



INTRODUCTION

Anti-IgE: changing lives in clinical practice?

S.T. Holgate

As physicians, we frequently encounter patients with severe persistent asthma who remain symptomatic despite receiving the best available treatment and optimal management efforts. If we are unable to achieve adequate asthma control despite using all available therapeutic options, these patients remain exposed to a high risk of serious exacerbations and asthma-related mortality. Addressing the unmet medical needs of this difficult-to-treat population is one of the greatest challenges in asthma management.

Asthma frequently has an allergic component. Immunoglobulin (Ig)E is central to the pathogenesis of allergic asthma and presents an ideal target for novel therapeutic agents. Omalizumab, the first anti-IgE treatment, suppresses IgE-mediated allergic/inflammatory reactions by binding to free IgE. In clinical studies, add-on omalizumab significantly reduced asthma exacerbation rates and the need for emergency medical interventions, and improved quality of life, in patients with severe persistent allergic asthma who were symptomatic despite taking regular high-dose inhaled corticosteroids and long-acting β_2 -adrenoceptor agonists.

I had great pleasure in chairing a Novartis-sponsored satellite symposium entitled “Anti-IgE: changing lives in clinical practice?” at the 16th Annual European Respiratory Society Congress (2006) held in Munich, Germany. The symposium provided an opportunity to bring together a distinguished faculty of experts in the field to discuss the role of anti-IgE therapy in addressing the unmet needs of patients with severe and poorly controlled asthma. In the symposium, we discussed the central role of IgE in the allergic/inflammatory cascade, the rationale for anti-IgE therapy, and the latest evidence regarding the efficacy and safety of omalizumab when used to treat inadequately controlled severe persistent allergic asthma. The important issues of patient selection and evaluation of treatment response to omalizumab were also covered. The proceedings of this important and timely symposium are reported in the present issue of the *European Respiratory Review*.

In the first paper of the present issue, HAMELMANN [1] provides an overview of the central role of IgE in the allergic asthma inflammatory cascade and the mechanism of action of omalizumab. By reducing serum IgE levels and high-affinity IgE receptor (Fc ϵ RI) expression on key cells in the inflammatory cascade, omalizumab blocks the release of inflammatory mediators from mast cells and reduces the subsequent infiltration of inflammatory cells, most notably eosinophils, into the airway. HAMELMANN [1] concludes that “the anti-inflammatory effects of omalizumab provide proof-of-concept of the key role played by IgE in allergic respiratory disease” and that “omalizumab represents a novel approach to the treatment of asthma, inhibiting the inflammatory cascade before it starts.”

PARTRIDGE [2] highlights the scale and impact of severe asthma and the need for careful diagnosis. The unmet needs in patients with severe asthma are illustrated by the findings of the Asthma Insights and Reality in Europe (AIRE) study [3], the Fighting for Breath survey [4], the International Asthma Patient Insight Research (INSPIRE) study [5] and the Gaining Optimal Asthma Control (GOAL) study [6]. PARTRIDGE [2] concludes that “despite treatment with currently available therapy, there remains a patient group who have ongoing morbidity, require significant use of health services and are at risk of severe exacerbations” and that “omalizumab may help address the clear and unmet need for an effective and safe treatment of patients with severe persistent allergic asthma who remain symptomatic despite optimised standard treatment.”

BUHL [7] reviews the efficacy and safety of omalizumab in clinical trials. Particular focus is given to the Investigation of Omalizumab in Severe Asthma Treatment (INNOVATE) study [8], which enrolled patients with inadequately controlled severe persistent allergic asthma despite high-dose inhaled corticosteroids (ICS) in combination with a long-acting β_2 -agonist (LABA) and additional controller medication if required. In the INNOVATE study, add-on omalizumab significantly reduced clinically significant exacerbation rates by 26% (0.68 *versus*

CORRESPONDENCE

S.T. Holgate
Southampton General Hospital
RCMB Division
Mailpoint 810
Level D
Centre Block
Southampton SO16 6YD
UK
Fax: 44 2380701771
E-mail: sth@soton.ac.uk

STATEMENT OF INTEREST

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0.91; $p=0.042$), severe exacerbation rates by 50% (0.24 *versus* 0.48; $p=0.002$) and emergency visit rate by 44% (0.24 *versus* 0.43; $p=0.038$) and significantly improved asthma-related quality of life ($p<0.001$), compared with placebo [8]. As patients enrolled in the INNOVATE study are the asthma patients with the greatest unmet need, these data are of great clinical importance and are highly encouraging. The results of the INNOVATE study are supported by pooled efficacy analyses [9, 10] and a good safety and tolerability profile [11]. BUHL [7] concludes that "omalizumab addresses an unmet medical need in patients with severe persistent allergic asthma whose symptoms persist despite receiving high-dose ICS and LABA, allowing these patients to live beyond the limitations of their asthma."

In my article [12], evidence showing that there is no reliable way to predict which patients will achieve a greater response to omalizumab is presented [13]. Physicians can easily and reliably identify patients who respond to omalizumab [13]; all patients eligible for omalizumab treatment should receive a 16-week trial and treatment, which is to be continued only if the physician judges that a marked improvement in asthma control has been achieved, as specified in the European Union (EU) label. As I point out, identifying responders, and continuing treatment only in these patients, minimises unwarranted drug exposure, whilst treatment benefit and cost-effectiveness of therapy are maximised.

In the final paper of the present issue, BEEH [14] provides specific details on the indication and clinical use of omalizumab. It is important to recognise that the indication for omalizumab varies in different countries. In the EU, omalizumab is indicated as add-on therapy to improve asthma control in adult and adolescent patients (≥ 12 yrs of age) with severe persistent allergic (total IgE 30–700 IU·mL⁻¹) asthma who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen, and who despite receiving daily high-dose ICS and a LABA have the following characteristics: reduced lung function (forced expiratory volume in one second $<80\%$); frequent daytime symptoms or night-time awakenings; and multiple documented severe asthma exacerbations. Patients who receive omalizumab should be assessed by their physician after 16 weeks and treatment continued only if there has been a marked improvement in asthma control. Omalizumab is administered by subcutaneous injection every 2 or 4 weeks at a dosage determined using a dosing table based on the patient's pre-treatment serum total IgE levels and body weight.

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