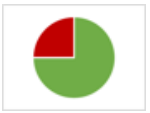
Omalizumab

We **cannot make a recommendation** with respect to the use of omalizumab for the treatment of AE.	**0**	>75%  (13/15) Expert Consensus

Omalizumab: in label for allergic asthma (≥ 6 years), chronic rhinosinusitis with nasal polyps (CRSwNP) (≥ 18 years) and chronic spontaneous urticaria (≥ 12 years)
Commonly used dosage:
Dosage (allergic asthma and CRSwNP): depends on baseline IgE (IU/ml), measured before the start of treatment, and body weight. The maximum recommended dose is 600 mg omalizumab every two weeks. Please refer to the SmPC for further details. Dosage (chronic spontaneous urticaria): 300 mg every four weeks.

Mechanisms of action and efficacy

Most AE patients have elevated serum IgE levels, but the pathogenic role of IgE in AE remains unknown. The anti-IgE antibody omalizumab has been used with great success for treatment of chronic spontaneous urticaria (CSU). A recent systematic review and meta-analysis has assessed the preclinical and trial data regarding omalizumab treatment of AE, which are conflicting.(1)

Omalizumab is licensed for treatment of asthma and CSU, but not for treatment for AE.

Omalizumab is binding free IgE, which leads to immune complexes of IgE and omalizumab. IgE bound to omalizumab cannot bind to the alpha chain of the high affinity receptor for IgE, thereby inhibiting its binding to mast cells, basophils and epidermal dendritic cells(2, 3), and subsequent immunological effects.

There are many case reports and case series,(1) but only few controlled trials studying omalizumab treatment of AE.(1, 4) In summary, the data show a measurable, but moderate efficacy of omalizumab for improving signs and symptoms of AE.(1, 5) There is no predictive marker linked to a better clinical response, and most of the published evidence is of low quality. The safety of omalizumab is very good(1), but the unpredictable and statistically low efficacy prevents a general recommendation for omalizumab regarding treatment of AE.

Dosage: acute flare, short term, long term

Adult:

Diffent dosages have been tested in AE patients, ranging from 150–450 mg every 2 weeks or every 4 weeks. A recent systematic review and meta-analysis by Wollenberg et al. found that patients with lower baseline IgE showed a positive response to treatment with omalizumab compared with patients with very high-to-extremely high serum IgE.(1)

An older systematic review and meta analysis by Wang et al. also found that IgE serum concentrations of lower than 700 IU/mL were associated with a better clinical response, compared with IgE concentrations of 700 to >5000 IU/mL. Age, sex, baseline clinical disease severity, the history of

concomitant asthma, and the use of 600 mg/month or more of omalizumab showed no significant association with the clinical results associated with omalizumab use.(6)

Children:

The ADAPT (Atopic Dermatitis Anti-IgE Paediatric Trial) trial evaluated the possible role of omalizumab in the management of severe paediatric AE with concomitant allergic disease (asthma, allergic rhinoconjuncitivitis or food allergies) for 24 weeks. The drug dose was determined by baseline total IgE (range: 30 to 1500 IU/ml), measured before the start of treatment, and body weight (kg) and calculated using the formula: 0.016 x weight (kg) x total IgE level (kU/l) in 2-4 weekly injections. The study showed that omalizumab significantly reduced disease severity and improve QoL in paediatric patients with severe AE and highly elevated IgE levels (median baseline total IgE of 8373 IU/L) compared with placebo.(4) However, this improvement was below the minimal clinically important difference for the main outcome (objective SCORAD).

Safety

There is a general consensus about the overall good safety profile of omalizumab with some controlled studies reporting excellent tolerability up to 4 years. A 2009 revision of data from controlled trials concluded that incidence of anaphylaxis was 0.14% in omalizumab-treated patients and 0.07% in control subjects. Of note, no serum-sickness attributable to the drug and no anti-omalizumab antibodies have been reported to date.(7)

There are no reported interactions of omalizumab with other medications used for AE or other allergic diseases. If clinically needed, omalizumab may be considered during pregnancy. More attention has been put over the appearance of gut parasite infections in treated patients, since IgE is an important player in the host defence against parasitic helminths. A randomized placebo-controlled trial in 137 adult subjects with respiratory allergy at high risk of helminth infection showed a modest increase of the incidence of parasitism in the active group.(8)

Monitoring

No biochemicals or instrumental exams are reported to be required for the monitoring of the therapy. IgE levels increase following administration of omalizumab and may remain elevated for up to 1 year following discontinuation of the drug.

References

1. Wollenberg A, Thomsen SF, Lacour J-P, Jaumont X, Lazarewicz S. Targeting immunoglobulin E in atopic dermatitis: A review of the existing evidence. World Allergy Organization Journal. 2021;14(3):100519.
2. Metz M, Maurer M. Omalizumab in chronic urticaria. Curr Opin Allergy Clin Immunol. 2012;12(4):406-11.
3. Bieber T, de la Salle H, Wollenberg A, Hakimi J, Chizzonite R, Ring J, et al. Human epidermal Langerhans cells express the high affinity receptor for immunoglobulin E (Fc epsilon RI). J Exp Med. 1992;175(5):1285-90.
4. Chan S, Cornelius V, Cro S, Harper JI, Lack G. Treatment Effect of Omalizumab on Severe Pediatric Atopic Dermatitis: The ADAPT Randomized Clinical Trial. JAMA Pediatr. 2019;174(1):29-37.
5. Belloni B, Ziai M, Lim A, Lemercier B, Sbornik M, Weidinger S, et al. Low-dose anti-IgE therapy in patients with atopic eczema with high serum IgE levels. J Allergy Clin Immunol. 2007;120(5):1223-5.
6. Wang HH, Li YC, Huang YC. Efficacy of omalizumab in patients with atopic dermatitis: A systematic review and meta-analysis. J Allergy Clin Immunol. 2016;138(6):1719-22.e1.
7. Corren J, Casale TB, Lanier B, Buhl R, Holgate S, Jimenez P. Safety and tolerability of omalizumab. Clin Exp Allergy. 2009;39(6):788-97.
8. Cruz AA, Lima F, Sarinho E, Ayre G, Martin C, Fox H, et al. Safety of anti-immunoglobulin E therapy with omalizumab in allergic patients at risk of geohelminth infection. Clin Exp Allergy. 2007;37(2):197-207.