

BRIEF COMMUNICATIONS

The use of omalizumab for treatment-refractory chronic spontaneous urticaria in a West Australian outpatient cohort

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omalizumab, chronic spontaneous urticaria, treatment, safety, treatment-refractory.

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Chronic spontaneous urticaria (CSU) is defined as daily pruritic hives and/or angioedema for 6 weeks or more, without an identifiable trigger. The disease may be self-limiting; however, in some cases, symptoms persist for years with a profound impact on patients' quality of life.¹ Treatments for CSU include antihistamines, leukotriene receptor antagonists and immunosuppressive drugs such as prednisolone and cyclosporin. Omalizumab is a recombinant humanised anti-IgE monoclonal antibody that targets the Fc region of IgE, reducing levels of free IgE.¹ Omalizumab was listed on the Pharmaceutical Benefits Scheme for the management of CSU in September of 2017. As a result, omalizumab will be more frequently prescribed by allergists and dermatologists, with general practitioners involved in administering injections in the community under specialist direction.

There is high-quality evidence from randomised controlled trials that omalizumab is a safe and effective treatment for CSU in patients who remain symptomatic despite treatment with high-dose antihistamines and leukotriene receptor antagonists.^{2–5} Recently published global guidelines recommend initiating treatment with omalizumab in patients with CSU unresponsive to dose-escalated second-generation H₁-antihistamines.⁶ Omalizumab carries a 'black box warning' regarding the risk of anaphylaxis, with an estimated frequency of 0.2%.⁷ Recent data suggest that the risk of anaphylaxis is lower among patients with CSU receiving omalizumab.⁸

Abstract

There is a lack of real-world data on the use of omalizumab in treatment-refractory chronic spontaneous urticaria (CSU). A single-centre retrospective cohort study was performed to assess the efficacy and safety of omalizumab for treatment-refractory CSU. The overall response rate of 67% is comparable with that reported in the literature. Disease control and sustained remission can be achieved with omalizumab, even in patients with treatment-resistant CSU.

There is a paucity of real-world and Australasian data addressing the efficacy of omalizumab for patients with CSU refractory to multiple lines of therapy. We therefore aimed to investigate the real-world efficacy and safety of omalizumab for treatment-refractory CSU in a West Australian outpatient cohort.

A retrospective cohort study was performed by the Immunology Department at Sir Charles Gairdner Hospital (SCGH). The study was approved by Safety, Quality & Performance at SCGH, an institutional ethics committee. The SCGH outpatient pharmacy database was used to identify all patients dispensed omalizumab for CSU. Data collected from medical records included patient demographics, duration of CSU, previous treatment received and response to treatment with omalizumab. Clinical response was defined as an improvement in disease activity, measured by the Urticaria Activity Score 7 (UAS7)⁹ or recorded qualitatively in clinical records. Disease control was defined as an ongoing clinical response during or after treatment with omalizumab. Relapse was defined as an increase in disease activity following cessation of omalizumab, indicated by either an increase in UAS7 score (≥ 16) or entry in the medical record. Sustained remission was defined as the absence of CSU symptoms (UAS7 score of 0 or clinical documentation) for >30 days after omalizumab treatment, with no concurrent use of other CSU medications including antihistamines.

Eighteen patients were prescribed omalizumab for the treatment of CSU either via the SCGH Drug and Therapeutics Committee or authorised via the WA Drug Evaluation Panel between October 2012 and September

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2017. Patient age ranged from 20 to 77 years, and 17 (94%) patients were female. About 11 (61%) of 18 patients had a history of at least one autoimmune or allergic condition. Disease duration ranged from 1 year to 45 years (median 7.5 years). Before omalizumab, patients had trialled an average of 5.2 drugs for CSU management. Before initiating omalizumab, 14 (78%) patients had required prednisolone, and all 18 (100%) patients had been previously treated with cyclosporin.

Clinical outcomes are summarised in Figure 1. Clinical improvement following an initial course of omalizumab 300 mg every 4 weeks (median duration 6 months) occurred in 12 (67%) of 18 patients. Following cessation, six patients (50% of initial responders) experienced a relapse of symptoms at an average of 63 days after the last dose of omalizumab (range 42 to 91 days). On re-initiation of omalizumab, all six patients had clinical improvement of symptoms. Three patients (25% of responders) experienced a sustained remission of CSU symptoms after completion of omalizumab therapy, and required no further treatment for CSU (duration of remission 5–18 months at time of study completion).

Seven patients (58% of responders) had sustained disease control at the end of the follow-up period with ongoing omalizumab treatment. Of these patients, five out of seven maintained disease control with an extended interval between doses (median dosing interval 8 weeks).

