9)	0.829	25 (54.4)	11 (47.8)	0.609
Nasal polyps	16 (23.2)	10 (23.3)	6 (23.1)	0.986	9 (20.9)	7 (26.9)	0.568	10 (20.4)	6 (30)	0.530	11 (25.6)	5 (19.2)	0.545	12 (26.1)	4 (17.4)	0.420
Asthma control status																
Partly controlled	25 (36.3)	17 (39.5)	8 (30.8)		17 (39.5)	8 (30.8)		21 (42.9)	4 (20)		18 (41.9)	7 (26.9)		17 (37.0)	8 (34.8)	
Uncontrolled	35 (50.7)	18 (41.9)	17 (65.4)		18 (41.9)	17 (65.4)		19 (38.8)	16 (80)		17 (39.5)	18 (69.2)		21 (45.7)	14 (60.9)	
Controlled	9 (13.0)	8 (18.6)	1 (3.9)		8 (18.6)	1 (3.9)		9 (18.4)	0 (0)		8 (18.6)	1 (3.9)		8 (17.4)	1 (4.4)	
Atopy	36 (52.2)	21 (48.8)	15 (57.7)	0.032	22 (51.2)	14 (53.9)	0.935	25 (51.0)	11 (55)	0.508	21 (48.8)	15 (57.7)	0.032	22 (47.8)	14 (60.9)	0.312
Laboratory findings																
WBC (10 ³ /μL)	8.1 ± 2.0	8.0 ± 1.9	8.1 ± 2.2	0.908	8.2 ± 2.0	7.9 ± 2.1	0.517	8.1 ± 2.1	7.9 ± 1.8	0.758	8.2 ± 2.1	7.9 ± 2.0	0.607	8.1 ± 2.1	8.0 ± 2.0	0.914
Eosinophils (cells/μL)	829.2 ± 604.0	844.5 ± 693.9	803.9 ± 427.3	0.765	839.6 ± 712.2	812.1 ± 373.9	0.834	808.4 ± 662.8	880.3 ± 438.2	0.657	785.0 ± 664.8	902.3 ± 490.9	0.439	863.7 ± 680.3	760.4 ± 416.7	0.439
Total IgE (ku/L)	402.3 ± 487.3	454.5 ± 559.8	291.7 ± 258.8	0.154	464.0 ± 567.7	291.8 ± 273.8	0.143	452.1 ± 535.3	232.3 ± 199.2	0.035	414.4 ± 476.9	376.5 ± 522.7	0.794	468.8 ± 563.1	261.4 ± 217.1	0.059
FeNO (ppb)	78.0 ± 54.6	86.2 ± 60.4	65.2 ± 41.8	0.098	75.7 ± 49.9	81.7 ± 62.1	0.667	77.9 ± 57.4	78.2 ± 48.7	0.986	85.0 ± 60.7	67.1 ± 42.0	0.194	86.5 ± 59.1	61.9 ± 41.2	0.080
Induced sputum eosinophil (%)	22.9 ± 28.3	25.7 ± 30.6	16.4 ± 23.2	0.274	19.3 ± 25.7	31.5 ± 33.0	0.165	23.3 ± 29.1	21.6 ± 26.7	0.855	21.2 ± 28.9	26.4 ± 27.7	0.546	24.7 ± 29.5	18.4 ± 25.4	0.488
Lung functions																
post-BD FEV1 (%)	67.3 ± 18.6	69.5 ± 15.8	62.9 ± 23.1	0.186	66.8 ± 15.3	68.0 ± 23.4	0.823	68.4 ± 16.9	64.7 ± 22.4	0.484	69.5 ± 18.9	63.7 ± 18.0	0.236	66.5 ± 17.4	68.7 ± 21.2	0.674
post-BD FEV1/FVC ratio	0.67 ± 0.12	0.68 ± 0.12	0.65 ± 0.14	0.465	0.67 ± 0.1	0.67 ± 0.16	0.984	0.68 ± 0.11	0.66 ± 0.15	0.632	0.68 ± 0.12	0.66 ± 0.13	0.449	0.65 ± 0.11	0.71 ± 0.13	0.071

Data are presented as number (%) or mean ± standard deviation.

SNOT, sino-nasal outcome test; BMI, body mass index; AE, acute exacerbation; ED, emergency department; ICU, intensive care unit; N/A, not applicable; OCS, oral corticosteroids; WBC, white blood cell; IgE, immunoglobulin E; FeNO, fractional exhaled nitric oxide; BD, bronchodilator; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

Table 3. Baseline characteristics according to SNOT domain responders in 114 dupilumab-treated subjects

