ALERGODATA: Sentinel registry of health outcomes in allergic patients treated with biological therapies from specialized allergology clinics in Spain

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Key words: Severe asthma. Chronic rhinosinusitis with nasal polyps. Chronic urticaria. Moderate to severe atopic dermatitis. Evidence based on clinical practice.

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 healthcare resources [1].

Biological drugs are therapeutic options very specific for immune system targets. They 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 the authorization of the biological drugs are completed and 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 Th2 diseases that may coexist simultaneously in an individual patient [3].

One of the Spanish Society of Allergology and Clinical Immunology (SEAIC) objectives is to promote activities that provide evidence on health outcomes in a clinical setting. To this end, it has been launched the Alergodata Registry 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 (see Table 1, Supplemental files) and coordinated by specific committees responsible for each disease under study (see Table 2, Supplemental files).

In line with the study plan, before inclusion in the Alergodata Registry, patients must be informed using the patient information sheet (PIS) and sign an informed consent form (ICF). The study initially involves an inclusion visit and at least one annual visit for the first five years, as the disease requires. Other visits will be conducted according to routine clinical practice. The investigator records the information in an electronic case report form (eCRF) designed specifically for the study (see Figure 1).

At the registry inclusion visit, screening criteria (see Table 3, Supplemental Files), patient sociodemographic variables, baseline clinical status of the patient's disease, diagnostic tests, and the patient's initial quality of life will be collected.

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

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

Quality of life (QoL) will be evaluated in all patients: in patients with **severe asthma,** it will be measured using the Mini Asthma Quality of Life Questionnaire (Mini-AQLQ)[11]. For patients with **chronic rhinosinusitis with nasal polyps**, QoL will be measured using the Sino-Nasal Outcome Test (SNOT22)[12]. For patients with **chronic urticaria,** quality of life will be measured using the Chronic Urticaria Questionnaire for Quality of Life (CU-Q2oL)[13] or the Dermatology Life Quality Index (DLQI)[14], and finally, for patients with **moderate to severe AD**, quality of life will be assessed using the Dermatology Life Quality Index (DLQI)[14]or the Children's Dermatology Life Quality Index (CLDQI)[15].

An annual statistical analysis will be performed to evaluate the primary and secondary objectives, stratified according to the disease(s) recorded for the patient. The results will be 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 (see 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 post-authorization prospective follow-up study (EPA-SP). Finally, in 2021, the protocol was evaluated by the autonomous community health agencies and Research Ethics Committees (RECs) of the hospitals that had confirmed their interest in participating in the SEAIC initiative, and the favorable opinion of the REC of the Hospital Clinic de Barcelona was obtained on March 4, 2021. Specifically, the study was submitted to or evaluated in 13 autonomous communities (see Table 5, Supplemental Files). In November 2021, eCRF access was opened, including patients who initiated biological treatment (or without biological treatment in the case of severe asthma) as of January 1, 2021.

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The Alergodata Registry is a SEAIC initiative for generating scientific knowledge in routine clinical practice in the field of allergology that will provide direct, accurate, evidence-based information on the management and treatment of patients with the allergic diseases in question, thus contributing to better healthcare decision-making. In short, real-life data in all these scenarios will be gathered, analyzed, and acted upon accordingly. Findings will be periodically re-analyzed 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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Conflict of interests

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

In the last three years, Ignacio Dávila has received payment for lectures, including service on speaker's bureaus from Allergy Therapeutics, Astra-Zeneca, Chiesi, Diater, GSK, Leti, Novartis, Sanofi; for a consultancy from Allergy Therapeutics, ALK-Abello, Astra-Zeneca, GSK, Merck, MSD, Novartis, Sanofi; and grants for Thermofisher Diagnostics, ISCIII, and Junta de Castilla y León.

In the last three years, Carlos Colás has received honoraria for consultancy and conferences from Novartis, GSK, Sanofi, Viatris, Chiesi, MSD, Takeda, Roxall, and ThemoFisher

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

In the last three years, Julio Delgado Romero has received fees for advisory boards from Bial and Sanofi, has received speaker's honoraria from AstraZeneca, Bial, Chiesi, GlaxoSmithKline Novartis, Sanofi, and TEVA, and received Grant/Research Support from AstraZeneca and Orion. He also received help assistance with meeting travel from Sanofi.

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

In the last three years, Ignacio Jáuregui Presa has received fees as 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 three years, Milagros Lázaro Sastre has received fees for advisory boards from Abbvie and has received speaker's honoraria from Sanofi, Abbvie, Novartis, Chiesi, Faes Farma, Organón, and LETI Pharma.

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

In the last three 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, Organon; and for a consultancy from Takeda, Abbvie, Novartis, Sanofi.

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

In the last three years, Beatriz Veleiro Pérez took part in an advisory board for Novartis. Received speaker's honoraria from Novartis and participated as a teacher-trainer supported by Novartis, Sanofi, Astra-Zeneca, and Cipla.

In the last three years, Carmen Vidal Pan has received personal fees for advisory boards from Stallergenes Freer and Leti and speakers' honoraria from Mundipharma, GSK, Leti, Chiesi, and ALK-Abelló.

In the last three years, Antonio Valero was an advisor for Sanofi, Uriach, AstraZeneca, ALK, and Allergy Therapeutics; received speaker's fees in meetings sponsored by AstraZeneca, Chiesi, Bial, and GSK; and received research project grants by Novartis and Uriach.

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Figure. Study plan.