

# Efficacy of long-term treatment with omalizumab in a food and inhalant allergy patient

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Omalizumab, a recombinant humanized immunoglobulin G1 (IgG1) monoclonal antibody, binds C-ε-3 region of free immunoglobulin E forming complexes that prevent the IgE interaction with their receptors [1]. Treatment with omalizumab produces a decrease in free immunoglobulin E (IgE) levels and consequently reduces the expression of the high affinity FcεRI receptor on the surface of mast cells and basophils [2].

In clinical practice, omalizumab is approved for treatment of patients with moderate-severe persistent perennial asthma and, since 2014, for treatment of chronic spontaneous urticaria (CSU) which are uncontrolled by conventional anti-H1 treatment [3].

In the literature there is increasing evidence of a possible efficacy of an anti-IgE therapy also in other allergic diseases (allergic rhinitis, nasal polyps, food allergy, eosinophilic gastrointestinal, etc.) [4] and in immune-mediated disorders including hypocomplementemic urticarial vasculitis syndrome (HUVS) [5].

We describe the case of a 10-year-old child with atopic dermatitis, hen's egg, cow's milk and peanut hypersensitivity (asthma, urticaria), persistent rhinitis and asthma since a few months of age.

We performed a complete allergological testing including:

- skin prick tests (SPTs), performed with major food and inhalant allergens (Lofarma, Milan, Italy), and positive and negative controls (histamine 10 µg/ml and saline solution) according to the EAACI recommendations [6];
- assays of serum total IgE, specific IgE and IgG4 for major inhalant and food allergens performed by UniCAP System (Pharmacia, Uppsala, Sweden);
- Basophil Activation Test (BAT) for major food allergens.

This evaluation showed a sensitization to dermatophagoides spp., alternaria, yolk and egg white, milk, dried fruits and lipid transfer protein (LTP).

During the years the patient's allergological evaluation was repeated to monitor his allergic conditions; moreover he continued to experience severe asthma exacerbations that were not controlled by symptomatic treatment and standard allergen-specific immunotherapy requiring recurrent high doses of oral corticosteroids. For these reasons, in 2014 the young patient started omalizumab treatment (300 mg monthly) according to guidelines [7].

The young patient immediately had a complete remission of his respiratory condition (allergic rhinitis and bronchial asthma); in fact, he obtained a good control of his bronchial asthma again (as demonstrated by an increase of his ACT score and enhancement of spirometry parameters) and he did not have any exacerbations which needed emergency therapies.

**Table 1.** sIgE and IgG4 trend from 2014 to 2017

Parameter	Value in 2014	Value in 2017
Yolk sIgE [U/ml]	0.29	0.74
Egg white sIgE [U/ml]	1.28	4.79
Milk sIgE [U/ml]	13.4	3.11
α lactoalbumin sIgE [U/ml]	0.40	0.95
β lactoglobulin sIgE [U/ml]	0.06	0.13
Casein sIgE [U/ml]	1.27	2.87
LTP sIgE [U/ml]	12.6	25.3
Yolk IgG4 [mg/l]	1.50	4.20
Egg white IgG4 [mg/l]	2.65	6.55
Milk IgG4 [mg/l]	0.84	1.23
α lactoalbumin IgG4 [mg/l]	1.66	4.74
β lactoglobulin IgG4 [mg/l]	0.51	0.35
Casein IgG4 [mg/l]	3.31	5.08
LTP IgG4 [mg/l]	1.02	1.64

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Moreover, he showed an almost complete remission of his multiple food allergies; in fact, he tolerated milk, cheese, dried fruits and cooked egg in any quantities, but continued to avoid raw egg for prudence.

After the beginning of the biological therapy, every year the patient repeated the allergy testing to monitor the possible changes in immunological and allergological features.

After 3 years, we observed an increase in total IgE (from 645 UI/ml to 2526 UI/ml) and in all the sIgE levels except for milk.