Variables		SNOT-22																
		Total score (n = 114)		Domain 1: rhinological symptoms		P value	Domain 2: extranasal rhinological symptoms		P value	Domain 3: ear/facial symptoms		P value	Domain 4: psychological dysfunction		P value	Domain 5: sleep dysfunction		P value
				Non- Responder (n = 66)	Responder (n = 48)		Non- Responder (n = 67)	Responder (n = 47)		Non- Responder (n = 76)	Responder (n = 38)		Non- Responder (n = 62)	Responder (n = 52)		Non- Responder (n = 61)	Responder (n = 53)	
Age (yr)	54.2 ± 10.2	55.5 ± 10.6	52.5 ± 9.6	0.133	55.3 ± 10.1	52.7 ± 10.4	0.183	54.8 ± 10.7	53.0 ± 9.3	54.8 ± 10.4	53.5 ± 10.0	0.488	55.8 ± 10.4	52.5 ± 9.8	0.084			
Male	58 (50.9)	37 (56.0)	21 (43.8)	0.194	38 (56.7)	20 (42.6)	0.137	39 (51.3)	19 (50)	33 (53.2)	25 (48.1)	0.584	35 (57.4)	23 (43.4)	0.136			
BMI (kg/m ²)	25.4 ± 3.8	25.6 ± 3.8	25.0 ± 3.9	0.352	25.8 ± 4.3	24.7 ± 3.1	0.136	25.5 ± 4.0	25.1 ± 3.6	24.9 ± 3.6	25.9 ± 4.1	0.206	25.6 ± 3.8	25.1 ± 3.9	0.560			
Asthma onset age (yr)	39.2 ± 13.1	39.4 ± 12.7	38.8 ± 13.8	0.797	39.3 ± 13.2	39.0 ± 13.2	0.891	39.2 ± 13.4	39.2 ± 12.7	39.1 ± 12.3	39.2 ± 14.2	0.955	39.0 ± 13.9	39.4 ± 12.3	0.887			
History of AE during last year																		
Unscheduled visit of outpatient	22 (19.3)	16 (24.2)	6 (12.5)	0.117	14 (20.9)	8 (17.0)	0.606	16 (21.1)	6 (15.8)	12 (19.4)	10 (19.2)	0.987	13 (21.3)	9 (17.0)	0.559			
Unscheduled visit to ED	16 (14.0)	13 (19.7)	3 (6.3)	0.041	11 (16.4)	5 (10.6)	0.382	13 (17.1)	3 (7.9)	9 (14.5)	7 (13.5)	0.872	8 (13.1)	8 (15.1)	0.762			
Hospitalization	13 (11.4)	9 (13.6)	4 (8.3)	0.379	8 (11.9)	5 (10.6)	0.830	9 (11.8)	4 (10.5)	7 (11.3)	6 (11.5)	0.967	7 (11.5)	6 (11.3)	1			
ICU admission	0 (0)	0 (0)	0 (0)	N/A	0 (0)	0 (0)	N/A	0 (0)	0 (0)	0 (0)	0 (0)	N/A	0 (0)	0 (0)	N/A			
Self-medication with steroid bursts	39 (34.2)	24 (36.4)	15 (31.3)	0.570	19 (28.4)	20 (42.6)	0.116	24 (31.6)	15 (39.5)	0.402	21 (33.9)	0.934	21 (34.4)	18 (34.0)	0.959			
OCS maintenance	50 (43.9)	33 (50)	17 (35.4)	0.121	31 (46.3)	19 (40.4)	0.536	35 (46.1)	15 (39.5)	0.505	28 (45.2)	0.760	24 (39.3)	26 (49.1)	0.297			
Previous use of biologics	51 (44.7)	30 (45.5)	21 (43.8)	0.857	29 (43.3)	22 (46.8)	0.710	35 (46.1)	16 (42.1)	0.690	28 (45.2)	0.921	28 (45.9)	23 (43.4)	0.788			
Comorbidities																		
Allergic rhinitis	83 (72.8)	45 (68.2)	38 (79.2)	0.193	47 (70.2)	36 (76.6)	0.446	56 (73.7)	27 (71.1)	0.766	43 (69.4)	0.366	43 (70.5)	40 (75.5)	0.551			
Chronic rhinosinusitis	63 (55.3)	37 (56.1)	26 (54.2)	0.841	35 (52.2)	28 (59.6)	0.438	38 (50)	25 (65.8)	0.110	30 (48.4)	0.107	29 (47.5)	34 (64.2)	0.075			
Nasal polyps	31 (27.2)	17 (25.8)	14 (29.2)	0.686	19 (28.4)	12 (25.5)	0.739	20 (26.3)	11 (29.0)	0.766	13 (21.0)	0.103	13 (21.3)	18 (34.0)	0.130			
Asthma control status				0.312			0.124			0.310		0.014			0.046			
Partly controlled	47 (41.2)	31 (47.0)	16 (33.3)		32 (47.8)	15 (31.9)		33 (43.4)	14 (36.8)		32 (51.6)		30 (49.2)	17 (32.1)				
Uncontrolled	48 (42.1)	23 (34.9)	25 (52.1)		24 (35.8)	24 (51.1)		28 (36.8)	20 (52.6)		18 (29.0)		21 (34.4)	27 (50.9)				
Controlled	16 (14.0)	10 (15.2)	6 (12.50)		8 (11.9)	8 (17.0)		13 (17.1)	3 (7.9)		10 (16.1)		10 (16.4)	6 (11.3)				
Atopy	45 (39.5)	24 (36.4)	21 (43.8)	0.314	20 (29.9)	25 (53.2)	0.017	25 (32.9)	20 (52.6)	0.172	23 (37.1)	0.934	23 (37.7)	22 (41.5)	0.629			
Laboratory findings																		
WBC (10 ³ /μL)	8.3 ± 2.8	8.8 ± 3.1	7.6 ± 2.1	0.021	8.7 ± 3.1	7.8 ± 2.2	0.090	8.7 ± 3.0	7.5 ± 2.1	0.020	8.4 ± 2.8	0.657	8.5 ± 3.0	8.1 ± 2.5	0.387			
Eosinophils (cells/μL)	494.9 ± 511.5	473.9 ± 454.7	523.8 ± 584.4	0.609	435.6 ± 418.8	579.5 ± 615.2	0.168	432.8 ± 416.6	619.3 ± 650.6	0.113	488.1 ± 461.7	0.877	521.5 ± 492.6	464.4 ± 535.5	0.555			
Total IgE (kU/L)	396.9 ± 453.6	386.5 ± 515.3	411.5 ± 354.6	0.773	379.7 ± 432.0	419.1 ± 484.2	0.667	368.6 ± 482.2	455.0 ± 388.4	0.372	380.8 ± 509.7	0.668	437.3 ± 552.1	355.6 ± 324.5	0.366			
FeNO (ppb)	61.5 ± 50.7	61.0 ± 53.7	62.1 ± 46.9	0.904	59.8 ± 47.6	63.8 ± 55.2	0.676	59.6 ± 53.5	65.1 ± 45.3	0.593	62.5 ± 57.7	0.810	62.5 ± 60.0	60.3 ± 38.1	0.812			
Induced sputum eosinophil (%)	16.3 ± 24.4	15.3 ± 24.4	17.7 ± 24.7	0.662	16.0 ± 25.4	16.8 ± 23.1	0.879	14.5 ± 23.4	20.1 ± 26.5	0.327	14.9 ± 24.1	0.567	13.0 ± 22.1	20.3 ± 26.6	0.169			
Lung functions																		
post-BD FEV1 (%)	67.5 ± 19.7	64.2 ± 20.3	72.4 ± 18.0	0.032	63.7 ± 20.7	73.0 ± 17.0	0.013	65.7 ± 21.2	71.1 ± 16.2	0.167	66.1 ± 21.1	0.393	63.9 ± 21.1	71.9 ± 17.2	0.032			
post-BD FEV1/FVC ratio	0.66 ± 0.15	0.64 ± 0.15	0.69 ± 0.14	0.078	0.63 ± 0.15	0.71 ± 0.13	0.005	0.65 ± 0.15	0.67 ± 0.13	0.512	0.64 ± 0.15	0.098	0.63 ± 0.15	0.7 ± 0.14	0.010			

Data are presented as number (%) or mean ± standard deviation.

SNOT, sino-nasal outcome test; BMI, body mass index; AE, acute exacerbation; ED, emergency department; ICU, intensive care unit; N/A, not applicable; OCS, oral corticosteroids; WBC, white blood cell; IgE, immunoglobulin E; FeNO, fractional exhaled nitric oxide; BD, bronchodilator; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

