

ALERGODATA: Sentinel Registry of Health Outcomes in Allergic Patients Treated With Biological Therapies at Specialized Allergology Clinics in Spain

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Palabras clave: Asma grave. Rinosinusitis crónica con pólipos nasales. Urticaria crónica. Dermatitis atópica moderada a grave. Evidencia basada en la práctica clínica.

The incidence of allergic diseases has grown steadily in recent decades, giving rise to a global public health problem that severely impacts health and available health care resources [1].

Biological drugs constitute a very specific therapeutic option for immune system targets and have helped improve

allergic patients' quality of life, especially those with the most severe and poorly controlled disease [2].

Once the clinical trials required for authorization are completed and the biologic drug is available, observational studies should be conducted in routine clinical practice to analyze the efficiency of the intervention in the real-world population. Moreover, there is a lack of evidence on how biologics can influence different concomitant type 2 helper T-cell diseases that co-occur in an individual patient [3].

One of the objectives of the Spanish Society of Allergology and Clinical Immunology (SEAIC) is to promote activities that provide evidence on health outcomes in a clinical setting. To this end, SEAIC launched the Alergodata Registry, which is the first registry designed to obtain data on the use of biological drugs in routine clinical practice by Spanish allergists.

The main objective of the Alergodata Registry, which was set in motion at the end of 2019, is to describe the profile of patients with severe asthma and/or chronic rhinosinusitis with nasal polyps and/or chronic urticaria and/or moderate-to-severe atopic dermatitis (AD) who are receiving biological drugs and are followed up in specialized allergology clinics.

The Alergodata Registry is led by a project team (Table 1, Supplemental files) and coordinated by specific committees responsible for each disease under study (Table 2, Supplemental files).

In line with the study plan and before inclusion in the Alergodata Registry, patients must be informed using the patient information sheet and sign an informed consent form. The study initially involves an inclusion visit and at least 1

annual visit for the first 5 years, as the disease requires. Other visits are arranged according to routine clinical practice. The investigator records the information in an electronic case report form (eCRF) designed specifically for the study (Figure).

The information collected at the registry inclusion visit comprises screening criteria (Table 3, Supplemental Files), patient sociodemographic variables, baseline clinical status of the patient's disease, diagnostic test results, and baseline quality of life.

The effectiveness of the treatments is measured according to the usual determinations performed for monitoring and evaluating patients as appropriate for their disease. In the case of severe asthma, disease control is classified according to the Asthma Control Test (ACT), lung function (including forced spirometry and bronchodilation) is measured, and the number and intensity of exacerbations and consumption of systemic corticosteroids is recorded [4]. The progress of patients with chronic rhinosinusitis with nasal polyps is evaluated based on the improvement in nasal symptoms based on the Total Nasal Symptom Score [5]. Reduction in polyp size is measured using endoscopy for the nasal passages and sinus computed tomography. In patients with chronic urticaria, the Urticaria Activity Score (UAS and UAS7) and the Urticaria Control Test are administered [6,7]. In patients with moderate-to-severe AD, severity scores (Eczema Area Severity Index and Scoring Atopic Dermatitis) are used [8]. The Investigator Global Assessment and the Patient-Oriented Eczema Measure are also included in the evaluation [9,10].

