Effectiveness of Benralizumab in Severe Eosinophilic Asthma Under Conditions of Routine Clinical Practice

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Benralizumab is a humanized IgG1κ, afucosylated, monoclonal antibody that binds to IL-5 receptor α on the surface of human eosinophils and basophils. It induces rapid and complete depletion of blood eosinophils, which persists for at least 2 to 3 months in patients receiving treatment [1,2].

Clinical trials have shown benralizumab to be efficacious and safe in patients with severe eosinophilic asthma by reducing annual exacerbations and improving symptoms and lung function [3,4]. Real-life studies are useful for checking the effect of a treatment in routine clinical practice, and several studies have shown the effectiveness of benralizumab [5,6]. Benralizumab is indicated in patients with severe uncontrolled eosinophilic asthma [7,8].

We report the results of a study performed by the Registry of Severe Asthma of the Region of Murcia (RE-ASGRAMUR) under conditions of routine clinical practice in 8 hospitals from the Region of Murcia, Spain. The study was approved by the Research Ethics Committee Area II-VIII of the Murcian Health System (SMS).

We present a series of 84 patients diagnosed with severe eosinophilic asthma after completing at least 1 year of treatment with benralizumab (mean duration of treatment, 18.8 months). We analyzed clinical characteristics, eosinophilia, total IgE, tolerance, and effectiveness (decreased exacerbations, Asthma Control Test [ACT], Asthma Quality of Life Questionnaire [AQLQ], lung function [FEV_1]), and use of oral corticosteroids. The statistical analysis was performed using the Wilcoxon signed rank test; the results are reported as median (IQR). The methods are described in detail in Appendix 2 of the Supplementary material.

The mean age was 59.5 years, and 49 patients were women (58.3%). The average body mass index was 29.5. Onset of asthma was before age 18 years in 16 patients (20.2%) and after in 63 (79.8%), and the mean duration of the disease was 23.5 years in the group with nasal polyps and 22 years in the group without polyps. Forty-three patients (51.2%) had never smoked, 38 (45.2%) were ex-smokers, and 3 were current smokers.

Thirty-two patients (38.1%) were atopic, 37 (44%) had chronic rhinosinusitis, and 32 (38%) had nasal polyposis. Thirty-nine patients (46%) were corticosteroid-dependent; the mean daily dose of prednisone was 16.5 mg. The mean eosinophil count was 682, IgE was 268.4, and FeNO was 51.9 ppb.

The mean number of exacerbations was 4.5, and 43 patients (51%) had to attend the emergency department at least once in the previous year. The mean ACT was 12.5 and the mean AQLQ was 3. Regarding lung function, the mean FEV_1 was 1840 mL (67.5%).

Previous treatment was with omalizumab in 32 patients (38%) and with mepolizumab in 16 (19%). In both cases, treatment was suspended owing to lack of response.

Patients' baseline characteristics are shown in Supplementary Table 1.

The results are shown in the Table. We found a very significant reduction in the number of exacerbations, from a median of 3 before treatment with benralizumab to 0 after treatment; this decrease was similar in patients with and without nasal polyposis. It is noteworthy that 70% of patients did not experience exacerbations during the year of treatment compared with 8% before treatment. This finding is consistent with data from other studies on benralizumab [9]. We observed this significant decrease in exacerbations in all groups, regardless of the baseline eosinophil level (Supplementary Table 2).

Median intake of oral prednisone by corticosteroid-dependent patients decreased from 10 mg before treatment to 0 mg after treatment, both in the group as a whole and in the subgroups (with and without polyposis). After treatment, 82% of patients did not take oral corticosteroids as maintenance therapy. The decrease in corticosteroid intake was observed in all groups in terms of eosinophil count, although it reached 0 mg per day in those with more than 300/µL, again confirming this effect of the drug [10].

As for asthma control (measured using the ACT score), we recorded a relevant increase from 13 to 22 in the group as a whole, well above the minimum important difference. This increase was greater in the polyposis subgroup.

Quality of life, which was measured using the miniAQLQ score, increased significantly, by 2.21 points, up to 5.07 points, well above the minimum important difference, as reported in other studies [11]. This increase was also greater in the subgroup with polyposis.