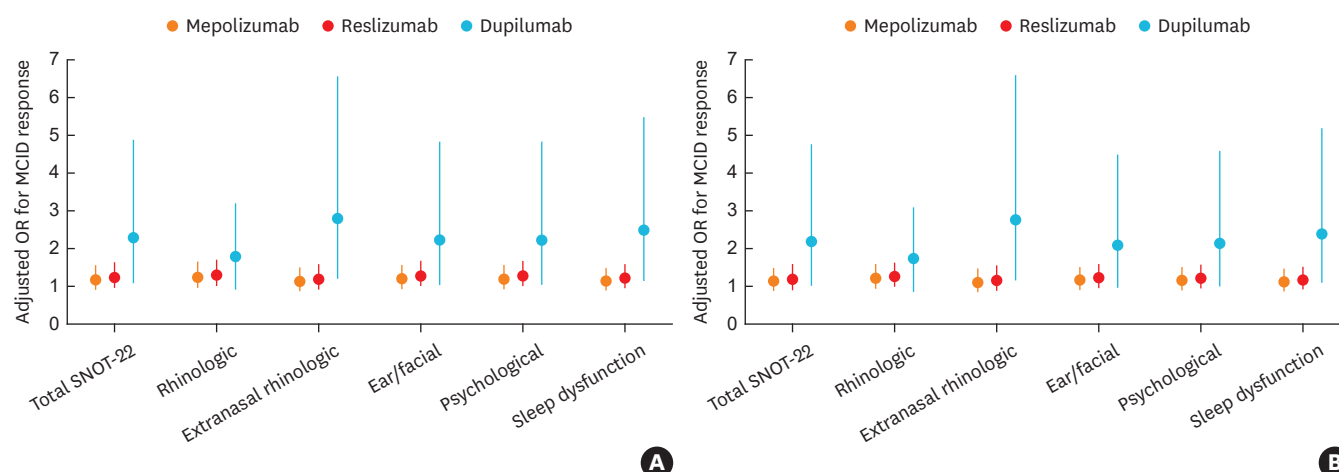


Fig. 1. Adjusted ORs and 95% confidence intervals for achieving the MCID in each SNOT-22 domain after 6 months of biologic treatment. (A) Adjusted for age, sex, forced expiratory volume in 1 second (%), and blood eosinophil count (n = 229). (B) Additionally adjusted for history of chronic rhinosinusitis diagnosis (n = 229). ORs are shown for each biologic (Mepolizumab, Reslizumab, and Dupilumab) across total and 5 SNOT-22 domains. The conventional treatment group was used as the reference (OR = 1.0). OR, odds ratio; MCID, minimal clinically important difference; SNOT, sino-nasal outcome test.

Table 4. Odds ratios for achieving MCID response in total and domain scores of SNOT-22 according to biologics (N = 229)

SNOT-22 score	Model 1: crude	Model 2: adjusted for age, sex, FEV1(%)	Model 3: adjusted for age, sex, blood eosinophil count	Model 4: adjusted for age, sex, FEV1(%), blood eosinophil count
Total				
Mepolizumab	1.32 (0.50–3.50)	1.06 (0.38–2.95)	1.04 (0.36–2.98)	1.03 (0.36–3.01)
Reslizumab	2.41 (0.99–5.85)	2.47 (0.98–6.17)	2.30 (0.90–5.86)	2.42 (0.95–6.21)
Dupilumab	2.37 (1.14–4.90)	2.30 (1.09–4.88)	2.31 (1.09–4.90)	2.29 (1.08–4.87)
Rhinologic				
Mepolizumab	1.09 (0.40–2.99)	0.99 (0.34–2.87)	0.87 (0.29–2.61)	0.96 (0.32–2.89)
Reslizumab	1.96 (0.80–4.83)	1.78 (0.70–4.52)	1.85 (0.72–4.76)	1.74 (0.67–4.52)
Dupilumab	1.85 (0.88–3.88)	1.89 (0.88–4.05)	1.81 (0.85–3.89)	1.87 (0.87–4.03)
Extranasal rhinologic				
Mepolizumab	2.74 (0.98–7.69)	2.74 (0.92–8.13)	2.03 (0.67–6.20)	2.36 (0.77–7.30)
Reslizumab	2.30 (0.87–6.13)	2.42 (0.88–6.64)	2.11 (0.76–5.87)	2.17 (0.78–6.10)
Dupilumab	2.88 (1.27–6.54)	2.90 (1.24–6.77)	2.70 (1.16–6.27)	2.80 (1.20–6.56)
Ear/facial				
Mepolizumab	1.45 (0.46–4.52)	1.29 (0.39–4.21)	0.90 (0.26–3.10)	0.94 (0.27–3.26)
Reslizumab	2.38 (0.86–6.54)	2.42 (0.86–6.78)	1.91 (0.67–5.49)	1.96 (0.68–5.64)
Dupilumab	2.38 (1.01–5.59)	2.22 (0.93–5.33)	2.06 (0.86–4.97)	2.07 (0.86–5.0)
Psychological dysfunction				
Mepolizumab	1.89 (0.71–5.05)	1.60 (0.57–4.48)	1.50 (0.52–4.34)	1.45 (0.50–4.24)
Reslizumab	1.59 (0.63–4.01)	1.60 (0.62–4.12)	1.44 (0.55–3.77)	1.49 (0.57–3.93)
Dupilumab	2.38 (1.12–5.05)	2.28 (1.06–4.93)	2.26 (1.04–4.89)	2.23 (1.03–4.83)
Sleep dysfunction				
Mepolizumab	1.03 (0.36–2.92)	0.95 (0.32–2.83)	0.92 (0.30–2.84)	1.03 (0.33–3.21)
Reslizumab	1.77 (0.71–4.45)	1.77 (0.68–4.56)	1.80 (0.68–4.72)	1.88 (0.71–4.97)
Dupilumab	2.46 (1.16–5.23)	2.44 (1.12–5.33)	2.43 (1.12–5.30)	2.50 (1.14–5.47)

Values are presented as odds ratio (95% confidence interval). Reference group: conventional treatment group. All adjusted variables were measured at the baseline visit.

MCID, minimal clinically important difference; SNOT, sino-nasal outcome test; FEV1, forced expiratory volume in 1 second.

Table 5. Odds ratios for achieving MCID difference response in total and domain scores of SNOT-22 according to biologics; additionally adjusted for history of CRS diagnosis (n = 229)

SNOT-22 score	Model 1: crude	Model 2: adjusted for age, sex, FEV1 (%), CRS	Model 3: adjusted for age, sex, blood eosinophil count, CRS	Model 4: adjusted for age, sex, FEV1 (%), blood eosinophil count, CRS
Total				
Mepolizumab	1.32 (0.50–3.50)	1.03 (0.37–2.89)	1.01 (0.35–2.92)	1.01 (0.35–2.94)
Reslizumab	2.41 (0.99–5.846)	2.36 (0.93–6.02)	2.20 (0.85–5.67)	2.33 (0.90–6.06)
Dupilumab	2.37 (1.14–4.90)	2.21 (1.02–4.78)	2.20 (1.02–4.75)	2.20 (1.02–4.77)
Rhinologic				
Mepolizumab	1.09 (0.40–2.99)	1.06 (0.36–3.11)	0.91 (0.30–2.74)	1.02 (0.34–3.12)
Reslizumab	1.96 (0.80–4.83)	1.99 (0.77–5.17)	2.01 (0.77–5.27)	1.94 (0.73–5.13)
Dupilumab	1.85 (0.88–3.88)	2.10 (0.95–4.62)	1.98 (0.90–4.33)	2.08 (0.94–4.59)
Extranasal rhinologic				
Mepolizumab	2.74 (0.98–7.69)	2.71 (0.91–8.10)	1.98 (0.65–6.05)	2.34 (0.75–7.29)
Reslizumab	2.30 (0.87–6.13)	2.38 (0.85–6.66)	2.01 (0.71–5.67)	2.15 (0.75–6.13)
Dupilumab	2.88 (1.27–6.54)	2.86 (1.20–6.80)	2.57 (1.09–6.07)	2.77 (1.16–6.60)
Ear/facial				
Mepolizumab	1.45 (0.46–4.52)	1.19 (0.36–3.93)	0.86 (0.25–2.96)	0.88 (0.25–3.08)
Reslizumab	2.38 (0.863–6.54)	2.17 (0.76–6.21)	1.73 (0.59–5.05)	1.78 (0.61–5.22)
Dupilumab	2.38 (1.01–5.59)	2.00 (0.82–4.91)	1.87 (0.76–4.58)	1.89 (0.776–4.64)
Psychological dysfunction				
Mepolizumab	1.89 (0.71–5.05)	1.44 (0.51–4.06)	1.39 (0.48–4.05)	1.31 (0.45–3.86)
Reslizumab	1.59 (0.63–4.01)	1.37 (0.52–3.60)	1.25 (0.47–3.35)	1.28 (0.48–3.45)
Dupilumab	2.38 (1.12–5.05)	1.98 (0.90–4.36)	1.98 (0.90–4.36)	1.94 (0.88–4.28)
Sleep dysfunction				
Mepolizumab	1.03 (0.36–2.92)	0.86 (0.29–2.59)	0.85 (0.27–2.61)	0.94 (0.30–2.94)
Reslizumab	1.77 (0.71–4.45)	1.53 (0.58–4.04)	1.54 (0.57–4.12)	1.63 (0.60–4.41)
Dupilumab	2.46 (1.16–5.23)	2.14 (0.96–4.76)	2.09 (0.95–4.64)	2.19 (0.98–4.88)