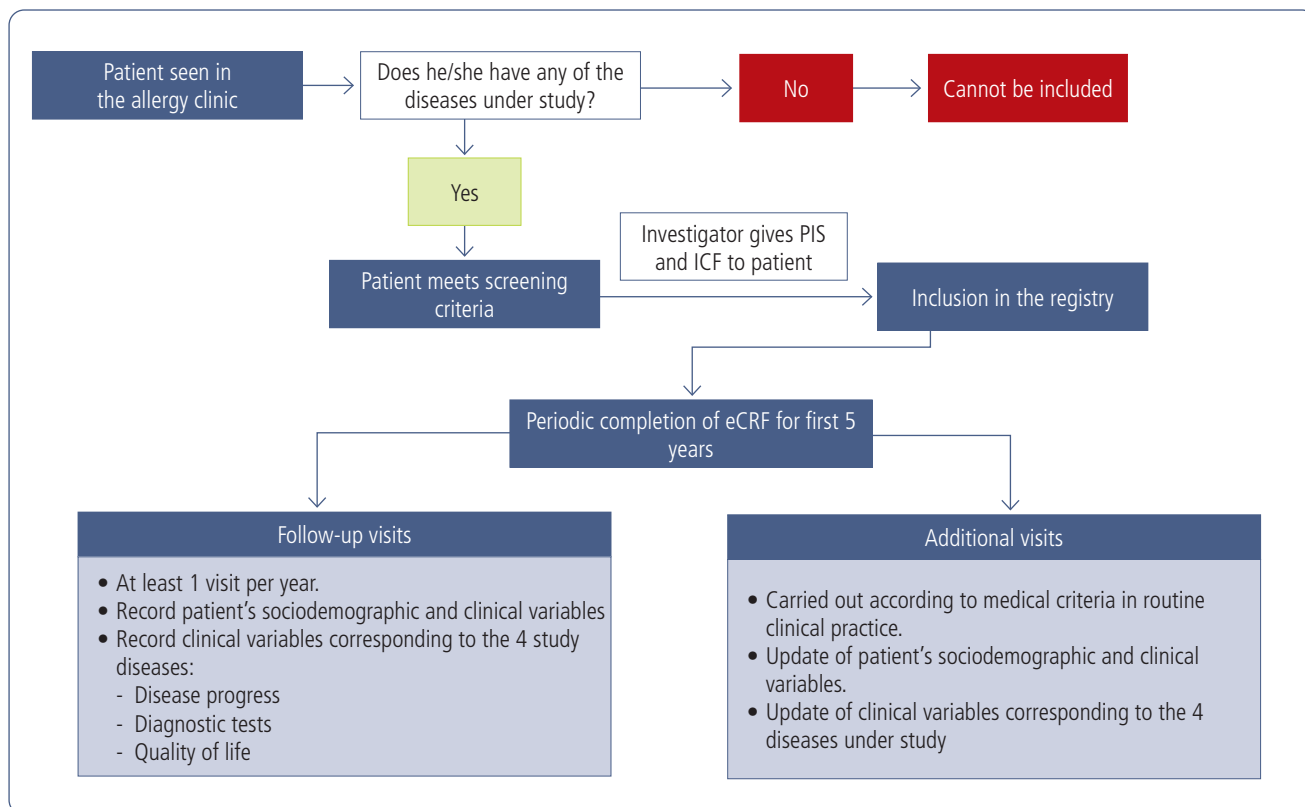


Figure. Study flow chart. PIS indicates patient information sheet; ICF, informed consent form; eCRF, electronic case report form.

Safety is assessed by recording adverse events associated with each biological drug.

Quality of life (QOL) is evaluated in all patients; in patients with severe asthma, it is measured using the Mini Asthma Quality of Life Questionnaire [11]. For patients with chronic rhinosinusitis with nasal polyps, QOL is measured using the Sinonasal Outcome Test [12]. For patients with chronic urticaria, quality of life is measured using the Chronic Urticaria Questionnaire for Quality of Life [13] or the Dermatology Life Quality Index (DLQI)[14], and finally, for patients with moderate-to-severe AD, QOL is assessed using the DLQI [14] or the Children's Dermatology Life Quality Index [15].

An annual statistical analysis is performed to evaluate the primary and secondary objectives, which are stratified according to the disease(s) recorded for the patient. The results are published in scientific journals.

Concerning implementation and conduct, all SEAIC members were invited to participate in the study. Confirmation was received from 62 Spanish hospitals, of which 61 finally participated (Table 4, Supplemental Files). The research protocol was drafted, and the documentation was prepared and presented to the health authorities. At the end of 2020, the Spanish Agency for Medicinal Products and Medical Devices classified the registry as a postauthorization prospective follow-up study (EPA-SP [Spanish initials]). Finally, in 2021, the protocol was evaluated by the autonomous community health agencies and research ethics committees of the hospitals that had confirmed their interest in participating in the SEAIC initiative, and the favorable opinion of the Research Ethics Committee of Hospital Clinic de Barcelona was obtained on March 4, 2021. Specifically, the study was submitted to or evaluated in 13 autonomous communities (Table 5, Supplemental Files). In November 2021, eCRF access was opened, and patients who initiated biological treatment (or were not taking biological treatment in the case of severe asthma) as of January 1, 2021 were included.

The Alergodata Registry is a SEAIC initiative for generating scientific knowledge in routine clinical practice in the field of allergology. It provides direct, accurate, evidence-based information on the management and treatment of patients with the allergic diseases in question, thus contributing to better decision-making in health care. In short, real-life data in all these scenarios is gathered, analyzed, and acted upon accordingly. Findings are periodically reanalyzed to build upon and strengthen the decision-making framework emerging from evidence-based medicine that cannot be obtained from clinical trials alone.

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Conflicts of Interest

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

In the last 3 years, Ignacio Dávila has received payment for lectures, including service on speakers bureaus from Allergy Therapeutics, AstraZeneca, Chiesi, Diater, GSK, Leti, Novartis, and Sanofi. He has also received payment for consultancy from Allergy Therapeutics, ALK-Abello, AstraZeneca, GSK, Merck, MSD, Novartis, and Sanofi and grants from Thermo Fisher Diagnostics, ISCIII, and Junta de Castilla y León.

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

In the last 3 years, Alfonso del Cuvillo has received honoraria for consultancy and conferences from MSD, AstraZeneca, Chiesi, Novartis, Sanofi, GSK, TEVA, Viartis, Alk-Abello, Faes Farma, Uriach, and Menarini.

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

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, Ignacio Jáuregui Presa has received the following: fees as an advisor from Sanofi, Novartis, and Faes Farma; congress support from Sanofi and Faes Farma; and speaker's honoraria from Sanofi, MSD, LETI Pharma, Novartis, Gebro Pharma, Organon, GSK, and Faes Farma.

