ORIGINAL REPORT

Dupilumab in Difficult-to-treat Chronic Spontaneous Urticaria: A Real-world Multicentre Cohort Study

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Chronic spontaneous urticaria (CSU) remains difficult to manage in patients refractory to antihistamines and omalizumab. Although dupilumab has recently been approved and incorporated into international guidelines, real-world evidence remains limited, particularly in treatment-refractory populations. We conducted a multicentre ambispective cohort study across 16 Spanish hospitals including adults with CSU, with or without concomitant chronic inducible urticaria, treated with dupilumab and followed for ≥4 weeks. The primary outcome was well-controlled disease within 24 weeks (Urticaria Control Test ≥12 and Urticaria Activity Score over 7 days≤6). Fifty-one patients were included; 92.0% had previously received omalizumab. At week 24, 69.7% (23/33) achieved well-controlled disease and 39.4% (13/33) complete control. Among patients with available week-52 data, 90.5% (19/21) and 61.9% (13/21), respectively, achieved these outcomes. Concomitant therapy use declined from 94.1% at baseline to 55.6% at week 52. Among omalizumab-experienced patients evaluable at week 24, dupilumab response was lower in prior nonresponders than in those with at least partial response to omalizumab (40% vs 85%, p=0.011). Atopic comorbidities were associated with greater UAS7 reduction (p=0.018). Dupilumab was well tolerated, with mostly mild adverse events. In routine clinical practice, dupilumab provides effective disease control in patients with difficult-to-treat CSU, including most omalizumab-experienced individuals.

Key words: urticara; chronic spontaneous urticaria; dupilumab.

Submitted Mar 11, 2026. Accepted after revision Jun 4, 2026

Published Jul 6, 2026.

SIGNIFICANCE

Chronic spontaneous urticaria is a skin condition that causes recurrent hives and severe itching, often disrupting sleep, work and daily life. It can be difficult to treat when standard treatments (antihistamines and omalizumab) do not work. In this study, dupilumab improved symptoms and quality of life in many patients, including some who had not responded well to omalizumab. It also reduced the need for additional treatments such as corticosteroids and immunosuppressants. These findings provide important evidence from routine clinical practice and may help to choose better therapeutic strategies for patients with severe chronic urticaria.

DOI: 10.2340/actadv.v106.adv-2026-0485

Acta Derm Venereol 2026; 106: adv-2026-0485.

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Treatment of chronic spontaneous urticaria (CSU) remains challenging, as more than 25% of patients are refractory to antihistamines, and up to one third of antihistamine nonresponders also partially or completely fail to respond to omalizumab (1, 2). This highlights the need for additional therapeutic options, with the development of potential disease-modifying treatments being a current priority (3). Recent advances targeting inflammatory pathways are transforming CSU management (4, 5). Type 2 inflammation, characterized by mast cell (MC) activation, Th2 cell responses and the activity of cytokines such as interleukin (IL)-4 and

IL-13, plays a substantial role in CSU pathogenesis (6). Beyond driving IgE production and mast cell recruitment, IL-4 and IL-13 also sensitize sensory neurons, contributing to histamine-independent pruritus (7–12).

Dupilumab, a fully human monoclonal antibody against the IL-4 receptor α, blocks IL-4 and IL-13 signalling through type I (IL-4Rα/γc) and type II (IL-4Rα/IL-13Rα) receptors, thereby reducing IgE synthesis, MC activation, inflammatory infiltration and neuronal sensitization (13–18). Clinical trials (LIBERTY-CSU CUPID A, B and C) have shown that dupilumab improves disease activity in patients with CSU inadequately controlled by antihistamines, although results were less robust in omalizumab-experienced patients (19, 20). Dupilumab has been approved for CSU in Japan, Brazil, the United States, the United Arab Emirates and by the European Medicines Agency and has been incorporated as a second-line treatment option in the published 2026 international urticaria guideline (5). Despite these regulatory advances, real-world evidence remains limited and is largely derived from small, heterogeneous case series, often including patients treated primarily for concomitant atopic disease rather than CSU itself. Robust data from routine clinical practice, particularly in patients with treatment-refractory or omalizumab-refractory CSU such as those included in this cohort, are therefore essential to understand treatment behaviour outside clinical trial settings and to guide individualized treatment decisions.

Here, we present our real-life experience in a multicentre ambispective cohort of CSU patients treated with dupilumab. The primary objective was to assess the effectiveness and safety of dupilumab under daily clinical practice. Secondary objectives were to analyse its impact on pruritus, quality of life and the use of concomitant medications.

