biologics

MDPI

Article

Real-World Long-Term Management of Chronic Urticaria Patients with Omalizumab: Safety, Effectiveness, and Predictive Factors for Successful Outcome

Ciro Romano [1,*], Domenico Cozzolino [2], Giuseppina Rosaria Umano [3] and Ernesto Aitella [4,5]

[1] Clinical Immunology Outpatient Clinic, Division of Internal Medicine, Department of Advanced Medical and Surgical Sciences, "Luigi Vanvitelli" University of Campania, 80131 Naples, Italy
[2] Division of Internal Medicine, Department of Precision Medicine, "Luigi Vanvitelli" University of Campania, 80131 Naples, Italy; domenico.cozzolino@unicampania.it
[3] Department of Woman & Child Health and General and Specialist Surgery, "Luigi Vanvitelli" University of Campania, 80131 Naples, Italy; giuseppinarosaria.umano@unicampania.it
[4] Allergy and Clinical Immunology Unit, "G. Mazzini" Hospital, ASL Teramo, 64100 Teramo, Italy; ernestoaitella@gmail.com
[5] Department of Clinical Medicine, Public Health, Life and Environmental Sciences, University of L'Aquila, 67100 L'Aquila, Italy
* Correspondence: ciro.romano@unicampania.it

Abstract

Background/Objectives: Omalizumab is a monoclonal anti-IgE antibody approved for the treatment of chronic urticaria. There are no established or validated prognostic markers currently available to identify likely responders. The aim of this study was to retrospectively analyze a cohort of chronic urticaria patients treated with omalizumab, in order to determine the clinical and laboratory characteristics associated with complete response to therapy. Methods: Medical records of chronic urticaria patients receiving omalizumab were reviewed. The following parameters were collected: age, sex, disease duration, Urticaria Activity Score over 7 days (UAS7), time to response, total serum IgE levels, presence or absence of atopy, neutrophil-to-lymphocyte ratio, eosinophil and basophil counts, presence or absence of autoimmune conditions, and treatment duration. Complete response was classified as dependent on continued drug administration or drug-free (sustained remission after discontinuation). Adverse events were also recorded. Results: Omalizumab was well tolerated by all patients, with no serious adverse events reported. Complete response was achieved in 81.3% of patients; partial and no responses were observed in 8.3% and 10.1%, respectively. The majority of responders (~79.5%) maintained complete control of hives with low-dose omalizumab; subsequently, most of these patients eventually achieved sustained, drug-free remission. Total serum IgE levels appeared to predict complete response, with 164.7 IU/mL identified as the cut-off value potentially distinguishing responders from nonresponders. Conclusions: Omalizumab is a safe and effective treatment for chronic urticaria. Total serum IgE levels may help identify complete responders. Long-term low-dose regimens could be considered to reduce the economic burden on healthcare systems, although this is currently an off-label approach.

Keywords: chronic urticaria; omalizumab; IgE; low-dose management

check for updates

Received: 30 July 2025
Revised: 11 October 2025
Accepted: 16 October 2025
Published: 22 October 2025

Citation: Romano, C.; Cozzolino, D.; Umano, G.R.; Aitella, E. Real-World Long-Term Management of Chronic Urticaria Patients with Omalizumab: Safety, Effectiveness, and Predictive Factors for Successful Outcome. *Biologics* **2025**, *5*, 33. https://doi.org/10.3390/biologics5040033

Copyright: © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

1. Introduction

Chronic urticaria is a condition characterized by the presence of hives for at least six weeks. Apart from autoimmune or autoallergic mechanisms, our understanding of the

possible trigger(s) and mechanism(s) responsible for the persistence of chronic urticaria remains largely incomplete [1–3]. The severity of chronic urticaria is commonly assessed using the Urticaria Activity Score over 7 days (UAS7), which assigns a daily score based on the number of wheals and the corresponding intensity of itch [4]. Although chronic urticaria is not a life-threatening disease, it is highly bothersome and significantly impairs quality of life [5–7]. Patients with chronic urticaria may experience poor sleep due to itching, reduced concentration during daily activities and, consequently, diminished performance at work or school; moreover, the visible presence of hives can hinder social interactions. For these reasons, the quality of life of individuals with chronic urticaria has been likened to that of patients with ischemic heart disease [6].

Unfortunately, the duration of chronic urticaria cannot be predicted: some patients suffer from the condition for only a few months, while many others experience daily hives for years [8–10]. Standard doses of antihistamines are often insufficient for the pharmacological management of chronic urticaria, and patients frequently require higher-than-recommended doses (up to two to four times the standard dose) [11–13]. Oral corticosteroids may be beneficial; however, hives often recur as the dose is tapered [14]. Consequently, the management of chronic urticaria has been challenging for both physicians and patients, until the introduction of omalizumab [15].

Omalizumab, a monoclonal antibody specific for human IgE, was initially developed for the treatment of severe allergic asthma refractory to standard therapies [16,17]; following several case reports suggesting its potential effectiveness in chronic urticaria [18–21], randomized clinical trials were conducted to evaluate its possible introduction into clinical practice [22–24]. Since its approval, omalizumab has markedly improved outcomes in chronic urticaria, with a substantial proportion of patients achieving complete or, at least, satisfactory control of hives [25–28].

