

Clinical
&
Experimental
Allergy

A next-generation anti-IgE monoclonal?

G. Roberts^{1,2,3}¹Clinical and Experimental Sciences and Human Development and Health, Faculty of Medicine, University of Southampton, Southampton, UK, ²NIHR Southampton Respiratory Biomedical Research Unit, University Hospital Southampton NHS Foundation Trust, Southampton, UK and ³The David Hide Asthma and Allergy Research Centre, St Mary's Hospital, Isle of Wight, UK

Back in 2014, a paper published in *Clinical and Experimental Allergy* reported that QGE031 suppressed free IgE, basophil FcεRI, surface IgE and skin prick test responses to allergen in atopic volunteers [1]. QGE031 is a humanized IgG1 monoclonal antibody against human IgE. It has a higher affinity for IgE than omalizumab and so potentially may be more effective. The results of the first dose-ranging study in patients with mild asthma have now been published [2]. Thirty-seven patients were randomized to subcutaneous QGE031, omalizumab or placebo injections for 10 weeks using a double-blind, parallel-group design. Inhaled allergen challenges at weeks 6, 12 and 18 revealed that QGE031 therapy gave a dose- and time-dependent increase in the provocative concentration of allergen causing a 15% decrease in FEV₁ (allergen PC15). The maximum dose resulted in a threefold greater change than omalizumab; QGE031 was well tolerated by participants. So might we have a more effective next-generation anti-IgE monoclonal in the pipeline? Will it be useful in our patients with very



Mark Hew

high levels of total IgE? We need to await the later phase clinical studies to find out.

Carrying on this theme, in this issue of *Clinical and Experimental Allergy*, Hew *et al.* [3] have looked at how effective omalizumab is in patients with high levels of total IgE. They compared the response to therapy in patients within ($n = 124$) and outside ($n = 55$) the total IgE prescribing criteria. After 6 months of therapy, there were similar improvements in asthma control and quality of life in both groups (Fig. 1). So it seems that omalizumab is effective for patients with high levels of total IgE, although only a quarter of this group had a total IgE >1747 IU/mL.

We now consider the epithelium to be important in the pathophysiology of asthma [4] with human rhinovirus (HRV) being a key trigger of exacerbations [5]. In this issue, Kicic *et al.* [6] examine the relationship between innate immune responses to HRV infection in asthmatic and control paediatric airway epithelial cells (AECs). In their *ex vivo* system, they found that viral production and release was higher in the asthmatic AECs, while there was less apoptosis and production of IFN-β and other inflammatory cytokines. HRV infection also inhibited the ability of epithelial cells to repair, particularly in the asthmatic AECs. Exogenous IFN-β restored some of these activities (Fig. 2). So it looks like we have a plausible mechanism via which HRV causes exacerbations of asthma in children.



Anthony Kicic



Philippe Devillier

Correspondence:

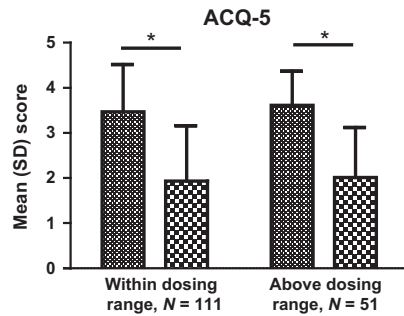
G. Roberts, Paediatric Allergy and Respiratory Medicine (MP803), Clinical & Experimental Sciences & Human Development in Health Academic Units, University of Southampton, Faculty of Medicine & University Hospital Southampton, Southampton SO17 1BJ, UK.

E-mail: g.c.roberts@soton.ac.uk

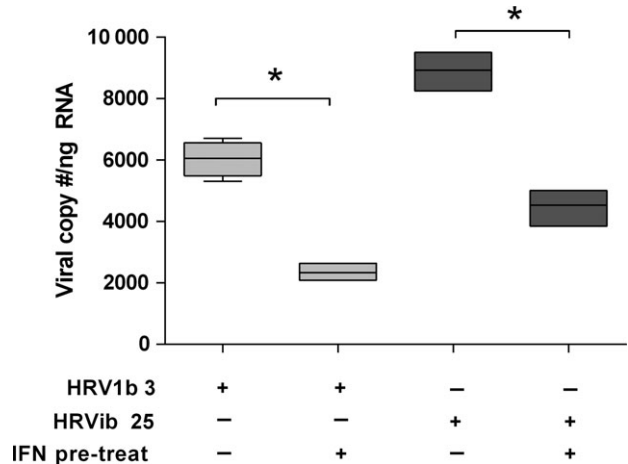
Cite this as: G. Roberts, *Clinical & Experimental Allergy*, 2016 (46) 1370–1371.

Caption to cover illustration: Multifaceted functions of IgA in mucosa. [See figure 1 in F. M. Carlier *et al.* (pp. 1372–1388).]

EB This logo highlights the Editor-in-Chief Editorial articles on the cover and the first page of each of the articles.



It has been said that hayfever is just a running nose, but our patients would say otherwise. Devillier *et al.* [7] have assessed over 500 teenagers and adults with grass pollen-driven allergic rhinoconjunctivitis using the Work Productivity and Activity Impairment Questionnaire plus Classroom Impairment Questions: Allergy Specific (WPAI-AS). The WPAI-AS only moderately correlated with the Rhinoconjunctivitis Quality of Life Questionnaire score, with lower correlations with the Rhinoconjunctivitis Total Symptom Score and a visual analogue scale. So measures of quality of life and symptoms do not adequately capture issues around school and work. This is important as many clinicians use quality-of-life tools



to make decisions around the need for immunotherapy. We might need to use additional assessments.

Lastly, please remember to complete the *Clinical and Experimental Allergy* readers' survey. This is open until the end of October 2016 and can be accessed at <http://bit.ly/ceasurvey>. We would encourage all our readers to complete the survey and help us improve your *Journal*.

References

- 1 Arm JP, Bottoli I, Skerjanec A *et al.* Pharmacokinetics, pharmacodynamics and safety of QGE031 (ligelizumab), a novel high-affinity anti-IgE antibody in atopic subjects. *Clin Exp Allergy* 2014; **44**:1371–85.
- 2 Gauvreau GM, Arm JP, Boulet L-P *et al.* Efficacy and safety of multiple doses of QGE031 (ligelizumab) versus omalizumab and placebo in inhibiting allergen-induced early asthmatic responses. *J Allergy Clin Immunol* 2016; **138**:1051–9.
- 3 Hew M, Gillman A, Sutherland M *et al.* Real-life effectiveness of omalizumab in severe allergic asthma above the recommended dosing range criteria. *Clin Exp Allergy* 2016; **46**:1407–15.
- 4 Loxham M, Davies DE, Blume C. Epithelial function and dysfunction in asthma. *Clin Exp Allergy* 2014; **44**:1365–2222.
- 5 Gern JE. How rhinovirus infections cause exacerbations of asthma. *Clin Exp Allergy* 2015; **45**:1365–2222.
- 6 Kicic A, Stevens PT, Sutanto EN *et al.* Impaired airway epithelial cell responses from children with asthma to rhinoviral infection. *Clin Exp Allergy* 2016; **46**:1441–55.
- 7 Devillier P, Bousquet J, Salvator H *et al.* In allergic rhinitis, work, classroom and activity impairments are weakly related to other outcome measures. *Clin Exp Allergy* 2016; **46**:1456–64.