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REDACTED REPORT BODY

Abbreviated report - CIGE025A2010- Efficacy of omalizumab in food allergic adults – A retrospective analysis

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Descriptive title

Efficacy of omalizumab in food allergic adults – A retrospective analysis

Qualified associate responsible for Discussion and Conclusion
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Rationale and background

Food allergies are a growing public health concern, with increasing prevalence and significant impacts on quality of life and can result in severe or even life-threatening symptoms [1]. The underlying pathophysiological mechanism of food allergy is a type I immunologic mechanism. The standard of care includes the short-term management of acute reactions and long-term strategies to reduce the risk of further reactions.

Omalizumab (OMA) is a humanized monoclonal anti-IgE antibody, which has been approved for the treatment of allergic asthma, chronic spontaneous urticaria and nasal polyposis for many years. Following the positive results of the OUtMATCH study in children [2], OMA was recently approved by the FDA in the U.S. for the treatment of food allergies. In Europe, however, its use for this indication remains off-label. While the combination of OMA and oral immunotherapy (OIT) has been studied for peanut and milk allergies, there is a lack of data on its use for lipid transfer protein (LTP) allergies—a major cause of severe reactions in Mediterranean populations. These allergies are particularly challenging due to their resistance to heat and digestion, making avoidance strategies less effective.

This retrospective analysis investigates real-world data on the use of OMA in adult patients with food allergy and food-induced anaphylaxis across several European centers.

Key milestones

- 11.2022–12.2022: Study concept finalized; questionnaire and study protocol developed.
- 01.2023–03.2023: Local ethics application submitted; European allergy centers contacted to identify eligible patients. Support provided to other centers for local protocols and ethics submissions.
- 05.2023: Ethics approvals received from committees in Berlin and Barcelona.
- 06.2023–07.2023: Patient data collected from medical records in Berlin and Barcelona.
- 07.2023–08.2023: Additional ethics approvals obtained and data collected from Basel and Leipzig.
- 09.2023: Data collection completed; study database created.
- 10.2023–12.2023: Statistical analysis conducted.
- 01.2024: Abstract submitted for EAACI 2024.
- 01.2024–04.2024: First Manuscript drafted.
- 05.2024: First manuscript draft shared with co-authors for feedback.
- 06.2024: Study findings presented at EAACI 2024 in Valencia.
- 06.2024–07.2024: Final manuscript prepared.
- 06.08.2024: Manuscript submitted for publication in World Allergy Organization Journal.
- 29.11.2024: Revised manuscript submitted.
- 12.03.2025: Manuscript accepted for publication.
- 03.04.2025: Article published online.

Research question, objectives, endpoints

The primary hypothesis was that omalizumab reduces the recurrence of anaphylactic reactions and improves the quality of life in patients with anaphylaxis. The secondary hypotheses were that omalizumab increases tolerance to higher amounts of allergen, reduces the severity of accidental reactions, and, when used as an adjuvant during immunotherapy, allows for more rapid and higher dosing as well as improved treatment tolerance.

The primary endpoint was the number of anaphylactic reactions recorded during treatment. The secondary endpoints included quality of life outcomes, the frequency of accidental reactions, changes in allergen threshold levels, and the severity of anaphylactic reactions

Names, titles, affiliations of investigators

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Study design

Retrospective, multi-center observational study conducted across four allergy departments in Europe (Berlin, Leipzig, Barcelona, and Basel). The study included patients with IgE-mediated food allergy who were treated with omalizumab, either as monotherapy or in combination with oral immunotherapy (OIT) between 2002–2022.

Study population and selection

The study included adult patients diagnosed with IgE-mediated food allergy who received omalizumab treatment between 2002 and 2022. Participants were identified through institutional records from allergy departments in Berlin, Leipzig, Barcelona, and Basel. Inclusion criteria required a confirmed history of food allergy—either with or without prior anaphylaxis—and treatment with omalizumab, either as monotherapy or in combination with oral immunotherapy.

Data sources and data collection methods

The assessment of the clinical data for research was approved by the ethics committee at the Charité (EA4/037/23) as the initiating center. In addition, local ethical approval was obtained in each center individually.

Data were collected retrospectively using a structured survey questionnaire based on patient medical records, ensuring anonymization. The questionnaire covered various parameters including demographics (sex, race, and year of birth), medical history (including relevant diseases, procedures, and medications), food allergy history (detailing specific allergies and anaphylactic reactions), diagnostic results (allergy tests and oral food challenges), OMA treatment details (including type, dosage, and safety), and information on oral immunotherapy for food allergy. Laboratory test results (total IgE, specific IgE, and basal serum tryptase) were obtained prior to treatment initiation.