MATERIALS AND METHODS

Study design, participants and setting

We conducted a multicentre ambispective cohort study across 16 Spanish hospitals. Eligible participants had a diagnosis of CSU with or without concomitant Chronic Inducible Urticaria (CIndU), confirmed according to clinical presentation and current international guideline criteria (5). Inclusion criteria were adult patients treated with dupilumab between July 2020 and February 2025, who provided written informed consent and had at least 4 weeks of follow-up after dupilumab initiation. Dupilumab was prescribed off-label for CSU in accordance with current local regulatory conditions. Most patients initiated with a 600 mg loading dose followed by 300 mg every 2 weeks. A small subset received dupilumab primarily for concomitant type 2 comorbidities and was included only if active CSU was present and CSU outcomes were assessed. The study combined retrospective data collection (from medical records and clinical images) with prospective follow-up to ensure consistency in outcome assessment. Exclusion criteria were absence of informed consent or legal protection status. The protocol was approved by the Clinical Research Ethics Committee of Hospital del Mar, Barcelona (institutional review board number 2024/11829/I). The study was conducted in accordance with the Declaration of Helsinki and reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (21). Two patients included in this cohort have been previously described in case reports (22).

Variables and data collection

The following data were collected: patient demographics (sex, age, body mass index [BMI]), comorbidities (including atopic dermatitis (AD), asthma or other allergic diseases) and previous medications. In patients previously treated with omalizumab, treatment response was classified based on the best clinical response achieved during prior omalizumab treatment, using UAS7, with assessments performed approximately every 3 months in routine clinical practice. Patients were categorized as nonresponders (UAS7>16), partial responders (UAS7 7–15), or good/complete responders (UAS7<7), irrespective of dose or interval adjustments (23, 24). Disease characteristics included urticaria subtype (CSU vs CSU with concomitant CIndU), presence of angioedema, disease duration, previous treatments and time to diagnosis. Disease severity was assessed at baseline using the UAS7, the peak pruritus numerical rating scale (NRS; previous 7 days), the Urticaria Control Test (UCT; previous 4 weeks) and the Dermatology Life Quality Index (DLQI; previous week). Biomarkers and predictors collected were baseline total IgE, eosinophil and basophil counts (including eosinopenia and basopenia), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), D-dimer, antinuclear antibodies (ANA) and anti-thyroid peroxidase (anti-TPO) IgG positivity. The date of the first dupilumab dose were defined as week 0. Concomitant treatments, as well as dupilumab dosing regimens, were also recorded.

Outcomes

The primary outcome was the proportion of patients achieving well-controlled CSU within 24 weeks after dupilumab initiation, defined as UCT≥12 and UAS7≤6. Secondary outcomes included the proportion of patients achieving well-controlled disease at weeks 4, 12 and 52, and complete control (UCT=16 and UAS7=0) at weeks

4, 12, 24 and 52, as well as changes from baseline in peak pruritus NRS, UAS7, UCT and DLQI. Additional secondary outcomes were the percentage reduction in concomitant treatment use and the evaluation of dupilumab safety. Adverse events (AEs) were recorded and classified as mild, moderate or severe, with severe events defined as invalidating or life-threatening. Timing and reasons for dupilumab discontinuation were also documented.

Statistical analysis

Continuous variables were summarized as median (interquartile range [IQR]) and categorical variables as counts and percentages. Between-group differences for continuous outcomes were assessed with the Wilcoxon rank-sum (Mann–Whitney) test, and differences in proportions with Pearson χ^2 test or Fisher exact test, as appropriate based on expected cell counts. To account for potential bias due to missing outcome data, a nonresponder imputation analysis was performed for the week-24 outcomes. Patients who discontinued treatment before week 24 due to lack of effectiveness and those with missing outcome data at week 24 despite reaching the visit were classified as nonresponders. Longitudinal changes in UAS7, UCT, peak pruritus NRS and DLQI were evaluated using linear mixed-effects models with a random intercept for each patient and visit/week included as a fixed effect. Models were fitted using maximum-likelihood estimation. From these models we obtained least-squares means (LSMs) and 95% CI at weeks 0, 4, 12, 24, 36 and 52.

To identify predictors of response to dupilumab, we used an analysis of covariance (ANCOVA) model to evaluate the change from baseline in UAS7 at week 24. Candidate variables we prespecified based on clinical relevance and previously identified treatment predictors, including age, sex, BMI, IgE≥40 IU/mL, the presence of atopic comorbidities (AD, asthma and/or allergic rhinoconjunctivitis), concomitant CIndU, angioedema, duration of CSU and CRP≥2 mg/dL (25). Each candidate was first assessed in univariable linear regression models. Variables with $p \leq 0.20$ were then considered for inclusion in the final multivariable model.