However, it remains unclear how to predict which patients will respond to omalizumab, which will achieve sustained remission after discontinuation, which will require continuous administration, and how best to manage long-term treatment [29–31]. Addressing these unmet needs is essential to optimize patient selection, tailor treatment duration, and improve cost-effectiveness. The aim of this study was to retrospectively analyze a cohort of chronic urticaria patients treated with omalizumab, in order to identify clinical and laboratory characteristics associated with complete response or low-dose maintenance, and to assess the safety of long-term management.

2. Patients and Methods

2.1. Patient Selection and Management

The medical records of forty-eight patients treated with omalizumab for chronic spontaneous urticaria refractory to standard treatments were retrospectively reviewed. Variables retrieved, entered into an electronic database, and analyzed included: age at diagnosis, gender, duration of chronic urticaria, total serum IgE levels, presence of concomitant atopic and/or autoimmune conditions, eosinophil and basophil counts, neutrophil-to-lymphocyte ratio (NLR), UAS7 scores before and during therapy, type of clinical response (complete, partial, or absent), time to clinical response, type of complete response (on or off drug), effect of low-dose management (i.e., half the approved dose of omalizumab [21,32]), and treatment duration up to July 2025. Table 1 summarizes the characteristics of the patient population.

Table 1. Demographic, clinical, and laboratory features of the study group.

Whole Patient Population, No. 48	
Gender, M/F	11/37
Age (yrs), mean ± sd/median	43.3 ± 13.5/43.5
CU duration (months), mean ± sd/median	29.1 ± 54.3/7.5
Total serum IgE (IU/mL), mean ± sd/median	189.5 ± 217/107.8
Concomitant atopy, %	38.6
Concomitant autoimmune diseases *, %	34.1
Circulating eosinophil counts (cells/μL), mean ± sd/median	166.9 ± 104.1/140
Circulating basophil counts (cells/μL), mean ± sd/median	35.3 ± 54.7/20
NLR, mean ± sd/median	2.2 ± 0.9/2
Response to omalizumab, no.	39 CR, 4 PR, 5 NR
Pre-omalizumab UAS7, mean ± sd/median	37.9 ± 6.4/42
Time to response to omalizumab (days), mean ± sd/median	15.3 ± 25.1/5
Treatment duration (months), mean ± sd/median	32.5 ± 38.4/17.5

Abbreviations: CR, complete response; CU, chronic urticaria; F, female; M, male; NLR, neutrophil-to-lymphocyte ratio; NR, no response; PR, partial response; sd, standard deviation; UAS7, Urticaria Activity Score over 7 days; yrs, years. * Autoimmune diseases included Hashimoto thyroiditis, Basedow disease, vitiligo, autoimmune gastritis. Normal values for total serum IgE: ≤100 IU/mL; normal values for eosinophil and basophil counts: ≤500 and ≤100 cells/μL, respectively.

To be eligible for omalizumab treatment, patients had to present with chronic spontaneous urticaria unresponsive to high doses of oral antihistamines (up to four times the recommended dose), either alone or in combination with leukotriene receptor antagonists or immunosuppressants (i.e., cyclosporine). Additionally, inability to taper oral corticosteroids was considered another eligibility criterion. Omalizumab was administered subcutaneously at the approved dose of 300 mg per month. Therapeutic response was monitored daily by the patients themselves using individual UAS7 questionnaires, with a definitive assessment conducted in hospital at 16 weeks. Follow-up visits were subsequently scheduled every three to four months. Complete response was defined as achieving a UAS7 score of 0. Partial response was defined as at least a 50% improvement in UAS7 compared to the baseline score. No response was defined as either no change or less than 50% improvement in the baseline UAS7 score. Patients who exhibited a consistent and complete response for at least three months during omalizumab treatment were permitted to reduce the monthly dose by half [21,32]. If the complete response persisted for an additional three months, the interval between doses was gradually extended until treatment discontinuation. Patients who experienced a recurrence of hives during omalizumab tapering were advised to return to the previously effective minimum dose and/or interval. This strategy, previously adopted by our group [21,32], although off-label, was used to classify complete responders as either definitive responders or on-drug responders, irrespective of the administered dose.

Since NLR, calculated by dividing the neutrophil count by the lymphocyte count, has been recognized as a surrogate marker of host immunoinflammation, due to its significant correlation with clinical outcomes in various diseases such as cardiovascular conditions, cancer, and even COVID-19 [33–35], it was evaluated as a potential predictive factor for clinical response.

2.2. Laboratory Investigations

Total serum IgE levels and complete blood counts, including neutrophils, lymphocytes, eosinophils and basophils, were assessed before starting omalizumab and at each follow-up visit, using standard laboratory kits and instrumentations.

2.3. Safety Assessment

All patients received omalizumab injections exclusively at the outpatient clinic, where they remained under observation for two hours to monitor for any local or systemic reactions to the monoclonal antibody therapy. Additionally, patients were instructed to document any adverse events potentially related to omalizumab that occurred outside the clinical setting.

2.4. Statistical Analysis

Patients were grouped according to treatment response (complete, partial, or absent). However, following the initial assessment, partial responders were excluded from statistical analysis to avoid generating confusing or conflicting results. Therefore, only complete responders and nonresponders were included in the statistical analyses.

Differences in continuous variables were assessed using the Mann–Whitney U test, while differences in categorical variables were evaluated using Fisher's exact test. Receiver operating characteristic (ROC) curve analysis was performed to assess the ability to predict complete responses to treatment, with reporting of the area under the curve (AUC) and corresponding confidence intervals (C.I.). Predictor cut-off values were determined using the Youden index.

