Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
www.all-imm.com

SHORT COMMUNICATION OPEN ACCESS

Benralizumab is effective in severe asthma with CRS, regardless of demographic and clinical basal outcomes

Diana Betancor Perez[a,b*], Marcela Valverde-Monge[a,b†], Ana Rosado[c], Mar Gandolfo-Cano[d,e], Teresa Robledo Echarren[f,g], María del Mar Moro-Moro[h], María del Mar Reaño Martos[i], Rafael Pineda-Pineda[j], Dario Antolin-Amérigo[k], Ines Torrado[l], Maria Vazquez de la Torre[m], Remedios Cardenas[n], Ismael García-Moguel[o,p†], Javier Domínguez-Ortega[b,l†], AIRE Group

[†]*Both authors contributed equally to this work.*

[a]*Department of Allergy, University Hospital Fundación Jiménez Díaz, Madrid, Spain*
[b]*Centro de investigación biomédica en enfermedades respiratorias (CIBERES), Instituto Carlos III, Madrid, Spain*
[c]*Department of Allergy, Hospital Universitario Fundación Alcorcón, Madrid, Spain*
[d]*Department of Allergy, Hospital Universitario de Fuenlabrada, Madrid, Spain*
[e]*RETIC ARADyAL, Instituto de Salud Carlos III, Madrid, Spain*
[f]*Department of Allergy, Hospital Clinico San Carlos (HCSC)*
[g]*Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdSSC), Madrid, Spain*
[h]*Department of Allergy, Complejo Hospitalario de Toledo, Toledo, Spain*
[i]*Department of Allergy, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain*
[j]*Department of Allergy, Hospital Universitario del Sureste, Madrid, Spain*
[k]*Department of Allergy, Hospital Ramón y Cajal, Madrid, Spain*
Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Madrid, Spain
[l]*Department of Allergy, La Paz University Hospital, Institute for Health Research (IdiPAZ), Madrid, Spain*
[m]*Department of Allergy, Hospital Infanta Leonor, Madrid, Spain*
[n]*Department of Allergy, Hospital Virgen del Rocío, Seville, Spain*
[o]*Department of Allergy, Hospital Universitario 12 de Octubre, Madrid, Spain*
[p]*Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), Madrid, Spain*

Received 27 June 2025; Accepted 3 December 2025
Available online 1 July 2026

KEYWORDS
benralizumab;
severe eosinophilic asthma;
SNOT-22;
self-administration;
safety

Abstract
Severe eosinophilic asthma (SEA) frequently coexists with chronic rhinosinusitis (CRS), with or without nasal polyps (CRSwNP/CRSsNP), exacerbating disease burden. The Sino-Nasal Outcomes Test (SNOT-22) assesses quality of life in CRS patients, but the impact of benralizumab on nasal symptoms remains controversial. This retrospective multicenter study analyzed SNOT-22 changes after 12 months of benralizumab treatment in SEA patients with comorbid CRS from the AUTOBENRA study, including data from nine Spanish hospitals. Among 121 screened SEA patients, 72 (59.5%) had CRS, with 31 providing complete SNOT-22 data

***Corresponding author:** Diana Betancor Perez, Department of Allergy, University Hospital Fundación Jiménez Díaz, Madrid, Spain. *Email address*: diana.betancor@quironsalud.es

https://doi.org/10.15586/aei.v54i4.1449

pre- and posttreatment. Subjects were predominantly female (74.2%), with a mean age of 56.4 ± 13.8 years. Most (85%) had CRSwNP, 71% reported anosmia, and 67.6% had undergone functional endoscopic sinus surgery (FESS) (mean: 2.3 ± 1.7 surgeries). The baseline SNOT-22 score averaged 55.7 ± 24.6 points. After 12 months, 21 (67.7%) achieved a minimal clinically important difference (MCID; ≥12 points). Notably, anosmic subjects were more likely to achieve the MCID (82% vs 33%; P = 0.005). No significant correlations emerged between SNOT-22 improvement and demographic, clinical, or biomarker profiles.

These findings suggest that benralizumab significantly improves quality of life in SEA patients with CRS, particularly those with anosmia, regardless of baseline characteristics or biomarker levels.

Introduction

Severe asthma is associated with chronic rhinosinusitis (CRS) with (CRSwNP) or without nasal polyps (CRSsNP) in over 35% of subjects, which significantly increases the disease burden.[1] The specific sino-nasal outcomes test 22 (SNOT-22) is used to measure the quality of life in these patients.[2] The addition of biologics such as benralizumab, an anti-IL-5 receptor antibody, has been shown to improve asthma control, particularly in individuals with the eosinophilic phenotype. However, the effect of this treatment on nasal symptoms remains controversial.