After 3 years, as regards sIgG4 for the major food allergens, the data showed an increase in all the values except for  $\beta$ -lactoglobulin (Table 1): this is important information because IgG4 is considered a predictor of acquired clinical tolerance. Finally, as regards BAT, we did not observe any significant changes except a decrease in the values for  $\beta$ -lactoglobulin and egg white.

Because of the excellent and encouraging results, we recommend that our patient should continue omalizumab therapy.

Omalizumab is the first immune-modifier to be approved for the treatment of allergic diseases. The excellent strength of evidence for the effectiveness of omalizumab in allergic asthma and chronic urticaria have resulted in the FDA approval for use in those diseases.

Since the use of anti-IgE treatment in other allergic conditions is still non-approved, there are only few studies about a possible role of omalizumab in food allergy treatment: it seems that may increase the safety and tolerability of oral immunotherapy to multiple foods [8] including cow's milk, peanut and hen's egg.

However, although these data suggest that an anti-IgE treatment may be beneficial for food allergy (almost in association with the immunotherapy), their findings are poor and actually certainly not conclusive in this field. Moreover, no data are available about long-term therapy and recurrence of allergic symptoms after the omalizumab discontinuation in food allergy use.

To our knowledge, there are no other reports in the literature that describe the time-course not only of total IgE and sIgE but also for other *in vitro* allergological parameters (IgG4 and BAT) after omalizumab treatment. For sIgG4, we observed an increase, generally present during the allergen specific immunotherapy, which is a predictor of acquired clinical tolerance [9].

As regards possible discontinuance of therapy, we are afraid of a possible and unpredictable recurrence of symptoms since there have been no reliable predictors of treatment efficacy until now.

In summary, we reported the first case of efficacy of omalizumab long-term treatment that leads to a remission of both respiratory and multiple food allergies in a child who was unresponsive to standard therapies.

Our excellent results are very promising for the use of omalizumab also in other allergological conditions and in

general in Th2-related diseases although we are not able to predict the long-term efficacy of this therapy after the discontinuance.

In conclusion, further larger-scale studies are needed to enlarge the indications of omalizumab use in other allergic diseases and to establish reliable markers to predict both the response to treatment and the possibility of therapy discontinuance without recurrence in symptoms.

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Eleonora Nucera MD and Raffaella Chini MD contributed equally to the work.

### Conflict of interest

The authors declare no conflict of interest.

### References

1. Fick Jr RB. Anti-IgE as novel therapy for the treatment of asthma. *Curr Opin Pulmon Med* 1999; 5: 76-80.
2. MacGlashan DW, Bochner BS, Adelman DC, et al. Down-regulation of Fc $\epsilon$ R1 expression on human basophils during *in vivo* treatment of atopic patients with anti-IgE antibody. *J Immunol* 1997; 158: 1438-45.
3. Package insert, Xolair (revision). (2017). Available from: [https://www.gene.com/download/pdf/xolair\\_prescribing.pdf](https://www.gene.com/download/pdf/xolair_prescribing.pdf)
4. Stokes J. Anti-IgE treatment for disorders other than asthma. *Front Med* 2017; 4: 152.
5. Nucera E, Basta F, Buonomo A, et al. A case of hypocomplementemic urticarial vasculitis syndrome successfully treated with omalizumab. *J Investig Allergol Clin Immunol* 2017; 27: 382-4.
6. Dreborg S. Allergen standardization and skin test. EAAI position paper. *Allergy* 1993; 48 (Suppl. 14): 49-82.
7. Genentech Inc. Xolair: FDA Prescribing Information. WWW document 2010. Updated July 2010. URL [http://www.gene.com/download/pdf/xolair\\_prescribing.pdf](http://www.gene.com/download/pdf/xolair_prescribing.pdf)
8. Bégin P, Dominguez T, Wilson SP, et al. Phase 1 results of safety and tolerability in a rush oral immunotherapy protocol to multiple foods using omalizumab. *Allergy Asthma Clin Immunol* 2014; 10: 7.
9. Scott Taylor TH, Axinia SC, Amin S, Pettengell R. Immunoglobulin G: structure and functional implications of different subclass modifications in initiation and resolution of allergy. *Immun Inflamm Dis* 2017; 6: 13-33.