Results are reported with 95% confidence intervals (CI); 2-sided p-values <0.05 were considered statistically significant. Analysis was performed with StataIC 17 (Stata Corp., College Station, TX, USA).

RESULTS

Patient characteristics

A total of 51 patients were included, of whom 34 (67.0%) were female. The number of patients evaluated at weeks 4, 12, 24, 36 and 52 of treatment was 51, 48, 35, 26 and 21, respectively. Baseline characteristics of the cohort are summarized in **Table I**. Prior to dupilumab, 47 patients (92.0%) had received omalizumab; among them, 19 were nonresponders, 24 were partial responders, and 4 achieved good/complete response. The median duration of omalizumab therapy before dupilumab initiation was 11 months (IQR 7–25). Previous omalizumab was discontinued in 40 patients, mainly due to lack of effectiveness (36 out of 40 patients, 88.0%), whereas 4 patients (10.0%) discontinued because of adverse events (in 1 patient, the reason for discontinuation was unknown). The main indication for dupilumab was uncontrolled CSU (90.0%), with 5 cases treated for concomitant conditions (3 AD, 1 asthma, 1 BP).

Table I. Baseline characteristics of the cohort

	Total*N*=51
Age, years, median (IQI)	51 (39–59)
Female sex, *n* (%)	34 (67)
Height, cm, median (IQI)	164 (159–172)
Body mass index, kg/m^2, median (IQI)	25 (22–31)
Chronic spontaneous urticaria duration, years, median (IQI)	6 (2–14)
Concomitant inducible urticaria, *n* (%)	
No	20 (39)
Symptomatic dermographism	12 (24)
Cold urticaria	3 (6)
Cholinergic urticaria	6 (12)
Pressure urticaria	7 (14)
Pressure+dermographism	3 (6)
Angioedema, *n* (%)	24 (48)
Extracutaneous symptoms, *n* (%)	
No	45 (88)
Arthralgia	4 (8)
Others	2 (4)
Atopic comorbidities, *n* (%)	10 (20)
Autoimmune comorbidities	9 (18)
Baseline UAS7, median (IQI)	32 (24–38)
Baseline UCT, median (IQI)	4 (2–7)
Baseline peak pruritus NRS, median (IQI)	9 (8–10)
Baseline DLQI, median (IQI)	20.5 (14–25)
Baseline total IgE, IU/mL, median (IQI)	63 (20–266)
IgE>40 IU/mL	26 (60)
Eosinopenia, *n* (%)	5 (10)
C-reactive protein, mg/dL, median (IQI)	0.3 (0.04–1.3)
D-Dimer, mg/L, median (IQI)	400 (250–574)
ANA≥1:160, *n* (%)*	5 (13)
CH50, U/mL (35-60), median (IQI)	57 (45–75)
IgG anti-TPO positivity,** *n* (%)	10 (26)
Previous treatments, *n* (%)	
SgAHs	51 (100)
Systemic corticosteroids	39 (76)
Cyclosporine	33 (65)
Omalizumab***	47 (92)
300 mg/4 w	11 (23)
450 mg/4 w	10 (21)
600 mg/4 w	21 (45)
450 mg/2 w	2 (4)
600 mg/2 w	3 (6)
Methotrexate	2 (4)
Sulfasalazine	2 (4)
Dapsone	2 (4)
Mycophenolate mofetil	2 (4)

*Available in 39 patients; **Available in 38 patients; *** Percentages for omalizumab dosing regimens are calculated among patients previously treated with omalizumab (*n*=47).
CH50:total hemolytic complement activity; DLQI:Dermatology Life Quality Index; IQI:interquartile Interval; NRS:numerical rating scale; sgAHs:second-generation antihistamines; UAS7:urticaria activity score over 7 days; UCT:urticaria control test.

Dupilumab was prescribed with an initial dose of 600 mg followed by 300 mg every 2 weeks in all patients; dosing modifications were uncommon, with a few patients later spaced to 3–4 weekly intervals or intensified to weekly dosing (Table SI). The median duration of treatment follow-up was 36 weeks (IQR 12–52). Eight patients discontinued dupilumab due to lack of response at weeks 16 (*n*=2), 24 (*n*=3), 36 (*n*=2), and 52 (*n*=1).

