Omalizumab (OMA) has been approved by the Drug Controller General of India (DCGI) in 2013 for the treatment of urticaria. OMA, a humanized monoclonal antibody against the constant region of the immunoglobulin E (IgE) molecule, was launched almost two decades ago for the treatment of severe allergic asthma. Chronic spontaneous urticaria (CSU) affects 1% of the world population and also their quality of life. Most of the patients suffering from chronic urticaria have no etiologic diagnosis or are considered as idiopathic. They continue to take oral antihistamines for symptomatic relief of troublesome wheals over a long duration of time. However, about 50% of these patients are refractory to H1-antihistamines because of varied reasons, including tachyphylaxis. Apart from antihistamines, there has been no good drug to nullify the effects of histamine or drugs that would directly decrease levels of free IgE which mediates Type-I hypersensitivity or IgE-mediated hypersensitivity reactions such as urticaria. OMA was developed as a humanized monoclonal anti-IgE antibody that binds with free IgE antibodies and reduces the circulating levels of free IgE. It does not bind to FcεRI receptors or receptor-bound IgE. OMA has been reported to work in solar urticaria, cold urticaria, and dermographism.[1]

OMALIZUMAB IN CHRONIC URTICARIA: DOSAGES AND INDICATIONS
The first-line therapy of CSU is non-sedating antihistamine, while the second-line therapy has now been revised to updosing of the same. OMA is a third-line therapy if updosing of antihistamines has failed to control urticaria.[2] OMA dose can be adjusted with increasing interval between doses or by decreasing dose, thus saving cost.

The recommended dose of OMA is 300 mg, 4 weekly in the management of CSU refractory to standard of care with H1-antihistamines in adults and adolescents ≥12 years of age. There have been reports of low-dose OMA with variable success rates. One-third of the patients may respond to 150 mg dose and a few may need >300 mg dose in real-life setting. In my experience, a fewer number of patients may need combination of cyclosporine and OMA for the control of urticaria.

In some patients, when OMA therapy was discontinued in patients of CSU due to various reasons and when it was restarted after some time, it was observed by Metz et al. that such retreatment with OMA was successful. This adds to the evidence that OMA can be restarted offering same efficacy. This could be because of less chances of neutralizing anti-OMA antibodies.[3]

OMALIZUMAB AND SERUM IMMUNOGLOBULIN E LEVELS
OMA binds to the constant region of the IgE molecule, inhibiting it from binding to its receptor, FcεRI. As a result, total IgE levels in the peripheral blood rise, but free IgE is reduced to very low levels. There has been a good correlation between baseline levels of serum IgE and response to OMA. This is predictable as OMA is an anti-IgE monoclonal antibody. Two studies found that low baseline IgE (<43 UI/mL) was associated with a poor response, while the complete responders had the highest serum baseline IgE values.[4,5]

FAST AND SLOW RESPONDERS
Patients with CSU respond differently to OMA. Among people with CSU, the clinical presentation might be indistinguishable, but the response to OMA can be fast (<1 week) or slower (1 week–3 months) or even very slow (12–24 weeks).[6] Basophil histamine release assay and in vivo autologous serum skin test correlate with slow responders, due to higher levels of autoantibodies. Autoimmune urticaria shows slow response to OMA. Angiotensin-converting enzyme inhibitors given along with OMA could interfere with its effect and efficacy.

OMALIZUMAB AND CURE OF URTICARIA
When a biological like OMA was introduced for chronic urticaria, it was looked upon with great hope, especially for patients suffering for trouble chronic urticaria. It needs to be remembered that like other biologicals, OMA cannot cure disease as it will only deplete allergen-specific serum IgE available for binding to FcεRI receptors on the mast cells releasing histamine responsible for urticarial reaction. OMA can reduce disease severity in patients who are taking antihistamines for a very long period of time or those who are not responding to even higher dosages of antihistamines. For such patients, OMA therapy offers better quality of life. However, each injection effect can last up to maximum 6–12 weeks and not more. Symptoms of urticaria come back rapidly in those who discontinue treatment, and it is dependent on initial urticarial activity score and early treatment response.[7]

OMA does not lose its effectiveness over time. There are no reports of antidrug antibodies demonstrated so far.