Values are presented as odds ratio (95% confidence interval). Reference group: conventional treatment group. All adjusted variables were measured at the baseline visit. SNOT, sino-nasal outcome test; CRS, chronic rhinosinusitis; FEV1, forced expiratory volume in 1 second.

Changes in SNOT-22 scores according to the type of treatment for 6 months

Changes in SNOT-22 score during 6 months were determined using a linear mixed effect model (**Fig. 2**). When adjusted for age, sex, the history of CRS diagnosis, FEV1 (%), and blood eosinophil count, no significant differences were observed in the psychological domain (**Fig. 2C**). Overall, a trend toward a decrease in total/domain scores of SNOT-22 was noted in the biologic-treated group compared to the conventional group, in which the decrease in these scores was more pronounced in the dupilumab-treated group as with the OR analyses.

DISCUSSION

This study compared changes in SNOT-22 (total/each domain scores) for 6 months in adult patients with severe asthma between the biologic-treated and conventional groups. Among them, dupilumab-treated group showed significantly higher OR of being responders in total, extranasal rhinological, psychological, and sleep dysfunction scores of SNOT-22 than the anti-IL-5-treated group or the conventional group. Moreover, when they were plotted at each time point (0, 1, and 6 months), an overall trend of decreased SNOT-22 was noted in the biologic-treated group, where dupilumab-treated group showed the most pronounced decrease. These findings suggest that dupilumab could be beneficial to control nasal symptoms in adult patients with severe asthma.

With the advancement of precision medicine in asthma management, biological therapies have expanded to encompass CRSwNP.³ Currently approved biologics for asthma and/or CRS include anti-IL-5 agents (mepolizumab, reslizumab), an anti-IL-5R α (benralizumab), an anti-IL-4R α

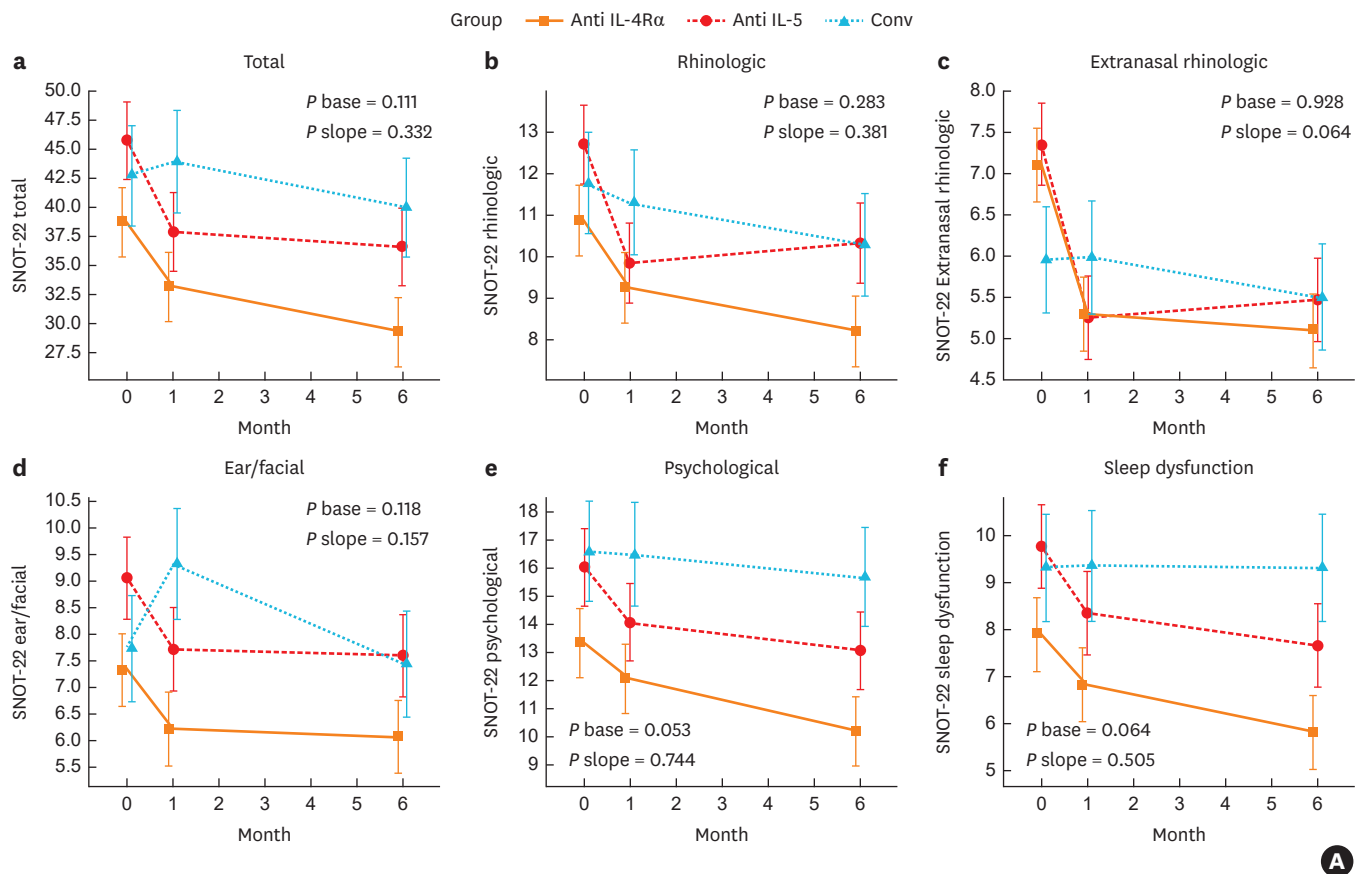


Fig. 2. Changes in SNOT-22 scores according to the type of asthma treatment for 6 months in adult patients with asthma requiring GINA Step 4–5 therapy using a linear mixed effect model. (A) Model 1: Adjusted for age, sex, history of CRS diagnosis, and FEV1(%). (B) Model 2: Adjusted for age, sex, history of CRS diagnosis, and blood eosinophils. (C) Model 3: Adjusted for age, sex, history of CRS diagnosis, FEV1(%), and blood eosinophils. Each panel represents the following: (a) Total SNOT-22, (b) Rhinologic symptoms SNOT-22, (c) Extranasal rhinologic symptoms SNOT-22, (d) Ear/facial symptoms SNOT-22, (e) Psychological dysfunction SNOT-22, and (f) Sleep dysfunction SNOT-22. Conv: conventional asthma treatment; anti-IL-4Rα: dupilumab; anti IL-5: mepolizumab and reslizumab. IL, interleukin; SNOT, sino-nasal outcome test; CRS, chronic rhinosinusitis; FEV1, forced expiratory volume in 1 second. (continued to the next page)