Four patients (22% of all patients) did not respond to omalizumab. Six patients reported side-effects of the treatment, with the most commonly reported side-effects including fatigue (four patients), headache (two patients) and injection site pain (two patients). Two patients ceased omalizumab due to side-effects. One patient ceased treatment secondary to headache, visual disturbance, malaise and rash, and the other patient ceased treatment secondary to headache, nausea and fatigue. No episodes of anaphylaxis occurred during 186 administered doses of omalizumab.

Discussion

This study confirms the safety and efficacy of omalizumab in real-world conditions. The patients captured in

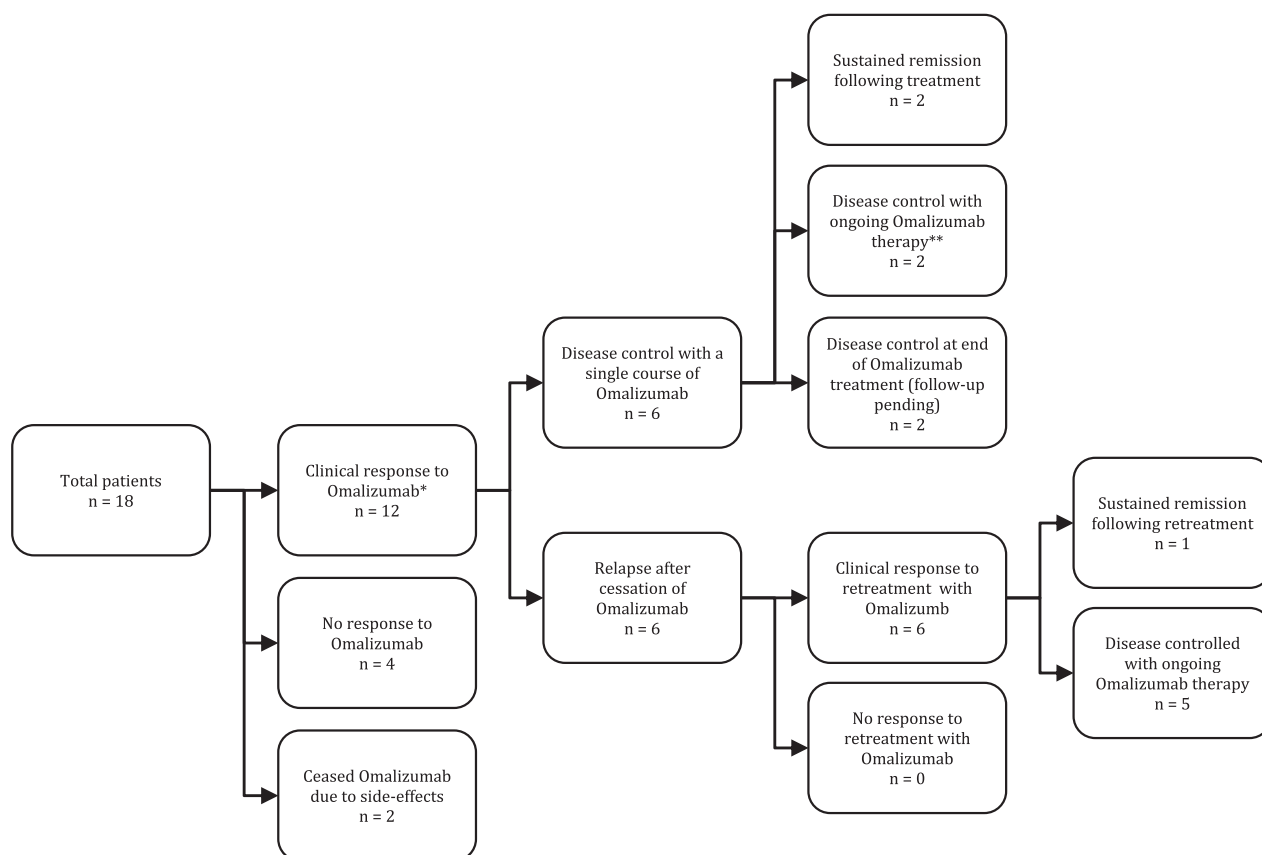


Figure 1 Clinical outcomes in the patient cohort. *Omalizumab 300 mg every 4 weeks, median duration 6 months. **Without a trial of omalizumab cessation.

this study had a long history of CSU and had failed multiple previous lines of therapy. Despite this, omalizumab induced disease control and/or sustained remission for most patients. The overall response rate of 67% is comparable with that reported in the literature. The pivotal phase III trials ASTERIA I, ASTERIA II and GLACIAL reported response rates of 51.9, 53 and 52.4% respectively. Of note, in ASTERIA I and II, patients only trialled

approved doses of H₁-antihistamines before commencing omalizumab.^{2–4} In comparison, our patients had trialled an average of 5.2 drugs before omalizumab and all received previous treatment with cyclosporin. In conclusion, while this study is of modest size, it has demonstrated that disease control and sustained remission can be achieved with omalizumab in patients with treatment-refractory CSU.

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