Data are presented as medians with interquartile ranges and frequencies, as appropriate. Means ± standard deviations (sd) are also provided. Statistical analyses were conducted using SAS OnDemand for Academics (©2025 SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Overall Outcome

Of the 48 patients in the study population, 39 showed a complete response, 4 a partial response, and 5 no response at the initial assessment conducted at 16 weeks. Figure 1 summarizes the results along with the corresponding UAS7 scores.

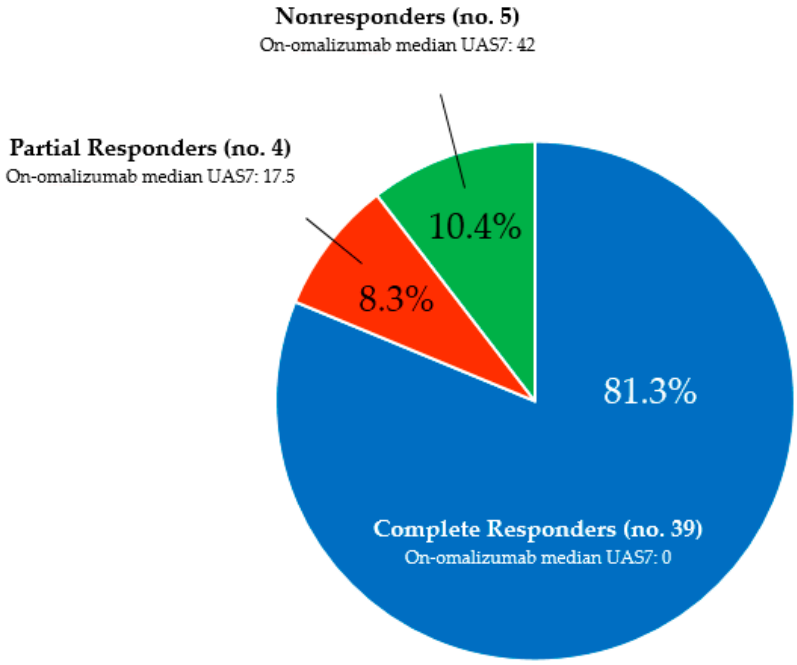


Figure 1. Summary of treatment outcomes. Prior to the initiation of omalizumab therapy, the median UAS7 score was 42 across all patient groups—complete responders, partial responders, and nonresponders. Following treatment, UAS7 scores remained unchanged in nonresponders, dropped to zero in complete responders, and showed substantial improvement in partial responders.

When patients were categorized as complete responders or nonresponders, total IgE levels appeared to be the key discriminant for treatment response (Table 2). Although on-treatment UAS7 scores and treatment duration also differed significantly between responders and nonresponders, these differences were considered consequences rather than determinants of the clinical outcome.

Table 2. Characteristics of complete responders and nonresponders.

	Complete Responders (No. 39)	**Nonresponders (No. 5)**	***p***
Age (years)	44 (35–53)	33 (32–72)	0.90
Sex (F, %)	74.4	80	0.99
Atopy (%)	42.9	0	0.14
Autoimmunity (%)	28.7	60.0	0.31
NLR	1.88 (1.43–2.69)	2.44 (1.24–3.69)	0.88
Basophils (cells/μL)	20 (10–40)	11 (10–30)	0.71
Eosinophils (cells/μL)	130 (100–200)	160 (158–170)	0.49
Total IgE (IU/mL)	112.5 (37.2–250.5)	18 (15.8–73.1)	0.04
Pre-omalizumab UAS7	42 (28–42)	42 (42–42)	0.13
On omalizumab UAS7	0 (0–0)	42 (42–42)	<0.0001
CU duration (months)	8 (4–12)	5 (4–26)	0.68
Treatment duration (months)	25 (8–52)	6 (4–12)	0.02

Abbreviations: CU, chronic urticaria; F, female; NLR, neutrophil-to-lymphocyte ratio; UAS7, Urticaria Activity Score over 7 days. Normal values for total serum IgE: ≤100 IU/mL; normal values for eosinophil and basophil counts: ≤500 and ≤100 cells/μL, respectively. Data are expressed as medians and interquartile ranges and frequencies, as appropriate.

Indeed, ROC curve analysis identified total IgE levels as a predictive factor for treatment response, with a cut-off value of 164.7 IU/mL distinguishing the two patient subgroups (Figure 2).

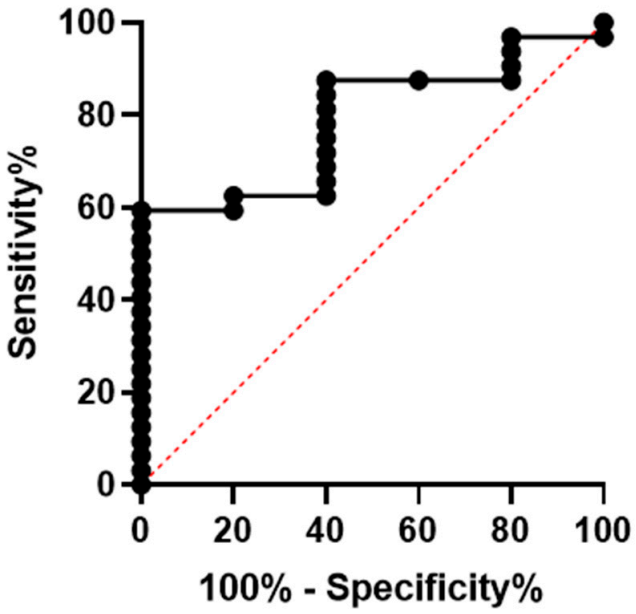


Figure 2. ROC curve analysis for total IgE levels as predictors of complete response to treatment. The area under the curve (AUC) was 0.79 (95% C.I. 0.62–0.96, $p = 0.04$). Youden test identified 164.7 IU/mL as the cut-off between responders and nonresponders.