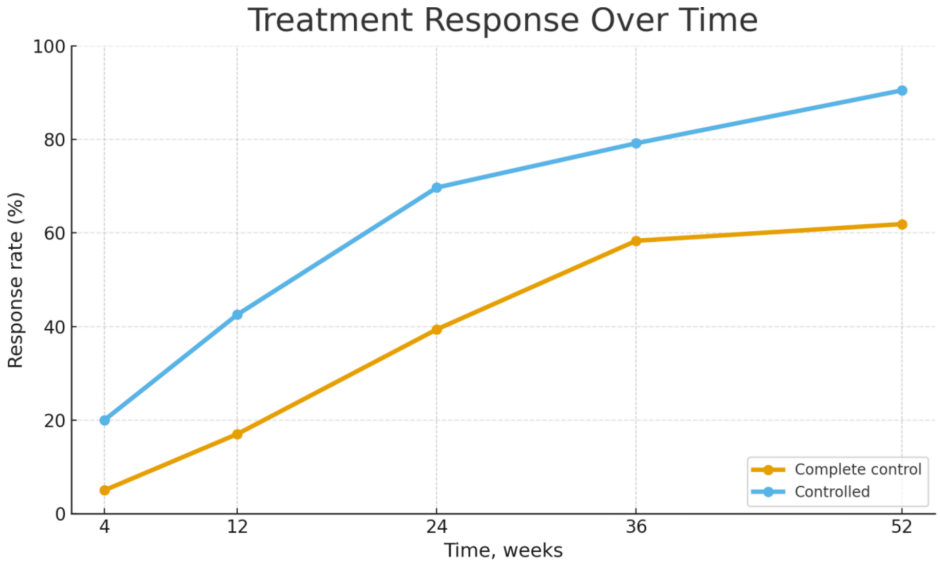
Outcomes

At the primary endpoint (week 24), 69.7% of patients achieved well-controlled disease and 39.4% achieved complete control. When UCT and UAS7 components were analysed separately, 3 patients met only the UCT criterion (9.1%) and were therefore not included in the primary endpoint, while none met only the UAS7 criterion; 21.2% of patients met neither criterion (Table SII). Among patients with available week-52 data, 90.5% achieved well-controlled disease and 61.9% complete control (**Fig. 1**), although these longer-term estimates should be interpreted cautiously given the limited number of evaluable patients. In the nonresponder imputation analysis, the corresponding rates were 60.5% and 34.2%, respectively. Furthermore, baseline characteristics were similar between patients with and without available week-24 and week-52 data, with a trend toward higher baseline severity in patients with available data (Tables SIII and SIV), suggesting limited risk of selection bias. Treatment with dupilumab resulted in a progressive sustained improvement in UCT, UAS7, peak pruritus NRS and DLQI through week 52 (**Fig. 2**A–D). The steepest decline in UAS7 scores occurred within the first 12 weeks (LSM change from baseline −14.8, 95% CI −17.4 to −12.2, $p<0.001$), followed by sustained reduction thereafter (−17.6, 95% CI −20.5 to −14.6 at week 24 and −20.1, 95% CI −23.7 to −16.6 at week 52, $p<0.001$ for both contrasts) (Fig. S1). Peak pruritus NRS and DLQI improved rapidly and progressively throughout treatment with greatest improvements occurring within the first 24 weeks (LSM change from baseline −5.53, 95% CI −6.49 to −4.58, $p<0.001$; and −15.31, 95% CI −18.02 to −12.60, $p<0.001$, respectively), with stable low values thereafter. Results expressed as LSM change from baseline for each scale are provided in Fig. S1.

No significant differences in response rates were observed between patients with CSU alone and those with concomitant CIndU at any timepoint (Table SV).

Concomitant treatments

At baseline, almost all patients (94.1%, *n*=48) required concomitant therapies, most commonly antihistamines (62.7%, *n*=32), corticosteroids (11.8%, *n*=6) and other systemic immunosuppressants such as cyclosporine or methotrexate (13.7%, *n*=7). In patients previously



Week	Well-controlled disease, n (%)	Complete control, n (%)	n
4	8 (20.0)	2 (5.0)	40
12	20 (42.6)	8 (17.0)	47
24	23 (69.7)	13 (39.4)	33
36	19 (79.2)	14 (58.3)	24
52	19 (90.5)	13 (61.9)	21

Fig. 1. Proportion of patients achieving well-controlled (UCT≥12 and UAS7≤6) and complete control (UCT=16 and UAS7=0) of disease during dupilumab treatment. *n* indicates the number of patients with available data at each follow-up week.