(dupilumab), and an anti-IgE (omalizumab).^{4,13} Moreover, an anti-thymic stromal lymphopoietin antibody has demonstrated promising preliminary results in CRS clinical trials.¹⁴

The observed differences in treatment responses on nasal symptoms between anti-IL-5 and anti-IL-4Rα biologics in the present study can be elucidated by investigating the distinct immunological roles of IL-5 and IL-4/IL-13 in T2-inflammatory processes. IL-5 primarily mediates eosinophil maturation in the bone marrow and facilitates its migration and peripheral tissue survival.^{15,16} Elevated IL-5 signaling results in increased blood and tissue eosinophil levels, with activated eosinophils releasing cytotoxic mediators including major basic protein, eosinophil peroxidase, and leukotrienes, ultimately leading to eosinophil-mediated tissue pathology.^{16,17}

Since the IL-4Rα facilitates both IL-4 and IL-13 signaling, dupilumab's blocking of this receptor enables a more comprehensive immunomodulatory intervention beyond eosinophil suppression.^{15,16} IL-4 promotes T2 cell differentiation and induces IgE class switching in B cells, thereby amplifying allergic inflammatory responses.^{16,18} IL-13 activates mast cells and basophils, stimulates mucus production through goblet cell hyperplasia, and promotes

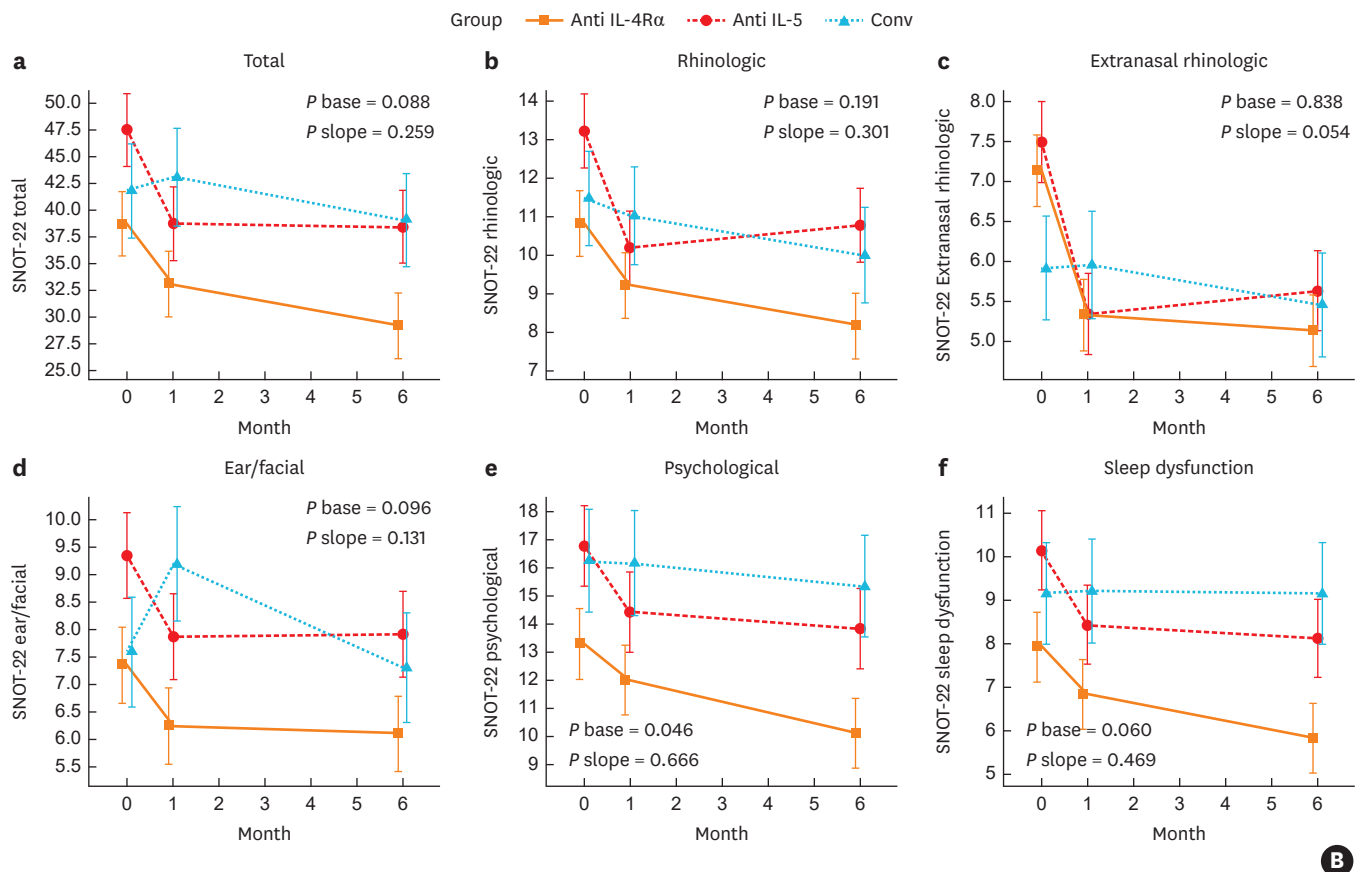


Fig. 2. (Continued) Changes in SNOT-22 scores according to the type of asthma treatment for 6 months in adult patients with asthma requiring GINA Step 4–5 therapy using a linear mixed effect model. (A) Model 1: Adjusted for age, sex, history of CRS diagnosis, and FEV1(%). (B) Model 2: Adjusted for age, sex, history of CRS diagnosis, and blood eosinophils. (C) Model 3: Adjusted for age, sex, history of CRS diagnosis, FEV1(%), and blood eosinophils. Each panel represents the following: (a) Total SNOT-22, (b) Rhinologic symptoms SNOT-22, (c) Extranasal rhinologic symptoms SNOT-22, (d) Ear/facial symptoms SNOT-22, (e) Psychological dysfunction SNOT-22, and (f) Sleep dysfunction SNOT-22. Conv: conventional asthma treatment; anti-IL-4Rα: dupilumab; anti-IL-5: mepolizumab and reslizumab. IL, interleukin; SNOT, sino-nasal outcome test; CRS, chronic rhinosinusitis; FEV1, forced expiratory volume in 1 second. (continued to the next page)

fibrosis and tissue remodeling via fibroblast activation.^{16,18} Both IL-4 and IL-13 additionally compromise epithelial barrier integrity by downregulating tight junction proteins.^{16,19}

Recent experimental evidence suggests that dupilumab's therapeutic efficacy may extend beyond inflammatory resolution. In a murine model of eosinophilic sinonasal inflammation, dupilumab not only reduced eosinophilic and neutrophilic infiltration but also ameliorated sensorineural olfactory dysfunction by attenuating microglial activation and neuroinflammatory signaling within the olfactory bulb.²⁰ This mechanism may explain more improved olfactory function observed with dupilumab compared to that with anti-IL-5 antibody in the present study.