Table. Results[a]

	Total N=84			Nasal Polyps n=32			No Nasal Polyps n=52		
	Baseline	After treatment	*P*	Baseline	After treatment	*P*	Baseline	After treatment	*P*
Exacerbations	3 (2-5)	0 (0-1)	<.00001	3 (2-5)	0 (0-0)	<.00001	4 (2-6.5)	0 (0-1)	<.00001
Oral prednisone	10 (5-20)	0 (0-5)	<.00001	10 (5-20)	0 (0-2.5)	.0013	10 (5.5-20)	0 (0-5)	<.00001
ED visits	1 (0-3)	0 (0-0)	<.00001						
ACT	13 (8-16)	22 (18.5-24)	<.00001	11 (9-14)	23 (19.5-24)	<.00001	13 (8-16)	21 (16-23)	<.00001
AQLQ	2.86 (2.27-3.7)	5.07 (4.07-5.85)	<.00001	2.86 (2-3.87)	5.6 (4.33-6.06)	<.00001	2,83 (2.4-3.5)	4.67 (3.8-5.27)	<.00001
FeNO, ppb	38 (14-68)	29 (19-51)	.011	29.5 (16-89)	32 (27-70)	NS	40 (10-59)	23.5 (8.5-46)	.0048
FVC, %	85 (70-97)	95.5 (78-104)	<.00001	86 (67-101)	98.5 (83-105)	.0014	83.5 (70.5-96)	90.5 (76.5-102)	.0003
FEV_1, %	69 (53-82)	81,5 (65-92)	<.00001	71 (51-84)	82.5 (72-95)	.0002	68 (54-76)	78.5 (63.5-91.5)	.0001

Abbreviations: ACT, Asthma Control Test; AQLQ, Asthma Quality of Life Questionnaire; FeNO, fractional exhaled nitric oxide; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity.
[a]Results are presented as median (IQR)

Overall, FeNO decreased from 38 before treatment to 29. By specific group, it decreased in patients without nasal polyposis and increased slightly in those who had polyposis. The median eosinophil count was 615/μL (410-865) before treatment and 0 (0-0) after (P<.00001) in the polyposis group and 600 (330-900) before treatment and 0 (0-0) after it (P<.00001) in the group without polyps.

With respect to lung function, we found an increase in FEV_1 from 1740 mL (69%) to 1985 mL (81.5%). This increase was greater in the group with polyposis (385 mL) than in the group without it (165 mL), thus confirming this comorbid condition as a potential indicator of enhanced response [12]. The median baseline FVC% was 85%, which increased to 95.5% after treatment; this increase was also higher in the group with polyps (12.5%) than in the group without polyps (7%). The FEV_1/FVC ratio was under the lower limit of normal before treatment in 51 patients, returning to normal values in 17 after treatment.

Five patients discontinued treatment because of adverse effects, as follows: local pain, asthenia, and refusal of treatment, 1 patient; influenza-like syndrome, 1 patient; headache, 1 patient; arthralgia, 1 patient; and bronchospasm plus headache, 1. Only 3 patients discontinued treatment owing to lack of response (persistence of exacerbations, with admission to hospital in 2 cases); all 3 were women (eosinophil counts of 300, 890, and 2300/μL), 2 of whom were obese. Two patients were atopic, and none had nasal polyps. One patient was previously in treatment with omalizumab, and another had received omalizumab and mepolizumab.

In conclusion, we found benralizumab to be a well-tolerated and effective treatment for patients with severe eosinophilic asthma, even in patients with eosinophils <300/μL. It decreased both the number of exacerbations and the intake of oral corticosteroids. Benralizumab improved disease control, quality of life, and lung function in our study. This improvement was more notable in patients with nasal polyposis.

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Conflicts of Interest

Juan Carlos Miralles López has received consultancy fees from Chiesi and speaker fees from Novartis, GSK, AstraZeneca, Sanofi, and Chiesi.

Rubén Espinosa Andújar has received speaker fees from Novartis, GSK, AstraZeneca, Sanofi, and Chiesi.

Francisco Javier Bravo Gutiérrez has received speaker fees from Novartis, Ferrer, GSK, AstraZeneca, Sanofi, and Chiesi.