In the last 3 years, Milagros Lázaro Sastre has received fees for advisory boards from AbbVie and has speaker's honoraria from Sanofi, AbbVie, Novartis, Chiesi, Faes Farma, Organon, and LETI Pharma.

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, Anna Sala-Cunill has received payment for lectures, including service on speaker's bureaus from Takeda, Behring, Allergy Therapeutics, Chiesi, Leti, Novartis, AbbVie, Sanofi, and Organon and for consultancy from Takeda, AbbVie, Novartis, and Sanofi.

In the last 3 years, Silvia Sánchez García has received payment or honoraria for lectures, presentations, speaker bureaus, and educational events from GSK, ALK-Abelló, Leti, GSK, Stallergenes and payment for acting as an advisor from GSK and Stallergenes.

In the last 3 years, Beatriz Veleiro Pérez has taken part in an advisory board for Novartis. She received speaker's honoraria from Novartis and participated as a teacher-trainer supported by Novartis, Sanofi, AstraZeneca, and Cipla.

In the last 3 years, Carmen Vidal Pan has received personal fees for advisory boards from Stallergenes Greer and Leti and

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In the last 3 years, Antonio Valero has acted as 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.

References

1. Ojeda P, Sastre J, Olaguibel JM, Chivato T. *Alergológica* 2015: A National Survey on Allergic Diseases in the Adult Spanish Population. *J Investig Allergol Clin Immunol*. 2018;28(3):151-64.
2. Matucci A, Micheletto C, Vultaggio A. Severe asthma and biologics: managing complex patients. *J Investig Allergol Clin Immunol*. 2023;33(3):168-78.
3. Pérez de Llano L, Cisneros C, Domínguez-Ortega J, Martínez-Moragón E, Olaguibel JM, Plaza V, et al. Response to Monoclonal Antibodies in Asthma: Definitions, Potential Reasons for Failure, and Therapeutic Options for Suboptimal Response. *J Investig Allergol Clin Immunol*. 2023;33(1):1-13.
4. Alobid I, Colás C, Castillo JA, Arismendi E, Del Cuvillo A, Gómez-Outes A, et al. Spanish consensus on the management of chronic rhinosinusitis with nasal polyps (POLIposis NAsal/POLINA 2.0). *J Investig Allergol Clin Immunol*. 2023;33(5):317-31.
5. Downie SR, Andersson M, Rimmer J, Leuppi JD, Xuan W, Akerlund A, et al. Symptoms of persistent allergic rhinitis during a full calendar year in house dust mite-sensitive subjects. *Allergy*. 2004;59(4):406-14.
6. García-Díez I, Curto-Barredo L, Weller K, Pujol RM, Maurer M, Giménez-Arnau AM. Cross-Cultural Adaptation of the Urticaria Control Test From German to Castilian Spanish. *Actas Dermosifiliogr*. 2015;106(9):746-52.
7. Weller K, Groffik A, Church MK, Hawro T, Krause K, Metz M, et al. Development and validation of the Urticaria Control Test: a patient-reported outcome instrument for assessing urticaria control. *J Allergy Clin Immunol*. 2014;133(5):1365-72, 72.e1-6.
8. Oranje AP, Glazenburg EJ, Wolkerstorfer A, de Waard-van der Spek FB. Practical issues on interpretation of scoring atopic dermatitis: the SCORAD index, objective SCORAD and the three-item severity score. *Br J Dermatol*. 2007;157(4):645-8.
9. Langley RG, Feldman SR, Nyirady J, van de Kerkhof P, Papavassilis C. The 5-point Investigator's Global Assessment (IGA) Scale: A modified tool for evaluating plaque psoriasis severity in clinical trials. *J Dermatolog Treat*. 2015;26(1):23-31.
10. Charman CR, Venn AJ, Williams HC. The patient-oriented eczema measure: development and initial validation of a new tool for measuring atopic eczema severity from the patients' perspective. *Arch Dermatol*. 2004;140(12):1513-9.
11. Juniper EF, Guyatt GH, Cox FM, Ferrie PJ, King DR. Development and validation of the Mini Asthma Quality of Life Questionnaire. *Eur Respir J*. 1999;14(1):32-8.
12. Khan AH, Reaney M, Guillemin I, Nelson L, Qin S, Kamat S, et al. Development of Sinonasal Outcome Test (SNOT-22) Domains in Chronic Rhinosinusitis With Nasal Polyps. *Laryngoscope*. 2022;132(5):933-41.
13. Baiardini I, Pasquali M, Braido F, Fumagalli F, Guerra L, Compalati E, et al. A new tool to evaluate the impact of chronic urticaria on quality of life: chronic urticaria quality of life questionnaire (CU-QoL). *Allergy*. 2005;60(8):1073-8.
14. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)-a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19(3):210-6.
15. Lewis-Jones MS, Finlay AY. The Children's Dermatology Life Quality Index (CDLQI): initial validation and practical use. *Br J Dermatol*. 1995;132(6):942-9.

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