Individuals were classified as treatment responders if an oral food challenge was negative (Responders- Group A), or a decrease of severity of food allergy during an oral food challenge was

determined (Responders- Group B) and no anaphylactic reactions occurred during treatment (Responders- Group C). Non-responders were those who experienced repetitive food anaphylactic reactions during treatment. Partial treatment responders were defined as individuals who experienced less than 1 food anaphylactic reaction despite undergoing treatment.

Statistical methods & Data analysis

The collected data were entered into a Microsoft Excel database and analyzed using IBM SPSS Statistics (version 27, Chicago, IL). Statistical analyses were descriptive in nature, focusing on summarizing patient demographics, treatment patterns, clinical outcomes, and safety data. Categorical variables were reported as frequencies and percentages, while continuous variables were presented as means, medians, and ranges.

Bias

As a retrospective study, the primary source of bias is selection bias—patients were identified from existing records, potentially excluding individuals with undocumented or less severe cases. Additionally, clinical outcomes were determined based on physician documentation and retrospective assessments, which may introduce observer bias. There was also variation in the use of oral food challenges across centers, further affecting consistency.

Limitations

This study has several limitations. The retrospective design may introduce selection bias, as the analysis depended on previously documented cases, which may not accurately reflect the broader population of patients with food allergy. Data were collected using paper-based questionnaires across multiple centers, employing a mix of closed and open questions, which may have led to variability and subjectivity in the responses. Quality of life (QoL) measures were not consistently captured, limiting the evaluation of patient-centered outcomes. Oral food challenge (OFC) data, when available, were not standardized across sites, complicating the interpretation of clinical response and allergic risk. Additionally, the study was conducted at a limited number of European centers, which may restrict the generalizability of the findings to other regions or healthcare systems.

Key Results

In total, 62 patients were included into this analysis. Of those, 52 were treated in the allergy department at Hospital Vall d'Hebron in Barcelona, Spain, 5 in the allergy department at Charité Universitätsmedizin in Berlin, Germany, 4 in the allergy department at the University of Leipzig, Germany, and 1 at the allergy department at the University Hospital Basel, Basel, Switzerland. Most patients were female (n=39/62, 62.9%), and all patients were Caucasian (n= 62/62, 100%). The age range of the patients was 9–59 years, with a mean age of 30.6 years at treatment initiation. Tables 1 and 2 present detailed demographic information and medical history data of the study population.

Seventeen individuals (n=17/62, 27.4%) underwent OMA monotherapy, while the remaining 45 patients (n=45/62, 72.6%) received OMA combined with oral immunotherapy (OIT). Among the latter group, OIT with cow's milk was performed in 22 cases (n=22/62, 35.5%), OIT with peach juice for LTP allergy in 20 cases (n=20/62, 32.6%) and OIT with egg in 3 cases (n=3/62, 5%).

In the majority of cases, OMA was administered at treatment initiation with a dose of 300 mg subcutaneously every 4 weeks (n=51/62, 82.3%). The primary medical indication for the treatment was "to reduce an accidental reaction" (n= 54/62, 87%), followed by "onset of repetitive anaphylactic reactions" (n=26/62, 41,9%) and "multiple food allergies" (n=10/62, 16.1%). The majority of the patients (n= 61/62, 98.4%) reported excellent safety with OMA treatment. One

patient (n=1/62, 1.6%) reported recurrent abdominal pain after receiving injections of OMA. Consequently, the treatment was discontinued due to this adverse event. No further known serious adverse events were observed.

The majority of patients (n=48/ 62, 77.4%) still receive OMA with or without OIT, with a mean duration of treatment of 5 and one-half years and a median duration of treatment of 5 years. Twelve patients received OMA treatment for longer than 7 years. The remaining patients (n=14/62, 22.6%) terminated the treatment. Seven of these patients continued the treatment with the OIT maintenance dose after OMA termination. The 7 patients who discontinued OMA are still avoiding the culprit foods.

Fifty-two patients (n= 52/62, 83.9%) were classified as treatment responders. Among these, 6 cases (Group A, n= 6/62, 9.7%) achieved desensitization, which was confirmed by an oral food challenge. Group B (n= 6/62, 9.7%) consisted of patients who demonstrated a decrease in the severity of food allergy, either demonstrated by an oral food challenge or based on the clinical assessment by the investigator. Group C included patients who did not experience any anaphylactic reactions during treatment (n=40/62, 64.5%). Nine patients (n=9/62, 14.5%) were classified as partial responders due to experiencing anaphylactic reactions during treatment. One patient (n= 1/62, 1.6%) was categorized as a non-responder. Figure 1 summarizes the main treatment outcomes observed in the study.