Manuel Castilla Martínez has received consultancy fees from GSK and AstraZeneca and speaker fees from Novartis, GSK, AstraZeneca, Sanofi, and Chiesi.

Isabel María Flores Martín has received speaker fees from Novartis, GSK, and Sanofi. María Loreto Alemany Francés has received speaker fees from Novartis, GSK, AstraZeneca, and Chiesi.

Manuel José Pajarón Fernández has received speaker fees from GSK.

José Valverde Molina has received consultancy fees from AstraZeneca, speaker fees from Novartis, GSK, Astra Zeneca, Sanofi, Teva, and Orion Pharma, and fees for advisory board participation from GSK and Novartis.

The remaining authors declare that they have no conflicts of interest.

References

1. Ghazi A, Trikha A, Calhoun WJ. Benralizumab – a humanized mAb to IL-5Rα with enhanced antibody-dependent cell-mediated cytotoxicity – a novel approach for the treatment of asthma. Expert Opin Biol Ther. 2012;12:113-8.
2. Dávila González I, Moreno Benítez F, Quirce S. Benralizumab: A New Approach for the Treatment of Severe Eosinophilic Asthma. J Invest Allergol Clin Immunol. 2019;29(2):84-93.
3. Bleecker ER, FitzGerald JM, Chanez P, Papi A, Weinstein SF, Barker P, et al. Efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists (SIROCCO): a randomised, multicentre, placebo-controlled phase 3 trial. Lancet. 2016;388:2115-27.
4. FitzGerald JM, Bleecker ER, Nair P, Korn S, Ohta K, Lommatzsch M, et al. Benralizumab, an anti-interleukin-5 receptor α monoclonal antibody, as add-on treatment for patients with severe, uncontrolled, eosinophilic asthma (CALIMA): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet. 2016;388:2128-41.
5. Miralles López JC, Escudero Pastor AI, Carbonell Martínez A, Navarro Garrido C, Bonilla Pacheco Y, Petrik Petrik Y. Benralizumab in real life. J Investig Allergol Clin Immunol. 2021;31(1):87-8.
6. Nolasco S, Crimi C, Pelaia C, Benfante A, Caiaffa MF, Calabrese C, et al. Benralizumab Effectiveness in Severe Eosinophilic Asthma with and without Chronic Rhinosinusitis with Nasal Polyps: A Real-World Multicenter Study. J Allergy Clin Immunol Pract. 2021;9(12):4371-80. doi: 10.1016/j.jaip.2021.08.004.
7. Dávila I, Quirce S, Olaguibel JM. Selection of Biologics in Severe Asthma: A Multifaceted Algorithm. J Investig Allergol Clin Immunol. 2019;29:325-8.
8. Delgado J, Dávila IJ, Domínguez-Ortega J. Clinical Recommendations for the Management of Biological Treatments in Severe Asthma Patients: A Consensus Statement. J Investig Allergol Clin Immunol. 2021;31:36-43.
9. Korn S, Bourdin A, Chupp G, Cosio BG, Arbetter D, Shah M, et al. Integrated Safety and Efficacy Among Patients Receiving Benralizumab for Up to 5 Years. J Allergy Clin Immunol Pract. 2021;9:4381-92.
10. Nair P, Wenzel S, Rabe KF, Bourdin A, Lugogo NL, Kuna P, et al. Oral Glucocorticoid-Sparing Effect of Benralizumab in Severe Asthma. N Engl J Med. 2017;376:2448-58.
11. Miralles López JC, Escudero Pastor AI, Carbonell Martínez A, Navarro Garrido C, Bonilla Pacheco Y, Petrik Petrik Y. Quality of life in severe asthmatic patients treated with benralizumab.

Eur Ann Allergy Clin Immunol. 2021 Jun 4. doi: 10.23822/EurAnnACI.1764-1489.218. Online ahead of print.
12. Mathur SK, Modena BD, Coumou H, Barker P, Kreindler JL, Zangrilli JG. Postbronchodilator lung function improvements with benralizumab for patients with severe asthma. Allergy. 2020 Jun;75(6):1507-10. doi: 10.1111/all.14178.

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