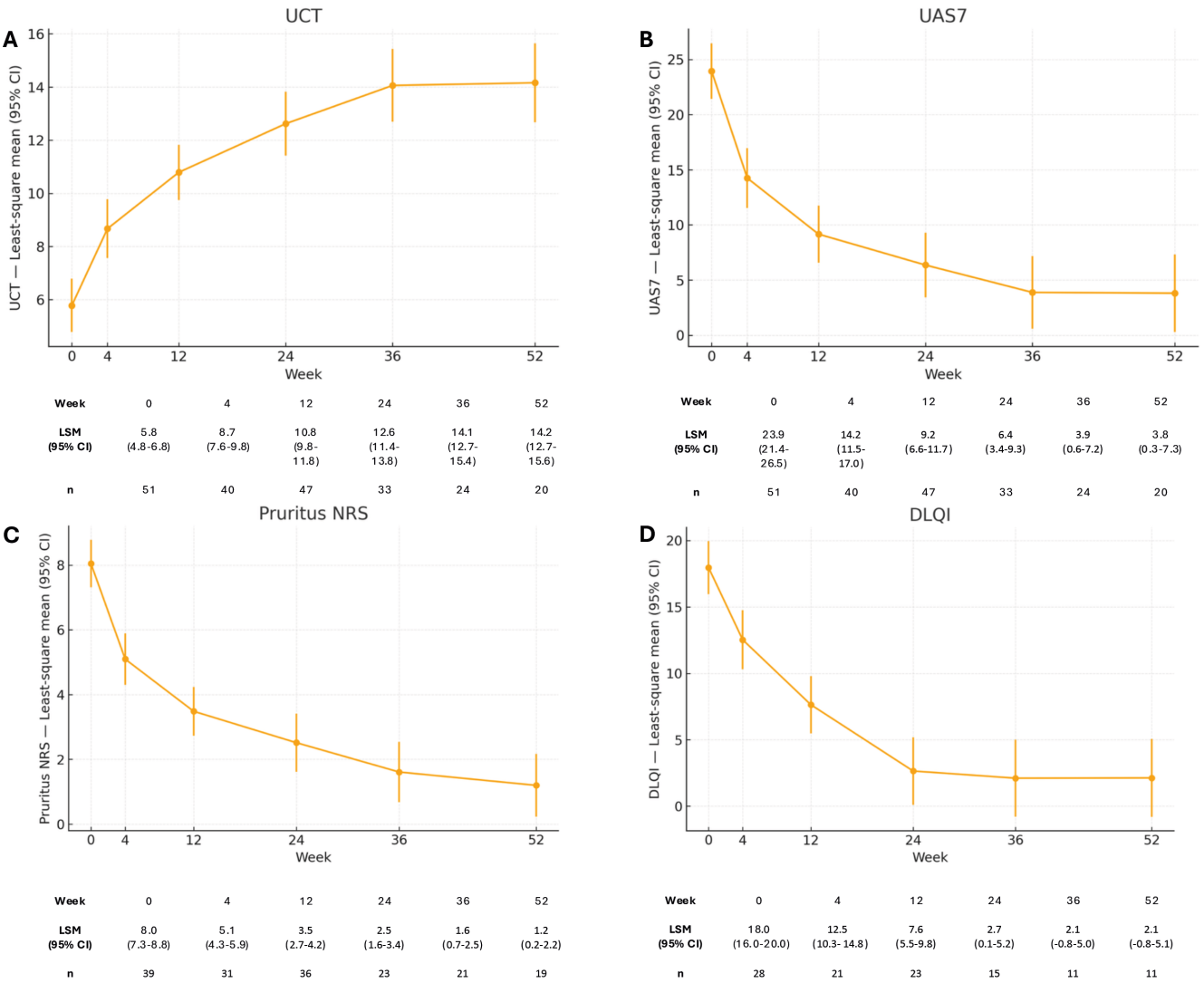


Fig. 2. Outcomes over time from baseline to week 52 during dupilumab treatment. (**A**) Urticaria Control Test (UCT; 0–16), (**B**) Urticaria Activity Score over 7 days (UAS7; 0–42), (**C**) peak pruritus numerical rating scale (Peak Pruritus NRS; 0–10), and (**D**) Dermatology Life Quality Index (DLQI; 0–30). Values are presented as least-squares means (LSM) with 95% confidence intervals (CI). *n* indicates the number of patients with available data at each follow-up week.