This study aimed to analyze the changes in SNOT-22 after 12 months of benralizumab treatment in real-life subjects with uncontrolled severe eosinophilic asthma (SEA) and comorbid CRS.

Methods

This was a retrospective multicenter study conducted in nine hospitals in Spain. It included patients with CRS and severe eosinophilic uncontrolled asthma who were treated with self-administered benralizumab as previously documented in AUTOBENRA study.[3] SNOT-22 scores before and after 12 months of benralizumab treatment were analyzed, along with data on demographics, clinical characteristics, comorbidities, lung function, and asthma-related parameters (annual exacerbation rate, use of oral corticosteroids, asthma control test, quality of life).

Additionally, CRS-related characteristics were collected (number of functional endoscopic sinus surgeries, subjective anosmia, SNOT-22 questionnaire), and inflammatory biomarkers, such as total IgE, blood eosinophils, fractional exhaled nitric oxide (FeNO), and atopy status, were evaluated.

Data were analyzed using descriptive statistics, with results expressed as means with standard deviations. The normality of the data distribution was assessed using the Kolmogorov–Smirnov test. Qualitative variables were expressed as absolute numbers and relative frequencies. A comparison of demographic and clinical characteristics between groups was conducted using the Mann–Whitney U-test, Student's t-test, chi-square test (χ^2), or Fisher's exact test, depending on the nature of the variables. The changes in quantitative characteristics between the basal and post-benralizumab states were compared using Student's paired t-test or McNemar's exact test. Correlations between variables and changes in SNOT-22 were calculated using Spearman's correlation coefficient. A significance level of 5% (P < 0.05) was used for all statistical analyses, which were performed using GraphPad Prism 8 (GraphPad Software Inc., San Diego, CA, USA).

The study protocol was approved by the Ethics Committee for Research with Medicinal Products at Hospital Universitario 12 de Octubre, Madrid, Spain, under code 21/031 for the project. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

Results

A total of 121 subjects with severe asthma were screened, of whom 72 (59.5%) had CRS. However, only 31 had information on SNOT-22 data before and 12 months after benralizumab treatment. These 31 subjects had a mean age of 56.4 ± 13.8 years, and were predominantly females (23/31). Among them, 29 (85%) had CRSwNP and 2 had CRSsNP. The initial SNOT-22 was 55.7 ± 24.6 points. Most subjects (22/31) reported anosmia, and 23 (67.6%) had previously undergone functional endoscopic sinus surgery (FESS) with a mean of 2.3 ± 1.7 surgeries per patient. Patients with SNOT-22 measurement in the follow-up had better lung function, quality of life measured by miniAQLQ, and were less dependent on prednisone. The characteristics of these patients are summarized in Table 1.

At 12 months of benralizumab treatment, the SNOT-22 score improved to an average of 25.2 ± 21.67 points, reflecting an average improvement of 30.5 points. Regarding the minimal clinically important difference (MCID) in SNOT-22, defined as an improvement of ≥12 points,2 this threshold was reached by 21 (67.7%) subjects. The baseline SNOT-22 value moderately correlated with a high NP score (r = 0.5, P < 0.05).

Subjects with subjective anosmia had worse baseline SNOT-22 scores (average 56.2 ± 26.8 points) compared to those with preserved sense of smell (average 36.8 ± 25.9; P = 0.05). Among the subjects with subjective anosmia, 18 out of 22 recovered their sense of smell after treatment,

Table 1 Baseline characteristics of the total population and the SNOT-22 subgroup.

Demographic characteristics	Total	12 m follow-up SNOT-22 subgroup	No SNOT-22 subgroup
	121	31	90
Female N (%)	72 (59%)	23 (74%)	49 (54.1%)
Age, years, mean ± SD	59.5 ± 12.5	56.7 ± 13.8	60.4 ± 13.7
Never smokers N (%)	77 (63%)	24 (77%)	53 (59.3%)
BMI	28.2 ± 5	27.2 ± 4.8	28.6 ± 5.2
Clinical characteristics			
Exacerbation with treatment/year, mean ± SD	3.2 ± 2.9	3.1 ± 2.7	3.2 ± 3.0
FEV1 pre-BD, %, mean ± SD	72.8 ± 21	82.4 ± 21.3*	69.6 ± 21.3*
FEV1/FVC, %, mean ± SD	70.6 ± 10.1	87.4 ± 25.5*	65.4 ± 14.4*
ACT, mean ± SD	15 ± 5	15.7 ± 4.9	14.8 ± 5.2
Mini-AQLQ, mean ± SD	4.1 ± 1.3	5.97 ± 0.8*	3.6 ± 1.2*
FeNO ppb, mean ± SD	49 ± 43	64.7 + 56	44.5 ± 43.8
IgE total kU/L, mean ± SD	540 ± 1060	552 + 1092	536 ± 1170
FESS, N (%)	32 (26)	23 (74)**	9 (10)**
Blood eosinophils/microliters, mean ± SD	775 ± 520	789 ± 505	771 ± 530
Prednisone dependent, N (%)	34 (26)	23 (74)**	11 (12)**
Comorbidities			
Atopy N (%)	75 (62)	23 (74)	52 (58)
GERD N (%)	46 (38)	15 (48.8)	31 (34)
Bronchiectasis N (%)	28 (21)	9 (29)	19 (21)
N-ERD N (%)	36 (27)	18 (58)*	18 (20)*