Figure 3 displays the individual values for complete responders and nonresponders. As previously mentioned, partial responders were excluded from the statistical analysis due to their "grey zone" characteristics, which could potentially interfere with the accurate interpretation of the results.

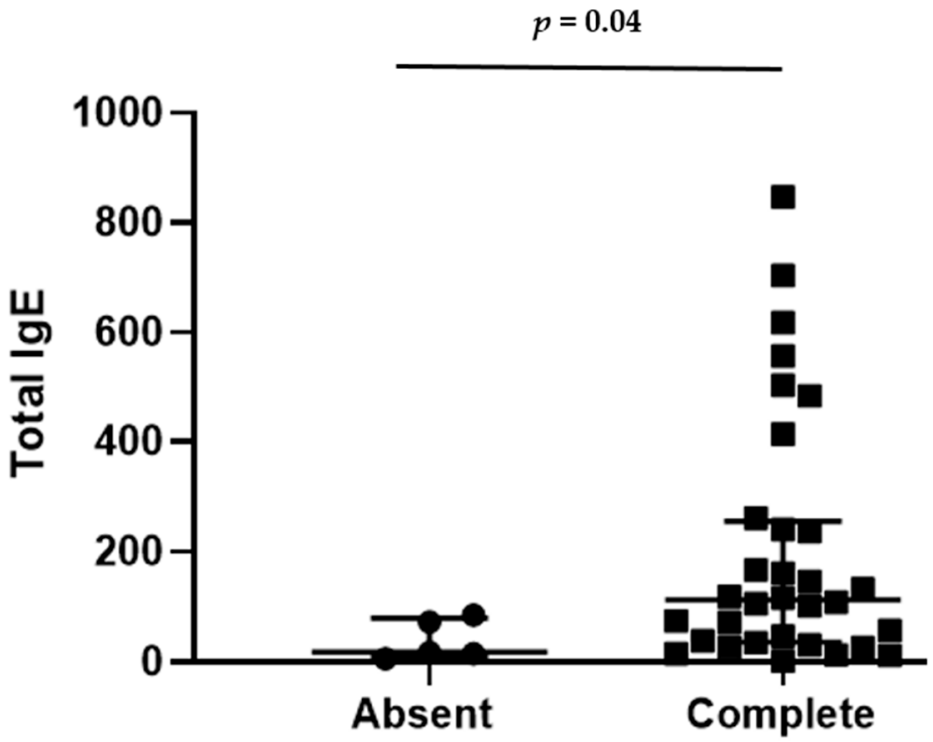


Figure 3. Scatterplot for individual total IgE values according to treatment outcome (absent response versus complete response).

3.2. Long-Term Management of Complete Responders

Complete responders, defined as patients with no occurrence of hives for at least three months, underwent progressive dose tapering and extension of dosing intervals in an effort to discontinue omalizumab treatment, as previously described with some modifications [21,32]. Briefly, complete responders were initially advised to reduce the monthly omalizumab dose from 300 mg to 150 mg for an additional three months. If complete disease control persisted, the dosing interval was gradually extended by 3–5 days until treatment withdrawal, typically when intervals reached approximately twice the drug's half-life (i.e., 45–50 days after the last injection). Patients who experienced a recurrence of hives were reinstated on the lowest effective dose and interval. Following this strategy, approximately 79.5% (31 out of 39) of complete responders were successfully managed with low-dose omalizumab without compromising disease control. The remaining 20.5% (8 out of 39) required the full therapeutic dose to prevent urticaria recurrence.

3.3. Differences Between Off-Drug and On-Drug Complete Responders

Complete responders could be further subdivided into those who achieved CU remission without the need for ongoing omalizumab injections (i.e., off-drug persistent remission), and those who maintained symptom control only with uninterrupted omalizumab administration (i.e., on-drug responders). Of the 39 complete responders, 21 (53.8%) who underwent dose reduction and progressive extension of dosing intervals were eventually able to discontinue omalizumab without experiencing a recurrence of urticaria during the subsequent six months. Conversely, ten complete responders receiving low-dose omalizumab could not be weaned off treatment without flare-ups. Figure 4 summarizes the

treatment outcomes for complete responders. Unfortunately, none of the variables included in the statistical analysis were able to predict the likelihood of sustained remission in the absence of continued therapy.