A comprehensive network meta-analysis encompassing 64 randomized controlled trials with 26,630 patients with eosinophilic asthma demonstrated dupilumab's superior efficacy in reducing exacerbations and improving lung function, while anti-IL-5 agents exhibited greater effectiveness in reducing oral corticosteroid utilization.¹³ Complementarily, a meta-analysis of 64 real-world studies involving 3,921 patients with CRSwNP revealed that dupilumab generated the most substantial improvements in NP scores, SNOT-22 outcomes,

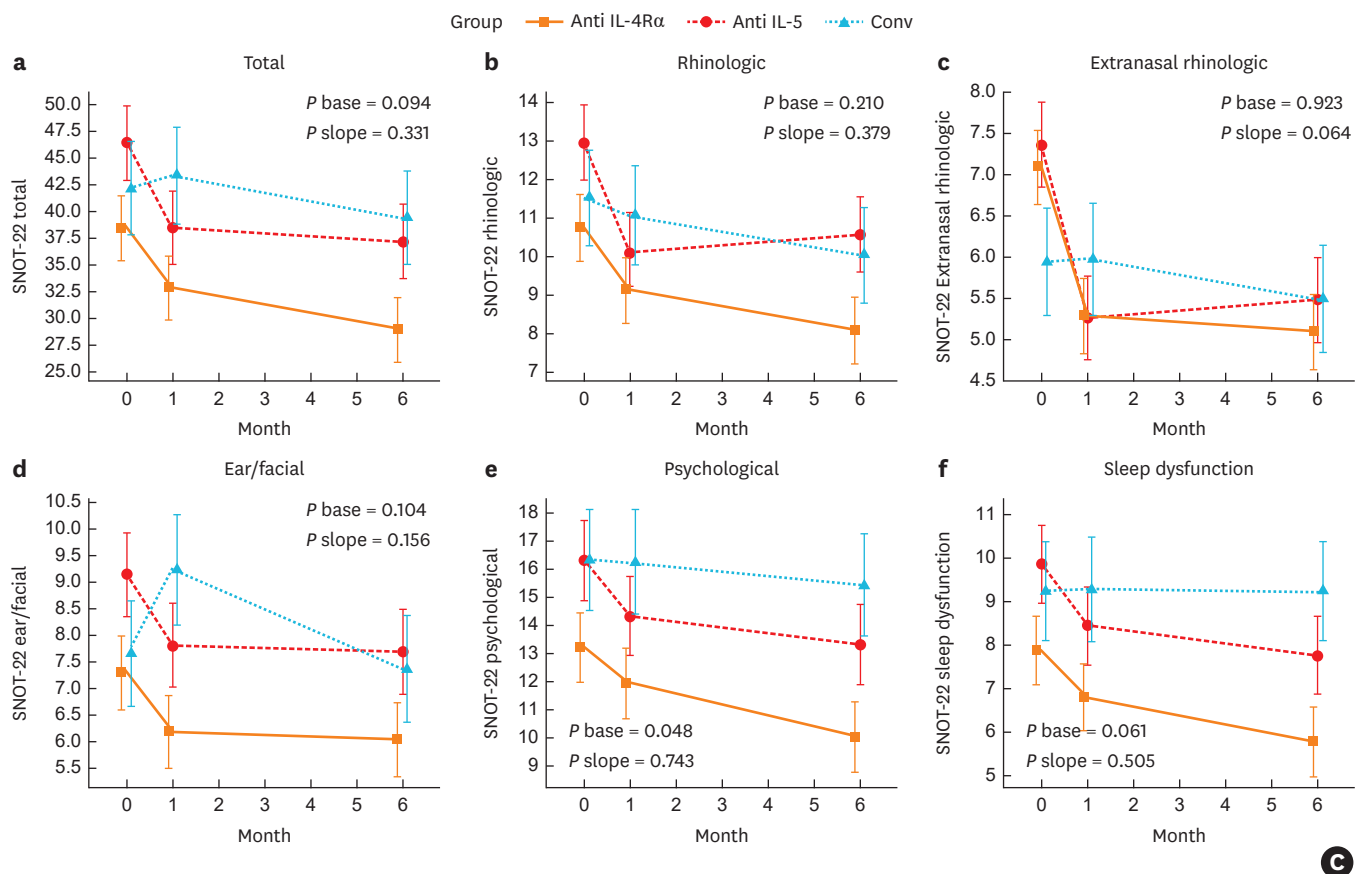


Fig. 2. (Continued) Changes in SNOT-22 scores according to the type of asthma treatment for 6 months in adult patients with asthma requiring GINA Step 4–5 therapy using a linear mixed effect model. (A) Model 1: Adjusted for age, sex, history of CRS diagnosis, and FEV1(%). (B) Model 2: Adjusted for age, sex, history of CRS diagnosis, and blood eosinophils. (C) Model 3: Adjusted for age, sex, history of CRS diagnosis, FEV1(%), and blood eosinophils. Each panel represents the following: (a) Total SNOT-22, (b) Rhinologic symptoms SNOT-22, (c) Extranasal rhinologic symptoms SNOT-22, (d) Ear/facial symptoms SNOT-22, (e) Psychological dysfunction SNOT-22, and (f) Sleep dysfunction SNOT-22. Conv: conventional asthma treatment; anti-IL-4Rα: dupilumab; anti-IL-5: mepolizumab and reslizumab. IL, interleukin; SNOT, sino-nasal outcome test; CRS, chronic rhinosinusitis; FEV1, forced expiratory volume in 1 second.

and secondary outcomes, including olfactory function assessments, when compared to mepolizumab, benralizumab, and omalizumab.²¹ Collectively, these findings substantiate the hypothesis that dual inhibition of IL-4 and IL-13 may provide more comprehensive therapeutic benefits in managing CRS-related symptoms in severe asthma, surpassing the efficacy of eosinophil-targeted interventions. However, CRS and allergic rhinitis demonstrate considerable pathophysiological heterogeneity across distinct endotypes. As our study utilized biologics without phenotypic classification of CRS and allergic rhinitis, drawing generalized conclusions requires caution.

Severe CRSwNP is defined as a bilateral disease with a NP score of ≥ 4 out of 8 and persistent nasal symptoms despite intranasal corticosteroid (INCS) therapy and requiring additional treatment.⁵ Uncontrolled CRSwNP is characterized by the need for long-term treatment with INCSs plus at least one course of systemic corticosteroids in the previous 2 years or persistent/recurrent symptoms despite previous sinus surgery.⁵ In severe uncontrolled CRSwNP, the addition of biologics may be considered based on the patient's type of inflammation. Given the high cost of biologics, it is crucial to evaluate whether the disease and symptoms have appropriately improved after treatment.