*P < 0.05; **P < 0.001.

[a]ACT: Asthma control test; [b]BMI: Body mass index; [c]CRSwNP: Chronic rhinosinusitis with nasal polyps; [d]FeNO: Fractioned exhaled nitric oxide; [e]FEV1: Forced exhaled volume in 1 s; [f]FVC: Forced vital capacity; [g]GERD: Gastroesophageal reflux disease; [h]IQR: Interquartile range; [i]IgE: Immunoglobulin E; [j]mini-AQLQ: Mini-Asthma Quality of Life Questionnaire; [k]N-ERD: Nonsteroidal anti-inflammatory drugs exacerbated respiratory disease; [l]SD: Standard deviation.

while 4 showed no changes. A higher proportion of subjects with subjective anosmia (82%) reached the MCID in SNOT-22 improvement compared to subjects with a conserved sense of smell (3/9; P = 0.005).

We found that the MCID for SNOT-22 improvement after benralizumab treatment was reached in a greater proportion of nonatopic subjects (10/11; 90%) compared to the atopic subjects (13/23; 56.5%). However, this difference was not statistically significant (P = 0.05). No other correlation with SNOT-22 values or significant MCID improvements were observed based on demographic or clinical characteristics, including disease severity, presence of exacerbations, asthma control status, or clinical remission. Similarly, no significant associations were found with biomarkers such as FeNO or peripheral eosinophilia. Results are presented in Table 2.

Discussion

Real-life improvement in SNOT-22 scores following benralizumab treatment has been demonstrated in other studies, with reductions of −19.8 reported by Le et al.[4] and by Chitguppi et al.[5] of −21.4 points. These improvements are lower than the −30.5 points observed in our study. Notably, both studies used a lower MCID threshold in SNOT-22 of nine points, whereas our study applied the cutoff point based on the Spanish expert consensus guidelines. We hypothesize that the anti-IL-5R mechanism of action of benralizumab may be insufficient to fully block the IgE-mediated inflammatory cascade associated with allergic rhinitis. In the RANS study,4 67.6% of participants with SEA and CRSwNP achieved the MCID for SNOT-22 improvement. The lower proportion of subjects with allergic rhinitis (13.3%) in the RANS study compared to our population (64.5%) may explain the reduced success rate in our atopic subjects.

Our population and the study by Chitguppi et al.[5] included a higher proportion of subjects with prior FESS (74 and 87%, respectively) compared to Le et al.'s population (65.7%). This difference may explain why benralizumab appears to yield a greater reduction in SNOT-22 scores in subjects who have undergone FESS.

The limitations of this study include the retrospective design and the small sample size, which likely restricted the statistical significance of some correlations between clinical characteristics or biomarkers. Nonetheless, our analysis is valuable as it highlights trends near statistical significance, which could be further investigated in larger sample sizes.

Table 2 Comparison of baseline characteristics between subgroups reaching and not reaching MCID in SNOT-22.