SAFETY PROFILE OF OMALIZUMAB
OMA has recently been assigned pregnancy category B risk status by the Food and Drug Administration.[8] Although not approved, OMA is considered a safe and effective therapy for those pregnant females not responding to antihistamines.

Side effect profile of OMA is good with only a few reports of hair loss, angioedema, and late-onset anaphylaxis. OMA...
is advised to be taken in the hospital setting and keep patient under observation for 2–4 h. As this a humanized monoclonal antibodies, allergenicity or chances of formation of antibodies against the OMA molecule is less. It contains only 5% of nonhuman (murine) amino acid residues.[9] OMA has good safety profile in clinical studies and in postmarketing studies. In a large Phase-III studies by Maurer et al. and Kaplan et al., there were little differences in side effects between placebo and OMA group. In my clinical practice, I have not observed any significant side effects with OMA therapy.[10,11]

In the coming years, it is expected that more data will be published about use of omalizumab in the treatment of chronic urticaria.

Kiran Godse
Department of Dermatology, DY Patil University School of Medicine, Navi Mumbai, Maharashtra, India

Address for correspondence:
Prof. Kiran Godse,
Shree Skin Centre and Pathology Laboratory, 21/22, L Market, Sector 8, Nerul West, Navi Mumbai - 400 706, Maharashtra, India.
E-mail: drgodse@hotmail.com

REFERENCES

1. Snast I, Kremer N, Lapidoth M, Enk CD, Tal Y, Rosman Y, et al. Omalizumab for the treatment of solar urticaria: Case series and systematic review of the literature. J Allergy Clin Immunol Pract 2018; pii: S2213-2198(18)30132-6.

2. Godse K, De A, Zawar V, Shah B, Girdhar M, Rajagopalan M, et al. Consensus statement for the diagnosis and treatment of urticaria: A 2017 update. Indian J Dermatol 2018;63:2-15.

3. Metz M, Ohanyan T, Church MK, Maurer M, Rajagopalan M, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. N Engl J Med 2013;368:924-35.

4. Ertas R, Ozurt K, Atasoy M, Hawro T, Maurer M. The clinical response to omalizumab in chronic spontaneous urticaria patients is linked to and predicted by IgE levels and their change. Allergy 2018;73:705-12.

5. Casale TB, Win PH, Bernstein JA, Rosén K, Holden M, Iqbal A, et al. Omalizumab response in patients with chronic idiopathic urticaria: Insights from the XTEND-CIU study. J Am Acad Dermatol 2018;78:793-5.

6. Ferrer M, Gimenez-Arnau A, Saldana D, Janssens N, Balp MM, Khalil S, et al. Predicting chronic spontaneous urticaria symptom return after omalizumab treatment discontinuation: Exploratory analysis. J Allergy Clin Immunol Pract 2018; pii: S2213-2198(18)30273-3.

7. Fda U. (Omalizumab): Safety Information 2015; 2015. Available from: http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/103976s5224lbl.pdf. [Last accessed on 2018 Jul 03].

8. Belliveau PP. Omalizumab: A monoclonal anti-IgE antibody. MedGenMed 2005;7:27.

9. Maurer M, Rosén K, Hsieh HJ, Saini S, Grattan C, Gimenez-Arnau A, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. J Allergy Clin Immunol Pract 2018. pii: S2213-2198(18)30273-3.

10. Maurer M, Rosén K, Hsieh HJ, Saini S, Grattan C, Gimenez-Arnau A, et al. Omalizumab in patients with symptomatic chronic idiopathic/spontaneous urticaria despite standard combination therapy. J Allergy Clin Immunol 2013;132:101-9.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.