Fourteen patients (n=14/17, 82.4%) who underwent OMA monotherapy were classified as responders. Twenty patients (n= 20/22, 90.1%) who received OMA combined with OIT with cow's milk were characterized as responders, as well as 15 (n=15/20, 75%) of those who received OMA with OIT with peach juice. Additionally, all 3 patients (n=3/3, 100%) who received OMA combined with OIT with egg were characterized as responders.

Ten patients experienced anaphylaxis during treatment (n = 10/62, 16.1%). Of these, three were in the OMA monotherapy group (n = 3/17, 17.6%), two in the cow's milk OIT group (n = 2/22, 9.1%), and five in the peach OIT group (n = 5/20, 25.0%). In five cases, the reactions were associated with cofactors such as exercise, NSAIDs, menstruation, or alcohol (n = 5/10, 50.0%). One case was related to non-compliance with the OIT protocol (n = 1/10, 10.0%). Treatment was discontinued due to these reactions in three patients (n = 3/10, 30.0%).

Among patients undergoing OIT, 26 had cow's milk allergy (n = 26/62, 41.9%) and 20 had LTP allergy (n = 20/62, 32.3%). Patients with LTP allergy had a higher mean age at treatment initiation (36.3 years) and showed lower total and specific IgE levels. In comparison, cow's milk-allergic patients had a mean total IgE level of 1024 kU/L and a mean cow's milk-specific IgE of 57 kU/L. The treatment response rate was higher in the cow's milk group (n = 20/22, 90.9%) compared to the LTP group (n = 15/20, 75.0%). However, both groups showed similarly favorable outcomes in terms of desensitization.

The results of the study were recently published (Alexiou A, Carreras-Kàtcheff S, Hartmann K, Treudler R, Tassinari P, Cardona V, Worm M. Efficacy of omalizumab in food allergic adults - A retrospective analysis. World Allergy Organ J. 2025 Apr 3;18(4):101048. doi: 10.1016/j.waojou.2025.101048.) and more detailed data can be found there.

Tables and Figures

	Entire cohort	Spain	Germany/ Switzerland
	N= 62	N=52	N=10
Age in years			
Mean age	30.60	29.40	37.40
Median age	27	25.50	35
Min.-Max. age	09-59 y.	09-59 y.	19-58 y.
Gender: n (%)			
Female	39 (62.9%)	33 (63.5%)	6 (60%)
Atopic history: n (%)			
Food allergy	62 (100%)	52 (100%)	10 (100%)
Allergic rhinoconjuctivitis	43 (69.4%)	37 (71.1%)	6 (60%)
Asthma	34 (54.8%)	28 (53.8%)	6 (60%)
Atopic dermatitis	7 (11.3%)	5 (9.6%)	2 (20%)
Chronic spontaneous urticaria	5 (8%)	2 (3.8%)	3 (30%)
IgE levels (kU/l)			
Mean IgE levels (kU/l)	606.6	635.1	435.3
Median IgE levels (kU/l)	289	289	361

Table 1: Demographics

	Entire cohort	Spain	Germany/ Switzerland
	N= 62	N=52	N=10
Poly- VS Monosensitised: n (%)			
Polysensitised	40 (64.5%)	34 (65.4%)	6 (60%)
Monosensitised	22 (35.5%)	18 (34.6%)	4 (40%)
Diagnosis of food allergy: n (%)			
Anaphylaxis*	52 (83.9%)	47 (90.4%)	5 (50%)
Oral food challenge**	8 (12.9%)	4 (7.7%)	4 (40%)
Medical History***	2 (3.2%)	1 (1.9%)	1 (10%)

Table 2. Food allergy history.
* (≥Grade 2, based on Ring & Messmer anaphylaxis grading score). ** With or without history of previous anaphylaxis. ***Based on previous symptoms in medical history, including Oral allergic symptoms and/or urticaria