It is recommended that treatment response is assessed 6 months after treatment with biologics.^{1,5} This assessment includes improved sense of smell (increase in smell score by ≥ 0.5), reduction in NP size (decrease by ≥ 1), improvement in nasal congestion score by ≥ 0.5 , and decreased SNOT-22 score by ≥ 8.9 , a simple yet significant measure of QoL.^{1,11} The SNOT-22 is a widely used and powerful patient-reported outcome measure (PROM) specific to CRS,²² with established validity in distinguishing between individuals with and without CRS and correlating with QoL in patients with CRS.²³ PROMs are particularly important for evaluating nasal symptoms in patients with CRS because objective measures such as laboratory tests, radiologic exams, and functional tests alone cannot fully assess the patient's condition. PROMs are essential tools for assessing patient health status, productivity, overall well-being, treatment response, and progression in patients with CRS.²⁴ A systematic review of PROMs related to CRS identified SNOT-22 as one of the highest quality validated measures among 14 PROM tools specific to adults with CRS.²⁵ The interquartile range for SNOT-22 is reported as mild 8–17, moderate 22.5–48, severe 54–83, with median values of mild 12, moderate 36, and severe 66.⁶ The MCID for SNOT-22 is established at 8.9, and a score > 40 indicates significant QoL impairment.²³ SNOT-22 also has been used as a PROM in other conditions such as allergic rhinitis,²⁶ obstructive sleep apnea (OSA),²⁷ and nasal septal deviation.^{28,29} There is a difference in SNOT-22 between OSA and CRS; even though both show high SNOT-22 scores, OSA has a high score in the psychological and sleep dysfunction domains but a low score in nasal discharge and loss of smell/taste.³⁰ Patients with preoperative SNOT-22 scores > 30 showed more benefit from functional endoscopic sinus surgery compared to those with lower scores, which could help to inform patient decisions for endoscopic sinus surgery using preoperative SNOT-22 scores.³¹

Randomized controlled trials and real-world studies on QoL changes in patients with CRS following biologics treatment indicate that the most common comorbidity in CRSwNP is asthma, particularly severe eosinophilic asthma.³ Most studies reported that biologics resulted in a significant improvement in SNOT-22 scores over the MCID compared to a placebo.³ In the present study, patients with severe asthma were enrolled and SNOT-22 improvements were evaluated after 6 months of GINA step 4–5 treatment. Among biologics, dupilumab showed significant improvements in total, extranasal rhinological, psychological, and sleep dysfunction domains regardless of CRS status. The significant improvements in total SNOT-22 scores appeared to be driven primarily by extranasal rhinological symptoms (cough, post-nasal drip, thick nasal discharge) and sleep/emotional well-being rather than core nasal symptoms such as nasal obstruction. This pattern may reflect our study design, where biologics were prescribed for severe asthma rather than specifically for nasal symptoms, and patients were enrolled regardless of CRS status.

Our study has several limitations. First, this study has inherent limitations due to its retrospective design and the selection of biologics based on routine clinical practice, which included subjective criteria influenced by physician experience. While this approach lacks the controlled precision of a randomized trial, it provides valuable real-world insights into the application and outcomes of biologics in clinical practice. This study enrolled adult patients with severe asthma treated with biologics regardless of CRS status even though we adjusted the ORs for achieving the MCID response in total and domain scores of SNOT-22 across different biologics. Secondly, potential baseline severity differences between treatment groups may have influenced therapeutic responses, as treatment allocation was not randomized and may have been influenced by unmeasured confounders related to disease severity, limiting our ability to draw definitive conclusions about comparative biologic

efficacy. Thirdly, the diagnosis of CRS and the evaluation of treatment response were based solely on patient self-reports—specifically, responses to whether they had ever been diagnosed with CRS by a physician—which highlights the lack of objective diagnostic measures such as nasal endoscopy, imaging studies, and nasal resistance scores, which represents a potential limitation of this study. Fourthly, we did not include omalizumab users, one of the biologics available for CRS, while we included reslizumab in the analysis despite its lack of indication for CRS. Finally, the utility of analyzing SNOT-22 by domains has not been yet well-established, and this study was unable to comprehensively evaluate the interconnections between different domains. Further research is needed to address these gaps.

In conclusion, biologic treatment in patients with severe asthma may lead to domain-specific improvements in SNOT-22 scores, particularly in the emotional and sleep domains. In our cohort, dupilumab demonstrated greater improvements not only in the total SNOT-22 score, but also in the extranasal rhinological, psychologic, and sleep dysfunction domains compared to conventional or anti-IL-5 antibody treatment in patients with severe asthma and nasal symptoms. We acknowledge that optimal management of CRS requires a comprehensive evaluation of NP type and disease severity, and that treatment decisions should be individualized—ranging from surgical approaches and corticosteroids to biologics or combination therapies—to achieve the best possible outcomes. Although our study was not designed to provide head-to-head comparisons among biologics, the inclusion of multiple agents within a single real-world cohort offers indirect comparative insights that may help inform clinical decision-making in the absence of formal randomized trials. Therefore, future studies should incorporate both subjective and objective outcome measures such as rhinomanometry, olfactometry, or other imaging modalities to provide a more comprehensive evaluation of biologic therapy effects on nasal symptoms. Despite such limitations, our findings provide valuable real-world evidence that biologics prescribed for severe asthma may offer meaningful nasal symptom benefits, with potential implications for treatment selection in patients with asthma-CRS overlap.

ACKNOWLEDGMENTS

This research was supported by the Bio & Medical Technology Development Program of the National Research Foundation (NRF) funded by the Korean government (MSIT) (2019M3E5D3073365). This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: RS-2024-00403700).

SUPPLEMENTARY MATERIALS

Supplementary Table S1

Categorized survey items for separate domains of the sino-nasal outcome test-22 instrument

Supplementary Table S2

Comparison of clinical characteristics according to the response of each SNOT-22 domain after 6 months in the biologic-treated and conventional groups

Supplementary Table S3

Odds ratios for achieving MCID response in total/domain scores of SNOT-22: asthma responders* vs. non-responders after 6 months of anti-IL-5 treatment (n = 69) and anti-IL-4 treatment (n = 114)

Supplementary Table S4

Odds ratios for achieving MCID response in total and each domain of SNOT-22 according to biologics (n = 229)

Supplementary Table S5

Odds ratios for achieving MCID response in total and each domain of SNOT-22 according to biologics; additionally adjusted for the history of CRS diagnosis (n = 229)

