Baseline Clinical Characteristics and Phenoendotypes of Patients With Severe Asthma in Alergodata: The Spanish Allergy Society Registry

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Asthma is a heterogeneous chronic condition comprising several phenotypes with similar clinical manifestations [1]. Between 5% and 10% of asthma patients have severe asthma

(SA) [2], and despite appropriate therapy, symptoms remain uncontrolled in approximately 50% [3].

Chronic rhinosinusitis is a group of disorders that also comprises several phenotypes, the most debilitating of which is CRS with nasal polyps (CRSwNP), which affects 2.1% to 4.4% of people in Europe [4]. The lack of highly effective therapy for CRSwNP means that adults experience severe lower airway disease [4].

SA and CRSwNP often co-occur [4]. Asthma is estimated to affect 40% to 70% of patients with CRSwNP, and the frequency of CRSwNP ranges from 57% to 62% in SA; both situations are associated with worse outcomes [4].

Recent studies showed that the pathophysiological mechanisms underlying CRSwNP and asthma are similar, with the type 2 (T2) endotype being the most frequent in developed countries [5]. Advances in the understanding of T2 inflammation mechanisms [4] have led to the development of new classes of biological drugs [6] and to the emergence of the united airway disease (UAD) concept, which highlights the need for an integrated approach to the diagnosis and treatment of airway diseases [7,8].

However, since upper and lower airway disease are still considered separate entities in routine clinical practice, further studies and real-world data are needed to address the lack of evidence in the management of UAD [8], as well as to determine the most appropriate biologics and how they can help when selecting treatment in the long term [8].

In this context, and as part of an action plan to provide real-word evidence on health outcomes in major allergic diseases, the Spanish Society of Allergology and Clinical Immunology (SEAIC) implemented the Alergodata Registry, whose primary objective was to describe patients'

Table. Main Clinical and Sociodemographic Variables of the Patients Included in the Alergodata Registry.

Clinical and sociodemographic variables	Severe asthma	Severe asthma[a] with CRSwNP
Mean (SD) age, y	N=170	N=30
Adults	50.6 (14.4) (n=158)	51.4 (12.4)
Children	13.8 (3.8) (n=12)	NA
Female sex	N=170 64.1%	N=30 50.0%
Comorbidities	N=170	N=30
CRSwNP[a]	44.1%	NA
CRS without nasal polyps	7.1%	NA
Atopic dermatitis[a]	10.0%	10.0%
Rhinitis	68.0%	65.5%
Gastroesophageal reflux	17.1%	10.0%
Psychiatric disturbance	11.8%	6.67%
Respiratory disease exacerbated by NSAIDs	18.2%	50.0%
Bronchiectasis	7.7%	10.0%
Obstructive sleep apnea	7.1%	6.9%
Mean no. of exacerbations	1.9 (2.3) (N=143)	NA
Level of uncontrolled asthma	79.5% (N=132)	NA
Phenotypes of asthma (%)	N=146	N=22
Eosinophilic (T2)	47.9%	77.3%
Allergic (T2)	50.7%	22.7%
Noneosinophilic	1.4%	0.0%
Prescribed biologic treatment		
Omalizumab	28.6% (N=168)	12.5% (N=24)
Dupilumab	27.9% (N=165)	69.6% (N=23)
Mepolizumab	23.4% (N=167)	20.8% (N=24)
Benralizumab	20.4% (N=157)	4.2% (N=24)
Reslizumab	3.8% (N=158)	4.0% (N=25)

Abbreviations: CRS, chronic rhinosinusitis; CRSwNP, chronic rhinosinusitis with nasal polyps; NA, not applicable; NSAIDs, nonsteroidal anti-inflammatory drugs.
[a]With or without associated biologic treatment.

characteristics and the use of biological drugs in SA and/or CRSwNP.

In the present manuscript, we present and discuss data on SA and CRSwNP collected at the baseline visits during the first year (from November 19, 2021, to December 1, 2022) of the Alergodata study.

The study population comprised patients with a diagnosis of SA and/or CRSwNP (EPOS2020) treated with biologic drugs and/or nonbiologics in allergy units. All patients signed the informed consent document (see inclusion/exclusion criteria in Table 1, Supplemental Files). Follow-up was for 5 years, with at least 1 annual visit. Each principal investigator recorded the patient's information on an electronic case report form designed specifically for the study. The data recorded were stored in a database and periodically reviewed to detect possible inconsistencies and/or missing items. This database includes ranges and internal consistency rules to ensure correct data completion and thus ensure optimal quality. The protocol was evaluated by the health agencies of the respective autonomous communities and the research ethics committees of the 61 hospitals participating in the study. The favorable opinion of the Research Ethics Committee of Hospital Clinic de Barcelona was obtained on March 4, 2021. The most relevant variables collected are presented in Table 2, Supplemental Files. Details of the methodology followed were published previously [9].

The study population comprised 279 patients with SA, of whom 170 received biological treatment (60.9%). Asthma was uncontrolled in 79.5% of patients. Of these 170 patients, 75 had comorbid CRSwNP (44.2%), which is consistent with the results of other series [10], even if lower than the usual prevalence [4]. Regarding the biologic treatments at inclusion, dupilumab was prescribed much more frequently than all other treatments in cases of SA with comorbid CRSwNP. It is also worth noting that even if benralizumab is not indicated for the treatment of CRSwNP, it was prescribed in 4.2% of cases of asthma and comorbid CRSwNP, consistent with the favorable results obtained in the phase 3 OSTRO Study [11]. The Table summarizes the main characteristics, comparing patients with SA and patients with both SA and CRSwNP.