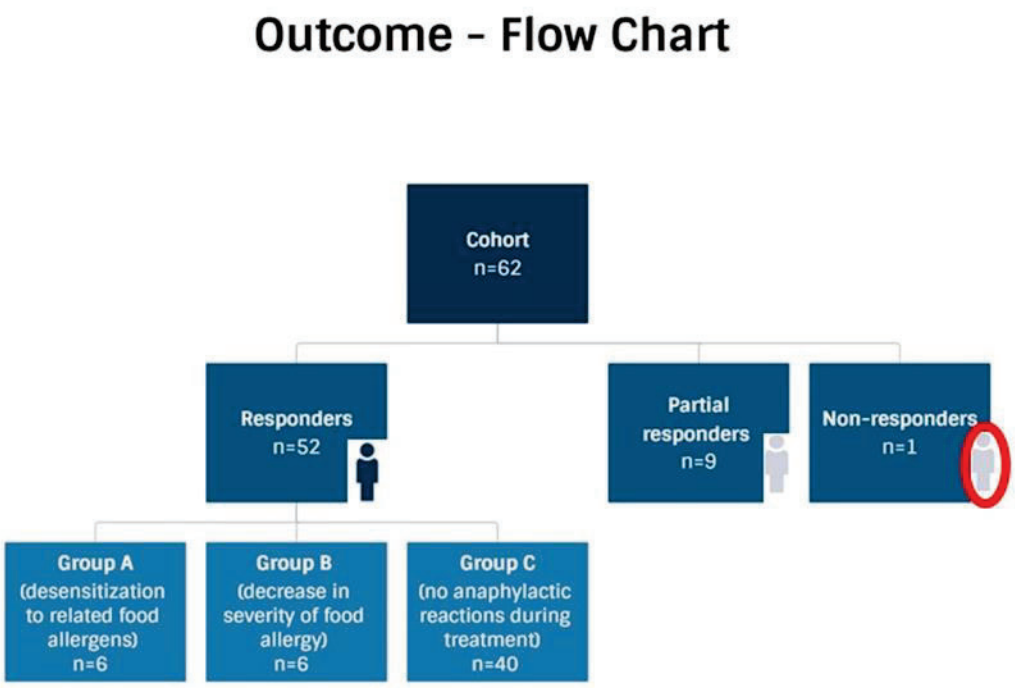

Figure 1: the outcome flowchart and the treatment response per treatment group. Treatment responders are highlighted, partial responders are marked in grey, and non-responders are marked with a red circle

Discussion of key results and interpretation

OMA is effective in reducing anaphylaxis in adults with food allergies, both as monotherapy and in combination with OIT. In the present study, real-world data on treatment of food allergy with OMA from various countries was analysed, encompassing patients with different sensitization patterns and subjected to various treatment protocols. This study involved a substantial cohort of adult patients throughout Europe and highlights the significant efficacy of OMA in managing food allergies.

This study is the first to publish the use of OMA in combination with OIT with peach juice for patients with proven LTP sensitization and highlights that OMA also facilitates OIT in patients with LTP allergy.

In 82.3% of cases, OMA was administered at a dose of 300 mg every 4 weeks, consistent with the dose approved for chronic spontaneous urticaria. This dosage was not predetermined but was adopted across various European allergy centers based on clinical experience, as it is also practical to implement.

Results suggest cofactors (exercise, NSAIDs, menstruation) significantly affect outcomes and should be addressed in clinical settings.

Conclusions

In conclusion, our data provide further evidence for the efficacy and tolerability of OMA in treating IgE-mediated food allergy, both alone and in combination with OIT. Notably, our study shows that OMA, particularly when combined with OIT, achieves higher response rates. OMA is a viable long-term treatment option for adult food allergy, offering good efficacy and tolerability. Cofactors should be considered in treatment planning.

Abstracts and publications in relation to this work:

1. Alexiou A. Omalizumab in food allergy – a retrospective analysis. Poster D1.370 presented at: EAACI Congress 2025; 2025 Jun 13–16; Valencia, Spain.
2. Alexiou A. Omalizumab in food allergy – a retrospective analysis. Presented as a Flash Talk at: EAACI Congress 2025; 2025 Jun 13–16; Valencia, Spain.
3. Alexiou A, Carreras-Kàtcheff S, Hartmann K, Treudler R, Tassinari P, Cardona V, Worm M. Efficacy of omalizumab in food allergic adults - A retrospective analysis. World Allergy Organ J. 2025 Apr 3;18(4):101048. doi: 10.1016/j.waojou.2025.101048.

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1. Santos, A.F., et al., *EAACI guidelines on the diagnosis of IgE-mediated food allergy.* Allergy, 2023.
2. Wood, R.A., et al., *Omalizumab for the Treatment of Multiple Food Allergies.* N Engl J Med, 2024. **390**(10): p. 889-899.