

## A description of the profile of patients with moderate to severe atopic dermatitis and chronic urticaria undergoing biological treatment evaluated in allergy hospital units in Spain: first report of the Alergodata Registry

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**Palabras clave:** Urticaria crónica. Dermatitis atópica moderada a grave. Evidencia basada en la práctica clínica. Registro.

Cutaneous immune-mediated diseases have become a significant global health concern, causing high healthcare costs worldwide, and their prevalence has steadily increased during the last decade [1, 2]. Fortunately for current and future patients, recent advances in understanding the pathophysiological mechanisms of these diseases, especially those implicating type 2 inflammation [3], have led to the development of new therapeutic alternatives, especially biological treatments [3-6].

Created at the initiative of the Spanish Society of Allergology and Clinical Immunology (SEAIC), Alergodata is the first registry designed to obtain data on the use of biologic drugs for the treatment of various severe diseases evaluated in allergy hospital units throughout Spain. The conditions studied in this registry can be divided into two groups: on the one hand, respiratory diseases, and on the other, skin diseases. In this paper, we will present the first-year results of the skin diseases group, collected from November 19, 2021 to December 1, 2022, and propose a description of the profile of recruited patients with chronic spontaneous urticaria (CSU) and with moderate-to-severe atopic dermatitis (AD). As the registry is still young, we will present only the first data, coming from the inclusion visit.

The study resulting from the registry is an observational, prospective, multi-centre, and national study, conducted under routine clinical practice conditions. The precise methodology was published previously [7].

Before inclusion in the Alergodata Registry, patients needed being informed by means of the patient information sheet (PIS) and sign an informed consent form (ICF). Then, to be included, patients must have been attended in allergy hospital units during the above-mentioned period and have a diagnosis of CSU or moderate-to-severe AD with indication for biologic treatment according to the summary of product characteristics (SmPC) approved in Spain. The minimum age for inclusion was therefore determined by the SmPC. The information was recorded by investigators on an electronic case report form (eCRF) designed specifically for the study.

A total of 200 patients with CSU were recruited from 38 centres, of which 173 were actually evaluable. In the case of moderate-to-severe AD, data came from 63 eligible patients evaluated in 58 centres. No imputation of missing data has been performed, resulting in data loss.

Patient profiles of the two pathologies of interest were established using sociodemographic variables (view online only supplementary table). In the case of moderate-to-severe AD, there were a slight predominance of men (51.7%), mostly Caucasian (86.8%), aged  $39.6 \pm 13.9$  y.o. on average. These data do not agree with previous findings of patients with moderate-to-severe AD regarding sex and ethnicity [8, 9]: a female preponderance has been widely observed in adults [6,

10, 11], and a higher prevalence in black-skinned people and Hispanics compared to white-skinned people[11]. Nevertheless, we must take our ethnic data with caution, as they are highly area-dependent and a hidden selection bias may exist.

Regarding CSU, there was a clear predominance of women (68.6% women vs. 31.4% men) and two predominant ethnic groups (80.1% Caucasian and 18.7% Hispanic) confirming the results of previous studies [5, 12]. The mean age was 47.9 y.o, slightly higher than that generally observed in this condition [5, 12, 13]. With respect to ethnic data, previous studies have shown that, also in the case of CSU, these data vary depending on each area, and attention should be paid again to a possible selection bias.

For either CSU or AD, no relationship could be established between disease and place of residence or educational level.

Disease activity and patients' quality of life (QoL) were measured using various scales and tools (view online only supplementary table) and in both cases, results were consistent with the diagnosis.

Among patients with CSU, 32.2% had associated angioedema (1-3 episodes) and 32.9% inducible urticaria (dermographism 70.2%, cholinergic 28.9%, pressure 19.6%). The other most frequently reported comorbidities were non-atopic diseases (42.4%) and rhinitis (20.3%). Regarding the AD registry, the most common comorbidities were rhinitis (77.2%), conjunctivitis (61.4%), and mild-to-moderate asthma (57.1%). Total IgE levels were elevated in both diseases with respect to normal levels ( $\leq 100$  UI/ml [14]), results that confirm previous data. However, in the case of CSU, only 24.9% of patients presented clinically significant allergic sensitization, compared to 76.7% of patients with AD. 94.8% of patients with CSU and 97.9% of patients recruited with moderate-severe AD, respectively, received antihistamine treatment.

The only biological treatment prescribed during the inclusion visit to patients with CSU was omalizumab, which is, in fact, the only monoclonal antibody (mAb) with an indication for CSU. Two cases of adverse effects were reported (arthralgia in the lower limbs and erythema/pruritus at the injection site) and led to treatment withdrawal. As for patients with AD, the vast majority were prescribed Dupilumab (91.7%), and the rest Tralokinumab (5%), Omalizumab (2%) and Benralizumab (2%), the latter in relation to comorbid asthma, in the hope of a double therapeutic benefit. Only two mild-moderate adverse events were recorded (one conjunctivitis and one labial herpes), in both cases attributed to Dupilumab.

Regarding other treatments prescribed before the initial visit, 87,2% of AD patients reported topical corticosteroids and 46,9% systemic immunosuppressants. Among the enrolled patients with CSU, only 15% reported prior treatment with systemic corticosteroids; a rather low figure, but one that can probably be explained by early up dosing of antihistamine treatment.

Although this study contains valuable data, it also has important limitations. One of them is that, despite the rather good quality of CSU data series, the AD data series are relatively low, probably because most AD patients consult dermatologists or primary care centres rather than allergy specialists. Alergodata is a potent registry but still too young to extract meaningful data. Since the registry will remain open for five years, it would be interesting to compare intermediate and final results with the results presented here, including safety and efficacy data on biologics collected from follow-up visits.

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## Author contributions

This document's authors contributed substantially to its conception and design. IJ and ML drafted the article, and all authors reviewed it critically for important intellectual content, approved the version to be published, and agreed to be accountable for all aspects of the work.

## Conflict of interests

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, Abbvie, MSD, LETI Pharma, Novartis, Gebro Pharma, Organon, GSK and Faes Farma.

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 Pharma, Novartis, Abbvie, Sanofi, Organon, Faes Farma, MSD, Chiesi; and for a consultancy from Takeda, Abbvie, Novartis, Sanofi, Pfizer.

In the last three years, María Nieto Cid declares no conflicts of interest.

In the last three years, Silvia Irene Corrales Vargas declares no conflicts of interest.

In the last three years, Jaume Martí-Garrido declares no conflicts of interest.

In the last three years, Susana Lizarza Mendizabal declares no conflicts of interest.

In the last three years, Maria Teresa Asensio Sánchez, declares no conflicts of interest.

In the last three years, Paula Ribó González has received personal fees for speakers' honoraria and advisory boards from Sanofi, Novartis and MartiTor Alergia.

In the last three years, Santiago Quirce, has been on advisory boards for and has received speaker's honoraria from ALK, Allergy Therapeutics, AstraZeneca, Chiesi, GlaxoSmithKline, Leti, Mundipharma, Novartis, Sanofi-Genzyme and Teva.

In the last three years, María Cesárea Sánchez Hernández has received personal fees for speakers' honoraria and advisory boards from Sanofi, Novartis, Faes Farma and Lilly.

In the last three years, Alejandro Joral Badas has received payment for lectures, including service on speaker's honoraria from Takeda, GSK, Allergy Therapeutics, Leti.

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, 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, 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.

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