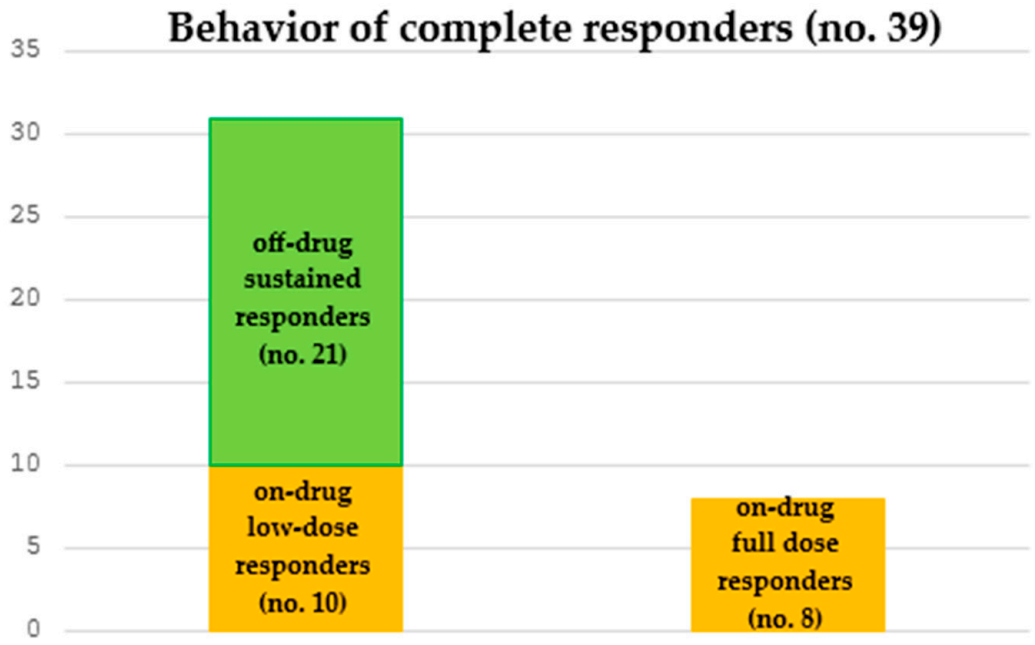


Figure 4. Summary of the long-term outcomes in complete responders. Of the 39 complete responders (represented across both columns), 31 patients (green-yellow column) were successfully managed long-term with low-dose omalizumab (150 mg) administered at extended intervals. Among these, 21 patients were able to completely discontinue treatment without relapse. The remaining 10 patients, although unable to fully withdraw from omalizumab, remained free of urticaria under the low-dose regimen. In contrast, eight patients (yellow column) were unable to modify the approved therapeutic dose and maintained symptom control only with the standard 300 mg monthly dose of omalizumab.

3.4. Safety

The mean ± sd treatment duration was 32.5 ± 38.4 months. Sixteen patients received omalizumab for at least 36 months, with two of them exceeding 10 years of treatment (123 and 209 months, respectively). None of the patients experienced major adverse effects requiring hospitalization (e.g., anaphylaxis). The only complaint, reported by nearly all patients (95.8%), was pain at the injection site. Consequently, no patients discontinued omalizumab due to safety concerns; treatment cessation occurred solely based on clinical decisions.

4. Discussion

This study confirms the effectiveness and safety of omalizumab in real-life patients with chronic urticaria. Specifically, over 80% of our patient population achieved complete clearance of hives within days or, at most, weeks after initiating anti-IgE therapy. Furthermore, we demonstrate that a substantial proportion of complete responders remained hive-free with very low doses of the monoclonal antibody, thanks to dose reduction and extended intervals between injections during long-term management. This approach could significantly reduce the economic burden of prolonged treatment, especially in countries where national health systems cover all patient expenses, while awaiting the market availability of more affordable alternatives (e.g., biosimilars).

The mechanism of action of omalizumab in chronic urticaria has yet to be fully elucidated [6,9,10,14]; consequently, predictive factors of treatment response remain an unmet clinical need [1,6,9,14]. In our study, among the numerous variables analyzed, only total serum IgE levels were found to correlate with clinical response, identifying 164.7 IU/mL as a potential cut-off value distinguishing responders from nonresponders. This finding aligns with the known mechanism of action of the monoclonal antibody (i.e., neutralization of free IgE) [15] and suggests that even in chronic urticaria—often referred to as "spontaneous" due to the absence of identifiable triggers—the IgE–mast cell axis [36] may play a pivotal role in disease pathogenesis. Furthermore, selecting chronic urticaria patients for omalizumab treatment based on serum total IgE levels may enhance the proportion of complete responders, thereby minimizing the risk of unnecessarily treating potentially unresponsive patients and reducing the waste of healthcare resources. However, it should be clarified that while higher IgE levels may increase the likelihood of a response to omalizumab, this does not imply that patients with low IgE levels cannot achieve complete disease control. In our experience, some patients with low IgE levels responded positively to omalizumab treatment. Therefore, the search for more robust predictive markers of response remains ongoing.

This is why we also evaluated the reliability of the neutrophil-to-lymphocyte ratio (NLR). The strong association between NLR and clinical outcomes across various diseases [33–35], combined with its ease of calculation from a standard, relatively inexpensive complete blood count, makes it a promising candidate as a biomarker. Specifically, NLR may reflect the balance between innate and adaptive immunity; consequently, the higher the NLR, the higher the predominance of systemic inflammation with respect to cell-mediated immunity.

Nevertheless, the behavior of NLR in chronic urticaria patients remains unclear. For example, these patients might theoretically exhibit elevated NLR values during active disease due to increased inflammation triggered by mast cell mediator release, with values decreasing during remission; persistence of high NLR values would indicate patients unlikely to achieve remission. Alternatively, NLR may be low in patients with chronic urticaria, as alterations in serum cytokine levels have been reported in this population [37], suggesting a predominance of lymphocytic activity. Whatever the case, it is important to note that both neutrophil and lymphocyte counts can be affected by a wide range of confounding factors—including viral and bacterial infections, coexisting autoimmune or chronic inflammatory conditions, malignancies, and even the medications used to manage acute urticaria flares (e.g., corticosteroids). Therefore, it is not surprising that NLR proved to be irrelevant in predicting disease outcomes.

