

Correspondence

Eosinophil count and efficacy of omalizumab treatment

To the Editor:

I read with interest the article by Busse et al¹ assessing the effect of omalizumab in a group of asthmatic patients in relation to their eosinophil counts. In their well-performed study they found that the primary end point (a decrease in asthma exacerbations) was not met. In the subgroup analysis, according to the eosinophil count (low, <300 cells/mL; high, >300 cells/mL), they were able to demonstrate efficacy in patients within the high-count group.

It is intriguing that the primary end point was not achieved despite omalizumab being a proved therapy for allergic asthma.^{2,3} To understand this paradox, it is necessary to take a closer look at this study. First, they chose patients who, despite being symptomatic, had normal lung function (FEV₁ >80%). Second, prior use of systemic corticosteroids (oral or intravenous), a classic sign of severity, was an exclusion and not an inclusion criteria.

Finally, after carefully reading the article and the additional information in the article's Online Repository, I did not find any reference about the allergens to which these patients were allergic. Defining asthma as atopic based only on the serum total IgE level (30-1300 IU/mL), as apparently was done, is certainly not enough.

The authors should clarify this last point and, if they have this information, plot it against the eosinophil level. It would probably show that (as expected) patients with positive results to allergen did much better than patients with negative results to allergen and had the highest eosinophil counts.

Once again, this study also shows that those who derive the most benefit from omalizumab have atopic asthma that is symptomatic despite optimal treatment, are in need of frequent steroid bouts, and have abnormal lung function test results.

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Disclosure of potential conflict of interest: J. Panasoff declares that he has no relevant conflicts of interest.

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Reply

To the Editor:

We would like to thank Dr Panasoff¹ for his comment on our report² of the EXACT trial (NCT00096954) of omalizumab, which studied patients with atopic asthma with preserved pulmonary function who remained symptomatic on inhaled

corticosteroids with or without other controller medications. To clarify, this study was done as a postmarketing commitment from the US Food and Drug Administration in which we were to evaluate patients with atopic asthma and normal lung function. Atopic asthma was not determined solely based on serum IgE levels; patients also had to have positive skin test responses or *in vitro* (RAST or ImmunoCAP) test responses to 1 relevant perennial aeroallergen, such as cat or house dust mite. The exclusion of prior use of systemic corticosteroids (oral or intravenous) was only if it had been in close proximity to the screening visit because this would indicate that the patient had a recent asthma exacerbation that could affect his or her lung function. The time restriction would also allow systemic steroids to have cleared from the patients' bodies so there would be no effect on baseline scores. Dr Panasoff was correct in noting that despite its proved efficacy in patients with allergic asthma, the study did not show a significant difference for omalizumab versus placebo in rate of exacerbations and that this might have been in part due to the patient population enrolled in the study. Reasons for poorly controlled asthma in the studied population might include poor compliance with therapy, improper use of inhaled medication, or chronic exposure to a potent antigen or the patients might be smokers. Omalizumab, by virtue of being administered every 2 or 4 weeks in the physician's office, might improve compliance. However, we believe that given the highly limiting patient eligibility for enrollment, the study was underpowered to demonstrate a statistically significant treatment effect in the primary end point. Because all patients in the study had positive results to allergen, we have not addressed Dr Panasoff's request to plot eosinophil levels against allergen-positive/allergen-negative status. We do appreciate his thorough review and the opportunity to provide a more in-depth explanation of the eligibility criteria and their effect on study outcome.

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Disclosure of potential conflict of interest: K. Rosén is employed by Roche and receives stock/stock options as part of her compensation. W. Busse receives compensation as a board member for Merck; has consultant arrangements with Novartis, GlaxoSmithKline, Genentech, Boston Scientific, and ICON; has received research support from the National Institutes of Health/National Institute of Allergy and Infectious Disease and the National Institutes of Health/National Heart, Lung, and Blood Institute; and receives royalties from Elsevier.

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1. Panasoff J. Eosinophil count and efficacy of omalizumab treatment. *J Allergy Clin Immunol* 2014;133:1231.
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Exhaled breath condensate eicosanoid levels in asthma: Still questioned

To the Editor:

We read with great interest the article by Kazani et al¹ who compared the levels of eicosanoid in exhaled breath condensate