treated with omalizumab, dupilumab was generally initiated immediately after omalizumab discontinuation, although a small proportion of patients received both drugs concomitantly (13.7%, *n*=7). At week 4, 6 patients (12.0%) were still on omalizumab alongside dupilumab; of these, 4 later discontinued omalizumab while continuing dupilumab, whereas 2 maintained combined therapy for a longer period. Over time, the need for additional medications declined substantially: by week 24, 22 of 33 patients (66.7%) still required concomitant therapy, and by week 52 this proportion had fallen to 10 of 18 patients (55.6%), corresponding to a 38.5% absolute reduction. Notably, no patients remained on systemic corticosteroids or immunosuppressants at week 52. Further details on concomitant medications can be seen in **Fig. 3** and Table SVI .

Prognostic factors of response

Response to dupilumab varied according to prior omalizumab outcome. Among patients previously treated with omalizumab and evaluable at week 24 (*n*=30), dupilumab response was significantly lower in those who had not responded to omalizumab compared with those who had shown at least partial response (40% vs 85%, *p*=0.011). Nevertheless, a substantial proportion of prior omalizumab nonresponders still achieved response to dupilumab.

Regarding the predictor model, in univariable analyses, longer disease duration was associated with a significantly smaller improvement in UAS7 at week 24 (coef.=−0.73 per year, 95% CI −1.19 to −0.27, *p*=0.003), while BMI, sex and atopic comorbidities showed nonsignificant trends (*p*<0.2) (Table SVII).

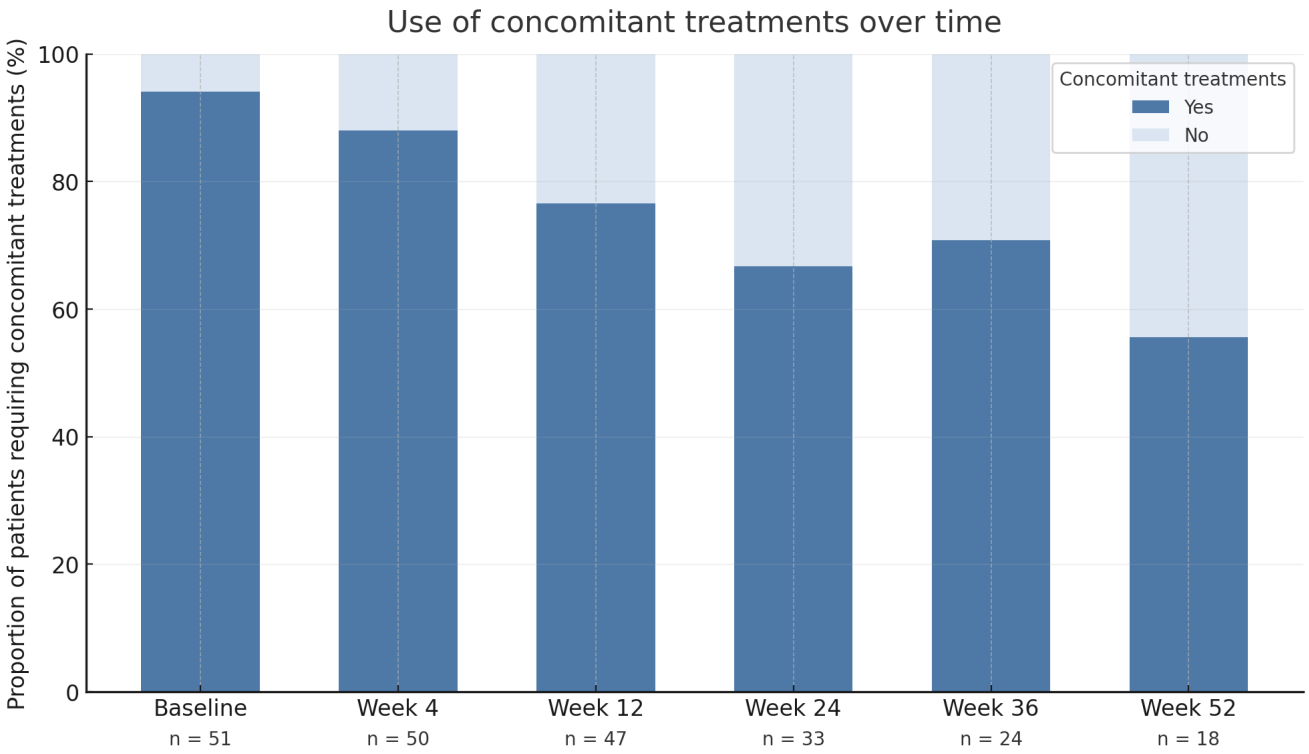


Fig. 3. Patients on concomitant therapy during dupilumab treatment. Proportion of patients requiring additional medication from baseline to week 52. *n* indicates the number of patients with available data at each follow-up week. Details on the specific concomitant treatments are provided in Table SVI