Unfortunately, we were unable to identify variables capable of predicting, at the start of therapy, which patients would benefit from sustained remission of chronic hives. Typically, patients who achieve clearance of hives during anti-IgE therapy have their treatment abruptly discontinued, followed by a watch-and-wait approach; in the event of recurrence, omalizumab is reintroduced [11–13].

In our long-term management strategy, sustained responders were identified when progressive extension of dosing intervals did not lead to urticaria recurrence. In our experience, this approach was preferred by patients, as it fostered a gradual sense of recovery. In contrast, abrupt discontinuation of therapy following hive resolution often left patients anxious about the potential return of symptoms.

Nonresponders remain an unmet clinical need in chronic urticaria. In some cases, the lack of response to omalizumab may stem from our incomplete understanding of the drug's mechanism of action. In other instances, pharmacokinetic and pharmacodynamic factors may theoretically contribute, as has been documented with other monoclonal

antibodies [38]. These aspects, however, have been rarely investigated in the context of omalizumab treatment, and primarily in patients with respiratory allergic diseases [39,40].

Finally, regarding safety, none of the most concerning side effects associated with omalizumab therapy were observed [41]. Specifically, no cases of anaphylaxis, thrombosis, cancer, parasitic infections, or other serious adverse events were reported. The only complaint, noted by nearly all patients, was pain at the injection site. A substantial proportion of patients received treatment for ≥3 years, and two patients continued periodic omalizumab injections for over 10 and 17 years, respectively, underscoring the excellent long-term safety profile of this drug.

5. Conclusions

Omalizumab proved to be safe and effective in real-life patients with chronic urticaria. Serum total IgE levels may assist in identifying individuals more likely to respond to treatment. Responders can be maintained urticaria-free through a personalized strategy involving low-dose administration (150 mg) at extended intervals, resulting in substantial reductions in healthcare costs. Long-term anti-IgE therapy was not associated with new safety concerns, with local pain at the injection site being the most commonly reported adverse effect.

For patients with severe disease refractory to omalizumab, still an unmet clinical need, the introduction of new therapeutic agents is eagerly anticipated. Among these, dupilumab, which targets the T helper cell–mast cell–IgE axis in various settings [42,43], holds particular promise.

Author Contributions: Conceptualization, C.R. and E.A.; methodology, C.R., D.C. and E.A.; software, G.R.U.; validation, D.C. and G.R.U.; formal analysis, C.R., D.C., G.R.U. and E.A.; investigation, C.R.; data curation, C.R.; writing—original draft preparation, C.R.; writing—review and editing, C.R., D.C. and G.R.U. and E.A.; supervision, C.R. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and its later amendments. Because of its retrospective nature, formal ethics approval was not required for this study; all the procedures being performed were part of routine care and all patients consented to the use of their clinical data under conditions of anonymity.

Informed Consent Statement: Informed consent for use of anonymous clinical data and adherence to the treatment protocol with omalizumab was obtained from all subjects involved in the study.

Data Availability Statement: Raw data are available from the corresponding author upon reasonable request.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Kolkhir, P.; Bonnekoh, H.; Metz, M.; Maurer, M. Chronic spontaneous urticaria: A review. *JAMA* **2024**, *332*, 1464–1477. [CrossRef]
2. Lang, D.M.; Sheikh, J.; Joshi, S.; Bernstein, J.A. Endotypes, phenotypes, and biomarkers in chronic spontaneous urticaria: Evolving toward personalized medicine. *Ann. Allergy Asthma Immunol.* **2025**, *134*, 408–417.e3. [CrossRef]
3. Lee, R.; Bernstein, J.A. Chronic spontaneous urticaria and chronic inducible urticaria. *J. Allergy Clin. Immunol.* **2025**, *156*, 546–556. [CrossRef]
4. Hollis, K.; Proctor, C.; McBride, D.; Balp, M.M.; McLeod, L.; Hunter, S.; Tian, H.; Khalil, S.; Maurer, M. Comparison of Urticaria Activity Score over 7 days (UAS7) values obtained from once-daily and twice-daily versions: Results from the ASSURE-CSU study. *Am. J. Clin. Dermatol.* **2018**, *19*, 267–274. [CrossRef] [PubMed]
5. O'Donnell, B.F.; Lawlor, F.; Simpson, J.; Morgan, M.; Greaves, M.W. The impact of chronic urticaria on the quality of life. *Br. J. Dermatol.* **1997**, *136*, 197–201. [CrossRef] [PubMed]