The Alergodata registry provides valuable data that can be compared with those reported in other series, for example, ENEAS [12] and the Spanish MEGA Cohort [13]. Specifically, we found that more than 50% of patients presented allergic asthma, whereas in the ENEAS series, most (58.1%) presented an eosinophilic endotype. However, these phenoendotypes may change and even overlap during the patient's lifetime [14]. In fact, allergens were one of the main reported triggers of asthma exacerbations (Table 2, Supplemental Files), although we must be cautious with these results, since exacerbations are usually triggered by various factors. Furthermore, clinically relevant allergic sensitization was reported in 65.7% of cases and, for the first time in a registry, the cumulative annual dose of corticosteroids was recorded. These last 3 observations highlight the originality of the Alergodata registry, given that they are not usually reported in series of this kind.

Our study is subject to limitations. First, the registry is still too young to enable meaningful and comparative data to be extracted. Nevertheless, we must keep in mind that it will remain open for 5 years, thus enabling us to compare initial, intermediate, and final results and to measure the impact of biological treatment on disease progression. Second, as the registry is based on clinical practice data, the sample size will depend on the fluctuation in the numbers of patients attending the clinic, which could lead to missing data. Third, the statistical analysis was performed per protocol, with the result that a subanalysis would be required to extract the full value of the data.

Patients with UAD, in particular SA and CRSwNP, are more refractory to treatment owing to increased airway obstruction and more frequent exacerbations [15]. A registry such as Alergodata will provide insight for clinicians regarding the real benefit of biological drugs, in terms of efficacy and safety and impact on reducing the use of nonbiological treatments.

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Conflicts of Interest

In the last 3 years, Javier Domínguez-Ortega has received fees for advisory boards from GSK, SANOFI, and AstraZeneca and speaker's honoraria from Sanofi, TEVA GSK, AstraZeneca, Bial, Novartis, Chiesi, and LETI Pharma.

In the last 3 years, Carlos Colás has received honoraria for consultancy and conferences from Novartis, GSK, Sanofi, Viatris, Chiesi, MSD, Takeda, Roxall, and Thermo Fisher.

In the last 3 years, Julio Delgado Romero has received the following: fees for advisory boards from Bial; speaker's honoraria from AstraZeneca, Bial, Chiesi, GlaxoSmithKline Novartis, and Sanofi; and grant/research support from AstraZeneca and Orion. He also received assistance with travel to meetings from Sanofi and Menarini.

In the last 3 years, Alicia Habernau Mena has received payment or honoraria for consultancy and conferences from ALK-Abelló, Leti, GSK, Sanofi, Chiesi, GlaxoSmithKline, Bioproject, AstraZéneca, MSD, and FaesPharma

In the last 3 years Ana Montoro has received the following: honoraria for consultancy and conferences from GSK, Astra Zeneca, Chiesi, and Letipharma; research/training support from Faes Farma, Allergy therapeutics, ALK, and DIATER; and assistance with travel to meetings from Roxall and Takeda.

In the last 3 years, Pilar Barranco has received speaker's honoraria from GSK.

In the last 3 years, Patricia Prieto Montaño has received payment or honoraria for presentations, speaking or educational events from Leti, Allergy Therapeutics, Diater, Astra Zeneca, GSK, and Sanofi and payment for expert testimony by Astra Zeneca, Sanofi, and GSK.

In the last 3 years, Juan Fraj Lázaro has received consulting fees from AstraZeneca and Sanofi and speaker fees from Gebro, AstraZeneca, GSK, Sanofi, Novartis, and Chiesi.

In the last 3 years, Pedro Galindo, has received honoraria for conferences from Novartis, GSK, Sanofi, Chiesi, and AstraZeneca.

In the last 3 years, Maria Gil Melcón has received honoraria for consultancy and conferences from AstraZeneca, Novartis, Sanofi, and GSK.

In the last 3 years, María Magdalena Lluch Bernal has received speaker's fees from GSK, and manuscript writing and assistance for attending meetings from Menarini.

In the last 3 years, Ruperto González-Pérez, has received fees related to advisory boards from GSK, AstraZeneca, Leo Pharma, and Sanofi. He has also received speaker's honoraria from GSK, AstraZeneca, Sanofi, Inmunotek, Diater, and Leti and research grants from SEAIC and FUNCANIS.

In the last 3 years, Darío Antolín-Amérigo has received payment or honoraria for lectures, presentations, speakers, bureaus, manuscript writing, and educational events from Astra Zeneca, GSK, Novartis, and Sanofi and payment for expert testimony from Astra Zeneca, GSK, and Sanofi.

In the last 3 years, Javier Montoro Lacomba has received speaker's honoraria from GSK, Sanofi, Diater, Chiesi, AbbVie, and Faes.

In the last 3 years, Antonio Valero has been an advisor for Sanofi, Uriach, AstraZeneca, ALK, and Allergy Therapeutics. He has received speaker's fees for meetings sponsored by AstraZeneca, Chiesi, Bial, and GSK and research project grants from Novartis and Uriach.

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