In the multivariable ANCOVA model, the presence of allergic comorbidities was independently associated with greater improvement in UAS7 at week 24 (coef.=11.6, 95% CI 0.7 to 22.5; p=0.039). Disease duration was associated with a lower magnitude of improvement, although this did not reach statistical significance (coef.=–0.39 per year, 95% CI –0.98 to 0.19; p=0.169) (**Table II**).

Safety

No AEs were reported in 42 of 51 patients (82.4%). Among the remaining 9, most were mild and did not require discontinuation. The most frequent was conjunctivitis (n=3), with one severe case leading to discontinuation at week 16. Other AEs included headache (n=2) and single cases of episcleritis, muscle pain, injection-site reaction, and asthenia.

DISCUSSION

In this multicentre study, dupilumab demonstrated substantial effectiveness and good tolerability in a population with difficult-to-treat CSU. Disease activity and control improved rapidly and were sustained through 1 year, as shown by marked reductions in UAS7 and pruritus severity, paralleled by improvements in UCT and DLQI. By week 24, nearly 70% of patients achieved well-controlled disease and almost 40% reached complete control, with response rates rising further at week 52. Dupilumab also enabled a progressive reduction in concomitant treatments, particularly systemic corticosteroids and immunosuppressants.

Our multicentre cohort represents the largest real-world series to date evaluating dupilumab specifically for uncontrolled CSU, with standardized outcome measures. Previous real-world reports, although supportive, have been limited by small sample sizes (7–33 patients) and heterogeneous treatment indications, often including patients treated primarily for uncontrolled AD or other type 2 comorbidities rather than CSU itself (22, 26–29). Despite these differences, the magnitude and kinetics of improvement in disease activity, pruritus, and quality of life observed in those studies are broadly consistent with our findings. Moreover, our results were also comparable to those reported in the pivotal phase 3 CUPID

Table II. Multivariable analysis of predictors of change in UAS7 at week 24; coefficients represent absolute change in UAS7 (baseline – week 24); positive values indicate greater improvement

Variable	Coefficient (B)	95% CI	*p*-value
Female sex	–3.34	–14.87 to 8.19	0.546
Disease duration (years)	–0.39	–0.98 to 0.19	0.169
Atopic comorbidities	11.61	0.68 to 22.55	**0.039**
Body mass index kg /m^2	0.48	–0.23 to 1.19	0.174

CI: confidence interval; UAS7: urticaria activity score over 7 days.

trials. At week 24, dupilumab treatment in our cohort led to a mean UAS7 reduction of –17.6 points, similar to the reductions seen in CUPID A (–20.5; omalizumab-naïve) and CUPID B (–14.4; omalizumab-incomplete responders or intolerant patients). Likewise, improvement in pruritus in our study (peak pruritus NRS –5.5) was broadly aligned with ISS7 reductions observed in CUPID A (–10.2, scale 0–21) and CUPID B (–7.7) (19).

Despite 92% of our patients having previously received omalizumab and discontinued it due to lack or loss of efficacy, the magnitude of dupilumab response in our cohort was comparable to that reported in the omalizumab-naïve CUPID A trial (19). This suggests that dupilumab may provide meaningful benefit in omalizumab-experienced patients, particularly those who had shown at least partial or transient responses. Conversely, dupilumab response was significantly lower in patients who had not responded to omalizumab compared with those who had previously shown benefit (40% vs 85%), although a substantial proportion of omalizumab nonresponders achieved disease control (19). These findings may suggest that early nonresponse to omalizumab identifies an endotype less dependent on type 2 inflammation, whereas patients with partial or time-limited responses could still benefit from IL-4/IL-13 blockade. In some patients, temporary overlap between omalizumab and dupilumab occurred during treatment transition, reflecting routine clinical practice rather than a predefined combination strategy. Given the multicentre nature of the study and the off-label use of dupilumab for CSU during much of the study period, no standardized recommendations were available regarding transition from omalizumab, and treatment sequencing was determined according to physician clinical judgement.