6. Sánchez-Borges, M.; Ansotegui, I.J.; Baiardini, I.; Bernstein, J.; Canonica, G.W.; Ebisawa, M.; Gomez, M.; Gonzalez-Diaz, S.N.; Martin, B.; Morais-Almeida, M.; et al. The challenges of chronic urticaria part 1: Epidemiology, immunopathogenesis, comorbidities, quality of life, and management. *World Allergy Organ J.* **2021**, *14*, 100533. [CrossRef] [PubMed]
7. Berberi, G.; Maazi, M.; Prosty, C.; McMullen, E.P.; Fein, M.; Lima, H.; Martinez-Jaramillo, E.; Ben-Shoshan, M.; Pourpanah, F.; Netchiporouk, E. Health-related quality of life in chronic urticaria: A systematic review and meta-analysis. *J. Allergy Clin. Immunol. Pract.* **2025**, *13*, 2317–2328. [CrossRef]
8. Kulthanan, K.; Jiamton, S.; Thumpimukvatana, N.; Pinkaew, S. Chronic idiopathic urticaria: Prevalence and clinical course. *J. Dermatol.* **2007**, *34*, 294–301. [CrossRef] [PubMed]
9. Zuberbier, T.; Ensina, L.F.; Giménez-Arnau, A.; Grattan, C.; Kocatürk, E.; Kulthanan, K.; Kolkhir, P.; Maurer, M. Chronic urticaria: Unmet needs, emerging drugs, and new perspectives on personalised treatment. *Lancet* **2024**, *404*, 393–404. [CrossRef]
10. Lang, D.M. Chronic urticaria. *N. Engl. J. Med.* **2022**, *387*, 824–831. [CrossRef]
11. Asero, R.; Calzari, P.; Vaienti, S.; Cugno, M. Therapies for chronic spontaneous urticaria: Present and future developments. *Pharmaceuticals* **2024**, *17*, 1499. [CrossRef]
12. Yosipovitch, G.; Biazus Soares, G.; Mahmoud, O. Current and emerging therapies for chronic spontaneous urticaria: A narrative review. *Dermatol. Ther.* **2023**, *13*, 1647–1660. [CrossRef]
13. Kolkhir, P.; Fok, J.S.; Kocatürk, E.; Li, P.H.; Okas, T.L.; Marcelino, J.; Metz, M. Update on the treatment of chronic spontaneous urticaria. *Drugs* **2025**, *85*, 475–486. [CrossRef]
14. Kaplan, A.P. Chronic spontaneous urticaria: Pathogenesis and treatment considerations. *Allergy Asthma Immunol. Res.* **2017**, *9*, 477–482. [CrossRef] [PubMed]
15. Chang, T.W.; Wu, P.C.; Hsu, C.L.; Hung, A.F. Anti-IgE antibodies for the treatment of IgE-mediated allergic diseases. *Adv. Immunol.* **2007**, *93*, 63–119. [CrossRef]
16. Humbert, M.; Beasley, R.; Ayres, J.; Slavin, R.; Hébert, J.; Bousquet, J.; Beeh, K.M.; Ramos, S.; Canonica, G.W.; Hedgecock, S.; et al. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE. *Allergy* **2005**, *60*, 309–316. [CrossRef] [PubMed]
17. Agache, I.; Rocha, C.; Beltran, J.; Song, Y.; Posso, M.; Solà, I.; Alonso-Coello, P.; Akdis, C.; Akdis, M.; Canonica, G.W.; et al. Efficacy and safety of treatment with biologicals (benralizumab, dupilumab and omalizumab) for severe allergic asthma: A systematic review for the EAACI Guidelines—recommendations on the use of biologicals in severe asthma. *Allergy* **2020**, *75*, 1043–1057. [CrossRef] [PubMed]
18. Spector, S.L.; Tan, R.A. Effect of omalizumab in patients with chronic urticaria. *Ann. Allergy Asthma Immunol.* **2007**, *99*, 190–193. [CrossRef]
19. Spector, S.L.; Tan, R.A. Advances in allergic skin disease: Omalizumab is a promising therapy for urticaria and angioedema. *J. Allergy Clin. Immunol.* **2009**, *123*, 273–274. [CrossRef]
20. Kaplan, A.P.; Joseph, K.; Maykut, R.J.; Geba, G.P.; Zeldin, R.K. Treatment of chronic autoimmune urticaria with omalizumab. *J. Allergy Clin. Immunol.* **2008**, *122*, 569–573. [CrossRef]
21. Romano, C.; Sellitto, A.; De Fanis, U.; Esposito, G.; Arbo, P.; Giunta, R.; Lucivero, G. Maintenance of remission with low-dose omalizumab in long-lasting, refractory chronic urticaria. *Ann. Allergy Asthma Immunol.* **2010**, *104*, 95–97. [CrossRef]
22. Saini, S.; Rosen, K.E.; Hsieh, H.J.; Wong, D.A.; Conner, E.; Kaplan, A.; Spector, S.; Maurer, M. A randomized, placebo-controlled, dose-ranging study of single-dose omalizumab in patients with H1-antihistamine-refractory chronic idiopathic urticaria. *J. Allergy Clin. Immunol.* **2011**, *128*, 567–573.e1. [CrossRef]
23. Maurer, M.; Rosén, K.; Hsieh, H.J.; Saini, S.; Grattan, C.; Gimenéz-Arnau, A.; Agarwal, S.; Doyle, R.; Canvin, J.; Kaplan, A.; et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *N. Engl. J. Med.* **2013**, *368*, 924–935. [CrossRef]
24. Saini, S.S.; Bindslev-Jensen, C.; Maurer, M.; Grob, J.J.; Bülbül Baskan, E.; Bradley, M.S.; Canvin, J.; Rahmaoui, A.; Georgiou, P.; Alpan, O.; et al. Efficacy and safety of omalizumab in patients with chronic idiopathic/spontaneous urticaria who remain symptomatic on H1 antihistamines: A randomized, placebo-controlled study. *J. Investig. Dermatol.* **2015**, *135*, 67–75. [CrossRef]
25. McCormack, P.L. Omalizumab: A review of its use in patients with chronic spontaneous urticaria. *Drugs* **2014**, *74*, 1693–1699. [CrossRef] [PubMed]
26. Akdaş, E.; Adışen, E.; Öztaş, M.O.; Aksakal, A.B.; İlter, N.; Gülekon, A. Real-life clinical practice with omalizumab in 134 patients with refractory chronic spontaneous urticaria: A single-center experience. *An. Bras. Dermatol.* **2023**, *98*, 240–242. [CrossRef] [PubMed]
27. Calzari, P.; Chiei Gallo, A.; Barei, F.; Bono, E.; Cugno, M.; Marzano, A.V.; Ferrucci, S.M. Omalizumab for the treatment of chronic spontaneous urticaria in adults and adolescents: An eight-year real-life experience. *J. Clin. Med.* **2024**, *13*, 5610. [CrossRef]
28. Seetasith, A.; Holden, M.; Hetherington, J.; Keal, A.; Salmon, P.; Bernstein, J.A.; Casale, T.B. Real-world outcomes in patients with chronic spontaneous urticaria receiving omalizumab: Insights from a clinical practice survey. *Curr. Med. Res. Opin.* **2024**, *40*, 1059–1066. [CrossRef]

