Omalizumab: now licensed as adjunct for urticaria

Steve Chaplin BPharm, MSc and **Clive Grattan** MA, MD, FRCP

Omalizumab (Xolair), which was originally licensed for IgE-mediated asthma, is now indicated as adjunctive therapy for chronic spontaneous urticaria. In our New products review, Steve Chaplin presents the data relating to its efficacy and adverse events, and Dr Clive Grattan discusses its place in therapy.

KEY POINTS

- omalizumab (Xolair) is an anti-IgE monoclonal antibody
- originally licensed as add-on therapy in severe persistant allergic asthma, it is now licensed as adjunctive treatment of refractory chronic spontaneous urticaria
- administered by subcutaneous injection, the recommended dose is 300mg once every four weeks; a month's treatment costs £512.30
- during 12 weeks' treatment it significantly reduced itch, reduced the number of weals and days with angioedema and improved quality-of-life scores in antihistamine-unresponsive patients
- adverse effects were similar to those occurring with placebo

European guidelines on the management of chronic spontaneous urticaria (CSU) recommend first-line treatment with newer nonsedating H_1-antihistamines, increasing the standard dose up to four-fold if required.[1] Second-line therapies include a leukotriene receptor antagonist (LRTA) or a triple regimen of an H_1- and H_2-antihistamine and an LTRA. Steroids are not recommended for long-term use due to their adverse effects. Current options when these drugs are unsuccessful include immunosuppressants such as methotrexate, sulfasalazine and ciclosporin, or dapsone.

Omalizumab

Omalizumab (Xolair) is a humanised monoclonal antibody that selectively binds to human immunoglobulin E (IgE). It was originally licensed as add-on therapy to improve asthma control in patients with severe persistent allergic asthma. It is now also licensed as add-on therapy for the treatment of CSU in adults and children aged at least 12 for whom treatment with an H_1 antihistamine is inadequate.

The recommended dose is 300mg by subcutaneous injection every four weeks. There is limited experience of treatment beyond six months' duration. No dose adjustment is recommended for elderly patients or those with impaired renal or hepatic function. There is no evidence of clinically significant drug interactions.

Clinical trials

The efficacy of omalizumab as adjunctive therapy of CSU has been evaluated in three placebo-controlled phase 3 trials,[2] of which two are published in full.[3,4] Two included multiple doses (n=79 and 81 at 300mg). One trial was primarily a safety study but included efficacy as a secondary end-point (n=252).[2]

All patients had CSU despite treatment with an H_1-antihistamine; in the safety study, CSU was additionally refractory to an H_2-antihistamine and/or a LRTA. Trial duration was 12 or 24 weeks, with 16 weeks follow-up. The primary end-point was the change in weekly itch score from baseline to 12 weeks.

In each study, omalizumab significantly reduced the itch score compared with placebo at 12 weeks, with a median time to response of about one

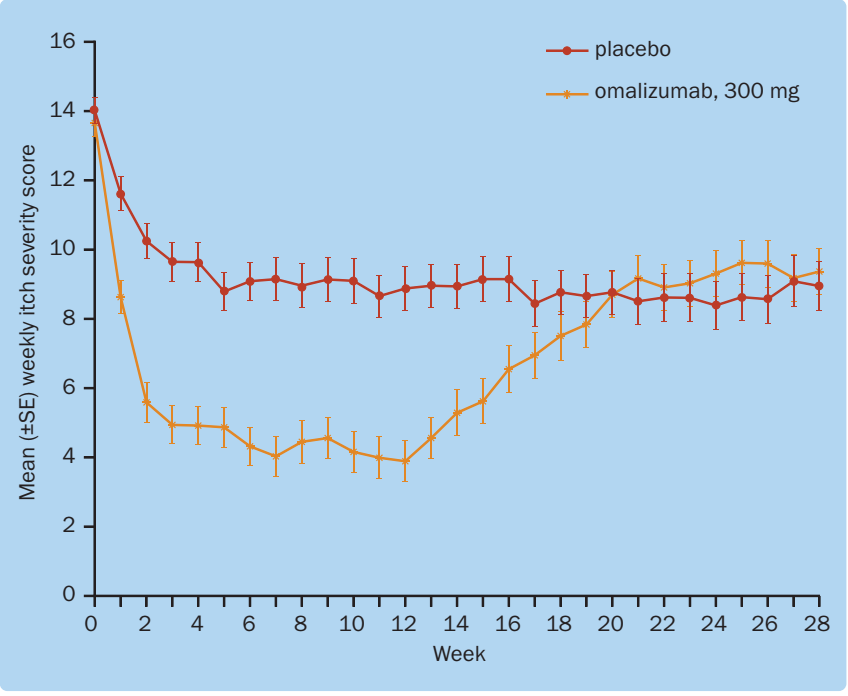

Figure 1. Itch severity score during and after adjunctive treatment with omalizumab and placebo – patients received doses at 0, 4 and 8 weeks, followed by a 16-week observation period; after reference 4

week. The proportion of patients with a minimum improvement in itch score of 5 points was 36–48 per cent with placebo and 70–79 per cent with omalizumab 300mg (the mean score at baseline was approximately 14). This was supported by reductions in the number of hives, more days free of angioedema and improvement in quality-of-life scores.

Efficacy was maintained with no evidence of tolerance during six months' treatment. After the final dose, the itch score remained low for one month then increased over a three-month period (see Figure 1).[4]

Adverse effects

Common adverse events in clinical trials included nasopharyngitis, headache, sinusitis, arthralgia, upper respiratory tract infection and cough, occurring with similar frequencies for both omalizumab and placebo.

References

1. Zuberbier T, *et al. Allergy* 2009;64:1427–43.
2. European Medicines Agency. *Xolair Assessment Report*. January 2013. www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Assessment_Report_-_Variation/human/000606/WC500164453.pdf.
3. Kaplan A, *et al. J Allergy Clin Immunol* 2013;132:101–9.
4. Maurer M, *et al. N Engl J Med* 2013;368:924–35.

Declaration of interests

Steve Chaplin has none to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics

Place in therapy

CSU is a relatively common condition lasting at least six weeks and sometimes years. It is characterised by itchy weals, angioedema or both. Patients are often very distressed by the itch that disturbs sleep when symptoms develop at night, resulting in underperformance the next day. They have to cope with the unsightly physical appearance of weals anywhere on the body with or without swelling of the face. Severely affected patients often experience additional symptoms including fatigue, lack of concentration, aching and hyperacidity. In short, the illness can have a substantial affect on quality of life.

The only licensed treatment of CSU is H_1-antihistamines. These may be very helpful in mild to moderate disease, reducing the itch and number of weals, but at licensed doses are only fully effective for about 40 per cent of patients.

Recent evidence supports up-dosing second-generation (nonsedating) antihistamines but around 30 per cent of patients still remain symptomatic despite off-label dosing up to four-fold.

As such, there is a clear need for better treatments in this subgroup of patients with antihistamine-unresponsive urticaria. A number of drugs are used off-licence to address this need with some success, though adverse effects may be dose-limiting and experience shows that some patients remain refractory to currently available therapies including immunosuppressives and oral corticosteroids.

It is therefore very encouraging that phase 3 studies of omalizumab have demonstrated a convincing benefit on itch and weal numbers for patients with antihistamine-unresponsive CSU, resulting in complete symptom control in some and a proportionate improvement in quality of life.

Declaration of interests

Dr Grattan has consultancies with Novartis and has been on an advisory board for Genentech.

Dr Clive Grattan is consultant dermatologist at Norfolk and Norwich University Hospital, Norwich, and St John's Institute of Dermatology, London