	Reaching MCID in SNOT-22 (≥12 points)	NOT reaching MCID in SNOT-22 (<11 points)	P
	N = 21	N = 10	
Demographic characteristics			
Age, years Mean (SD)	56.6 (14.6)	60.2 (11.2)	n.s.
Sex: Female N (%)	12 (57.1)	8 (80)	n.s.
IMC Mean (SD)	26.2 (4.2)	29.0 (6.0)	n.s.
Atopy, N (%)	11 (53.3)	9 (90)	n.s.
Years with asthma, Mean (SD)	21.6 (13.8)	27.2 (11.6)	n.s.
Subjective anosmia, N (%)	18 (85.7)	4 (40)	0.01
Previous surgery	17 (80.95)	6 (60)	n.s.
Number of previous surgeries, Mean (SD)	2.28 (1.69)	2.2 (1.71)	n.s.
≥ 2 surgeries	13 (61.91)	2 (20)	n.s.
≥ 3 surgeries	4 (19.05)	0 (0.0)	n.s.
T2 Biomarkers			
IgE Mean (SD)	378.7 (595.1)	184.0 (160.4)	n.s.
Highest blood eosinophils on record, Mean (SD)	668.3 (302.1)	990.0 (895.7)	n.s.
Subjects ≥ 300 eos, N (%)	23 (100%)	11 (100%)	n.s.
FeNO Mean (SD)	64.1 (50.6)	56.1 (65.5)	n.s.
Lung Function			
FEV1, L Mean (SD)	1,5 (1,2)	2.1 (0.9)	n.s.
FEV1 %, Mean (SD)	77.99 (20.0)	89.2 (20.7)	n.s.
FVC, L Mean (SD)	2.1 (1.6)	2.8 (1.1)	n.s.
FVC %, Mean (SD)	89.9 (17.6)	104.0 (14.7)	0.04
FEV1/FVC Mean (SD)	87.4 (17.0)	85.1 (10.3)	n.s.
Clinical characteristics			
Number of asthma exacerbations per year, Mean (SD)	4.1 (3.4)	3.8 (3.5)	n.s.
Clinical remission of asthma, N (%)	12 (57.1)	7 (70.0)	n.s.
ACT, Mean (SD)	14.9 (4.1)	17.8 (5.3)	n.s.
Mini AQLQ, Mean (SD)	8.4 (16.2)	8.5 (10.8)	n.s.

[a]ACT: Asthma control test; [d]FeNO: Fractioned exhaled nitric oxide, [e]FEV1: Forced exhaled volume in 1 s, [f]FVC: Forced vital capacity; [i]IgE: Immunoglobulin E; [j]mini-AQLQ: Mini-Asthma Quality of Life Questionnaire; [l]SD: Standard deviation.

Conclusion

We conclude that benralizumab is effective in improving the quality of life, as measured by SNOT-22, in individuals with severe uncontrolled eosinophilic asthma and comorbid CRS, especially among those experiencing subjective anosmia. The improvement is evident regardless of other clinical characteristics or biomarker levels.

Ethics Approval and Informed Consent

The Ethics Committee for Research with Medicinal Products at Hospital Universitario 12 de Octubre, Madrid, Spain, approved the study protocol and assigned code 21/031 to the project. Signed informed consent from all subjects was included as an inclusion criterion.

Mandatory Disclosure on Use of Artificial Intelligence

The authors declare that no AI-assisted tools were used in the preparation of this manuscript. All references have been manually verified for accuracy and relevance.

Author Contributions

All authors contributed equally to this article.

Conflicts of Interest

The authors declare no potential conflicts of interest with respect to the publication of this article.

Funding

This research did not receive any specific grant from the funding agencies in public, commercial, or not-for-profit sectors. The AIRE Group meetings were sponsored by AstraZeneca.

References

1. Guía Española para el Manejo del Asma (GEMA) Versión 5.4. Spain: Luzan cinco health consulting. [cited 2024 May 31]. Available from: www.gemasma.com
2. Documento de consenso sobre rinosinusitis crónica con poliposis nasal: Guía POLINA. Versión 2023. Spain: Luzancinco

health consulting. [cited 2024 May 31]. Available from: https://www.seaic.org/profesionales/noticias-para-profesionales/guia-polina.html

3. García-Moguel I, Rosado A, Gómez-Cardeñosa A, Gandolfo-Cano M, Echarren TR, del Mar Moro Moro M, AIRE Group et al. Reliability, satisfaction and effectiveness of benralizumab home self-administration in patients with severe eosinophilic asthma in real-world practice: The Auto-Benra Study. J Asthma Allergy. 2022;13(15):623–32. https://doi.org/10.2147/JAA.S358738
4. Le TT, Emmanuel B, Katial R, Tran TN, Kwiatek JJ, Cohen DS, et al. Benralizumab in severe eosinophilic asthma and chronic rhinosinusitis with nasal polyps: The real-world, multi-country RANS observational study. J Asthma Allergy. 2024;17:313–24. https://doi.org/10.2147/JAA.S437190
5. Chitguppi C, Patel P, Gandler A, Murphy K, Md TK, Monostra P, et al. Effect of benralizumab in patients with severe eosinophilic asthma and chronic rhinosinusitis with nasal polyps: A case series. Am J Rhinol Allergy. 2021;35(5):559–67. https://doi.org/10.1177/1945892420978351