29. Terhorst-Molawi, D.; Fox, L.; Siebenhaar, F.; Metz, M.; Maurer, M. Stepping down treatment in chronic spontaneous urticaria: What we know and what we don't know. *Am. J. Clin. Dermatol.* **2023**, *24*, 397–404. [CrossRef] [PubMed]
30. Brás, R.; Costa, C.; Limão, R.; Caldeira, L.E.; Paulino, M.; Pedro, E. Omalizumab in chronic spontaneous urticaria (CSU): Real-life experience in dose/interval adjustments and treatment discontinuation. *J. Allergy Clin. Immunol. Pract.* **2023**, *11*, 2392–2402. [CrossRef]
31. Batyrbayeva, A.; Ispayeva, Z.; Pashimov, M.; Kaibullayeva, J.; Baidildayeva, M.; Kapalbekova, U.; Tokmurzayeva, E.; Plakhotina, O.; Maldybayeva, A.; Salmanova, A.; et al. Clinical phenotypes and biomarkers in chronic urticaria. *Clin. Chim. Acta* **2025**, *571*, 120233. [CrossRef] [PubMed]
32. Romano, C.; Sellitto, A.; De Fanis, U.; Balestrieri, A.; Savoia, A.; Abbadessa, S.; Astarita, C.; Lucivero, G. Omalizumab for difficult-to-treat dermatological conditions: Clinical and immunological features from a retrospective real-life experience. *Clin. Drug Investig.* **2015**, *35*, 159–168. [CrossRef] [PubMed]
33. Dong, C.H.; Wang, Z.M.; Chen, S.Y. Neutrophil to lymphocyte ratio predict mortality and major adverse cardiac events in acute coronary syndrome: A systematic review and meta-analysis. *Clin. Biochem.* **2018**, *52*, 131–136. [CrossRef]
34. Carrión-Barberà, I.; Lood, C. Performance of the neutrophil-to-lymphocyte ratio as a prognostic tool for survival in solid cancers. *Front. Oncol.* **2025**, *15*, 1616477. [CrossRef]
35. Xiaoyan, L.; Zhongying, B.; Shuhong, D.; Jing, S.; Yijie, Z.; Jie, Z.; Jingxin, L. Predictive model for coronavirus disease 2019 severity based on blood biomarkers: A retrospective study. *Front. Med.* **2025**, *8*, 1597082. [CrossRef]
36. Aitella, E.; Romano, C.; Ginaldi, L.; Cozzolino, D. Mast cells at the crossroads of hypersensitivity reactions and neurogenic inflammation. *Int. J. Mol. Sci.* **2025**, *26*, 927. [CrossRef]
37. Zeng, W.; Xia, J.; Zeng, Q. Levels of serum inflammatory cytokines and their correlations with disease severity in patients with chronic spontaneous urticaria. *Postepy Dermatol. Alergol.* **2024**, *41*, 85–90. [CrossRef]
38. Trotta, M.C.; Alfano, R.; Cuomo, G.; Romano, C.; Gravina, A.G.; Romano, M.; Galdiero, M.; Montemurro, M.V.; Giordano, A.; D'Amico, M. Comparison of timing to develop anti-drug antibodies to infliximab and adalimumab between adult and pediatric age groups, males and females. *J. Pediatr. Pharmacol. Ther.* **2022**, *27*, 63–71. [CrossRef]
39. Corren, J.; Casale, T.B.; Lanier, B.; Buhl, R.; Holgate, S.; Jimenez, P. Safety and tolerability of omalizumab. *Clin. Exp. Allergy* **2009**, *39*, 788–797. [CrossRef]
40. Ohta, K.; Yamamoto, M.; Sato, N.; Ikeda, K.; Miyamoto, T. One year treatment with omalizumab is effective and well tolerated in Japanese patients with moderate-to-severe persistent asthma. *Allergol. Int.* **2010**, *59*, 167–174. [CrossRef] [PubMed]
41. Pongdee, T.; Li, J.T. Omalizumab safety concerns. *J. Allergy Clin. Immunol.* **2025**, *155*, 31–35. [CrossRef] [PubMed]
42. Romano, C.; Cozzolino, D.; Corona, M.E.; Aitella, E. Efficacy and safety of dupilumab across different Th2-type-mediated diseases: A real-life preliminary experience. *Biologics* **2025**, *5*, 3. [CrossRef]
43. Romano, C. Safety and effectiveness of dupilumab in prurigo nodularis. *J. Investig. Allergol. Clin. Immunol.* **2021**, *31*, 162–163. [CrossRef] [PubMed]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.