REFERENCES

1. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, et al. European position paper on rhinosinusitis and nasal polyps 2020. *Rhinology* 2020;58:1-464. [PUBMED](#) | [CROSSREF](#)
2. Orlandi RR, Kingdom TT, Smith TL, Bleier B, DeConde A, Luong AU, et al. International consensus statement on allergy and rhinology: rhinosinusitis 2021. *Int Forum Allergy Rhinol* 2021;11:213-739. [PUBMED](#) | [CROSSREF](#)
3. Mullol J, Azar A, Buchheit KM, Hopkins C, Bernstein JA. Chronic rhinosinusitis with nasal polyps: quality of life in the biologics era. *J Allergy Clin Immunol Pract* 2022;10:1434-1453.e9. [PUBMED](#) | [CROSSREF](#)
4. Fokkens WJ, Viskens AS, Backer V, Conti D, De Corso E, Gevaert P, et al. EPOS/EUFORÉA update on indication and evaluation of biologics in chronic rhinosinusitis with nasal polyps 2023. *Rhinology* 2023;61:194-202. [PUBMED](#) | [CROSSREF](#)
5. Bachert C, Han JK, Wagenmann M, Hosemann W, Lee SE, Backer V, et al. EUFORÉA expert board meeting on uncontrolled severe chronic rhinosinusitis with nasal polyps (CRSwNP) and biologics: definitions and management. *J Allergy Clin Immunol* 2021;147:29-36. [PUBMED](#) | [CROSSREF](#)
6. Toma S, Hopkins C. Stratification of SNOT-22 scores into mild, moderate or severe and relationship with other subjective instruments. *Rhinology* 2016;54:129-33. [PUBMED](#) | [CROSSREF](#)
7. DeConde AS, Mace JC, Bodner T, Hwang PH, Rudmik L, Soler ZM, et al. SNOT-22 quality of life domains differentially predict treatment modality selection in chronic rhinosinusitis. *Int Forum Allergy Rhinol* 2014;4:972-9. [PUBMED](#) | [CROSSREF](#)
8. Lee JH, Dixey P, Bhavsar P, Raby K, Kermani N, Chadeau-Hyam M, et al. Precision Medicine Intervention in Severe Asthma (PRISM) study: molecular phenotyping of patients with severe asthma and response to biologics. *ERJ Open Res* 2023;9:00485-2022. [PUBMED](#) | [CROSSREF](#)
9. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014;43:343-73. [PUBMED](#) | [CROSSREF](#)
10. Global Initiative for Asthma. Global strategy for asthma management and prevention. Fontana (WI): Global Initiative for Asthma; 2023.
11. Chowdhury NI, Mace JC, Bodner TE, Alt JA, DeConde AS, Levy JM, et al. Investigating the minimal clinically important difference for SNOT-22 symptom domains in surgically managed chronic rhinosinusitis. *Int Forum Allergy Rhinol* 2017;7:1149-55. [PUBMED](#) | [CROSSREF](#)
12. McGlothlin AE, Lewis RJ. Minimal clinically important difference: defining what really matters to patients. *JAMA* 2014;312:1342-3. [PUBMED](#) | [CROSSREF](#)
13. Pitre T, Jassal T, Angjeli A, Jarabana V, Nannapaneni S, Umair A, et al. A comparison of the effectiveness of biologic therapies for asthma: a systematic review and network meta-analysis. *Ann Allergy Asthma Immunol* 2023;130:595-606. [PUBMED](#) | [CROSSREF](#)
14. Lipworth BJ, Han JK, Desrosiers M, Hopkins C, Lee SE, Mullol J, et al. Tezepelumab in adults with severe chronic rhinosinusitis with nasal polyps. *N Engl J Med* 2025;392:1178-88. [PUBMED](#) | [CROSSREF](#)
15. Kuruvilla ME, Lee FE, Lee GB. Understanding asthma phenotypes, endotypes, and mechanisms of disease. *Clin Rev Allergy Immunol* 2019;56:219-33. [PUBMED](#) | [CROSSREF](#)

16. Ogulur I, Mitamura Y, Yazici D, Pat Y, Ardicli S, Li M, et al. Type 2 immunity in allergic diseases. *Cell Mol Immunol* 2025;22:211-42. [PUBMED](#) | [CROSSREF](#)
17. Siddiqui S, Bachert C, Bjermer L, Buchheit KM, Castro M, Qin Y, et al. Eosinophils and tissue remodeling: relevance to airway disease. *J Allergy Clin Immunol* 2023;152:841-57. [PUBMED](#) | [CROSSREF](#)
18. Manson ML, S  fholm J, James A, Johnsson AK, Bergman P, Al-Ameri M, et al. IL-13 and IL-4, but not IL-5 nor IL-17A, induce hyperresponsiveness in isolated human small airways. *J Allergy Clin Immunol* 2020;145:808-817.e2. [PUBMED](#) | [CROSSREF](#)
19. Sugita K, Steer CA, Martinez-Gonzalez I, Altunbulakli C, Morita H, Castro-Giner F, et al. Type 2 innate lymphoid cells disrupt bronchial epithelial barrier integrity by targeting tight junctions through IL-13 in asthmatic patients. *J Allergy Clin Immunol* 2018;141:300-310.e11. [PUBMED](#) | [CROSSREF](#)
20. Yeh CF, Lan MY, Lin CC, Hung YW, Huang WH, Lai YL. Dual blockade of IL-4 and IL-13 with dupilumab ameliorates sensorineural olfactory dysfunction in mice with eosinophilic sinonasal inflammation. *Rhinology* 2025;63:32-42. [PUBMED](#)
21. Cai S, Xu S, Zhao Y, Zhang L. Efficacy and safety of biologics for chronic rhinosinusitis with nasal polyps: a meta-analysis of real-world evidence. *Allergy* 2025;80:1256-70. [PUBMED](#) | [CROSSREF](#)
22. Liu M, Liu J, Weitzel EK, Chen PG. The predictive utility of the 22-item sino-nasal outcome test (SNOT-22): a scoping review. *Int Forum Allergy Rhinol* 2022;12:83-102. [PUBMED](#) | [CROSSREF](#)
23. Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item sinonasal outcome test. *Clin Otolaryngol* 2009;34:447-54. [PUBMED](#) | [CROSSREF](#)
24. Ting F, Hopkins C. Outcome measures in chronic rhinosinusitis. *Curr Otorhinolaryngol Rep* 2018;6:271-5. [PUBMED](#) | [CROSSREF](#)
25. Rudmik L, Hopkins C, Peters A, Smith TL, Schlosser RJ, Soler ZM. Patient-reported outcome measures for adult chronic rhinosinusitis: a systematic review and quality assessment. *J Allergy Clin Immunol* 2015;136:1532-1540.e2. [PUBMED](#) | [CROSSREF](#)
26. Husain Q, Hoehle L, Phillips K, Caradonna DS, Gray ST, Sedaghat AR. The 22-item sinonasal outcome test as a tool for the assessment of quality of life and symptom control in allergic rhinitis. *Am J Rhinol Allergy* 2020;34:209-16. [PUBMED](#) | [CROSSREF](#)
27. Bengtsson C, Jonsson L, Theorell-Haglow J, Holmstrom M, Janson C, Lindberg E. Sinonasal outcome test-22 and peak nasal inspiratory flow - valuable tools in obstructive sleep apnoea. *Rhinology* 2020;58:341-8. [PUBMED](#) | [CROSSREF](#)
28. Poirrier AL, Ahluwalia S, Goodson A, Ellis M, Bentley M, Andrews P. Is the sino-nasal outcome test-22 a suitable evaluation for septorhinoplasty? *Laryngoscope* 2013;123:76-81. [PUBMED](#) | [CROSSREF](#)
29. Aydođdu I, Atar Y, Aydođdu Z, Salt  rk Z, Ata   E, Dođan   , et al. Comparison of olfactory function and quality of life with different surgical techniques for nasal septum deviation. *J Craniofac Surg* 2019;30:433-6. [PUBMED](#) | [CROSSREF](#)
30. Ji K, Risoli TJ, Kuchibhatla M, Chan L, Hachem RA, Jang DW. Symptom profile of chronic rhinosinusitis versus obstructive sleep apnea in a tertiary rhinology clinic. *Ann Otol Rhinol Laryngol* 2019;128:963-9. [PUBMED](#) | [CROSSREF](#)
31. Rudmik L, Soler ZM, Mace JC, DeConde AS, Schlosser RJ, Smith TL. Using preoperative SNOT-22 score to inform patient decision for endoscopic sinus surgery. *Laryngoscope* 2015;125:1517-22. [PUBMED](#) | [CROSSREF](#)