CSU comprises a type 2–high endotype, characterized by elevated total serum IgE, eosinophilia, and atopic comorbidities, and an autoimmune/type IIb endotype, defined by low IgE and the presence of IgG autoantibodies against FcεRI or IgE (3, 30). Our results suggest that patients with a Th2-driven profile may respond more favourably to dupilumab, as the presence of atopic comorbidities was associated with greater UAS7 reductions throughout follow-up. However, this observation requires confirmation in larger prospective studies. Both omalizumab and dupilumab act on the same type 2 inflammatory axis – omalizumab by neutralizing circulating IgE and dupilumab by inhibiting its upstream drivers IL-4 and IL-13 – explaining why their clinical response patterns may often overlap (18).

Despite the suggested association of a Th2-skewed CSU profile and better outcomes, baseline total IgE≥40 IU/mL showed only a trend toward greater UAS7 reduction at week 24, without reaching statistical significance. This exploratory cut-off was based on omalizumab studies where IgE below this threshold predicted poor response (31, 32). Although higher baseline IgE levels have been associated with improved dupilumab response in asthma (33) and alopecia areata (34), IgE is not a reliable predictor in other atopic diseases such as AD, likely because most patients already exhibit elevated IgE levels, limiting its discriminatory value (35–37). Consistent with our findings, phase 3 subanalyses from LIBERTY-CSU CUPID A also failed to identify baseline total IgE as a predictor of dupilumab response (13, 19). Larger prospective cohorts will be needed to clarify whether IgE can serve as a reliable biomarker of dupilumab responsiveness in CSU. This is in line with the updated 2026 urticaria guideline, which positions dupilumab mainly in omalizumab-naïve patients based on phase 3 trial data (5); however, our findings suggest that selected omalizumab-experienced patients, particularly those with prior partial or transient responses, and possibly those with atopic comorbidities, may still derive clinically meaningful benefit.

Several limitations of our study should be pointed out. Variations in treatment protocols among different healthcare providers could generate heterogeneity in patient management and outcomes. As this was a real-world, multicentre study, the frequency and timing of clinical evaluations varied across centres, resulting in missing data for some outcome scales at specific follow-up visits. Additionally, not all patients reached the 52 week follow-up, which may limit the long-term insights and robustness of our findings. The ambispective design may have introduced variability in data capture, and the relatively small sample size limited the power of subgroup analyses, including exploratory biomarker evaluation. Finally, follow-up beyond 1 year was available only for a subset of patients, precluding firm conclusions about long-term durability.

In conclusion, this study supports dupilumab as an effective and well-tolerated treatment for difficult-to-treat CSU. Dupilumab achieved sustained improvements in disease activity, pruritus and quality of life, while enabling progressive withdrawal of systemic therapies. Although prior nonresponse to omalizumab was associated with lower dupilumab response rates, a substantial proportion of these patients still achieved meaningful disease control. Atopic comorbidities may be associated with better response and warrant further study. These findings

support dupilumab as a valuable therapeutic option for difficult-to-treat CSU.

ACKNOWLEDGEMENTS

This investigation was performed during Nidia Planella's studies at the UPF.

Funding sources: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability statement: The data underlying this article will be shared on reasonable request to the corresponding author.

Ethics committee: The study was approved by the ethical committee of Hospital del Mar (n° 2024/11829/I) in Barcelona, Spain. A written informed consent for scientific diffusion was obtained.

Conflict of interest: AGA is or recently was a speaker and/or advisor for and/or has received research funding from Almirall, Amgen, AstraZeneca, Avene, Blue-Print, Celldex, Escient Pharmaceutials, Genentech, GSK, Harmonic Bio,Incyte, Instituto Carlos III- FEDER, Jaspers, Leo Pharma, Menarini, Mitsubishi Tanabe Pharma, Noucor, Novartis, Sanofi–Regeneron, Septerna, Servier and Thermo Fisher Scientific, Uriach Pharma all outside the submitted work. JMM has served as a speaker, medical advisor, and/or consultant for ADIMYF, Astra Zeneca, Bocentium Consulting, Fundacio Clinic Per La Recerca, Fundació Institut de Recerca Hospital de la Santa Creu i Sant Pau, Fundacion Piel Sana de la AEDV, Grupo Español de Trasplantes Hematopoyéticos y Terapia Celular, Janssen, Laboratorios Viñas, MFAR, Organon Salud, Sanofi-Aventis and Viatris Pharmaceuticals all outside the submitted work. JS was a speaker and/or advisor for Novartis, Sanofi-Regeneron and Noucor all outside the submitted work. Other authors declare no conflicts of interest.

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