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Raymond G. Slavin & Pablo Jimenez

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LETTER TO THE EDITOR

Reduction of the Total IgE Level by Omalizumab in Children and Adolescents

RAYMOND G. SLAVIN,[1,*] AND PABLO JIMENEZ[2]

[1]*Saint Louis University School of Medicine, Saint Louis, Missouri, United States*
[2]*Novartis Pharmaceuticals Inc, East Hanover, New Jersey, USA*

To the Editor:

In a recent article in the *Journal of Asthma*, Steiß et al. report findings from a study of omalizumab in nine patients with severe allergic asthma (1). Consistent with previous large-scale, randomized, controlled trials, Steiß et al. note that omalizumab was well tolerated and associated with clinical improvements (reduction in systemic corticosteroids and exacerbations and improvement in quality of life) in patients with severe asthma. However, their finding that total immunoglobulin (IgE) concentration decreased during omalizumab therapy (evaluated after 6 months in the majority of patients) contrasts with previous studies. The apparent inconsistency between the findings reported by Steiß et al. and those documented in previous studies requires some clarification and comment.

Several randomized, double-blind, placebo-controlled trials have shown that omalizumab suppresses free IgE (2-6), while total IgE (free and omalizumab-bound IgE) increases during treatment and returns towards baseline after discontinuation of therapy (3-5, Novartis, data on file). Concentrations of omalizumab and free IgE have been shown to correlate well with changes in clinical outcomes, based on a pharmacokinetic and pharmacodynamic model (7). The increase in total IgE and decline in free IgE is a consequence of the formation of small complexes of omalizumab and IgE, which are cleared relatively slowly compared with free IgE. Consequently, administration of omalizumab results in an increase in total IgE on standard assays that quantify both free and omalizumab-bound IgE.

Steiß et al. state that the ADVIA Centaur-specific IgE assay that they used apparently binds to the same epitope as omalizumab. If this is the case, it would not measure omalizumab-bound IgE and in effect provides an approximation of free IgE. The association between "total IgE" and improved clinical outcomes reported by Steiß et al. therefore, may have some similarity to the previously documented association between free IgE and clinical outcomes. However, the ADVIA Centaur-specific IgE assay has not been demonstrated to be robust and reproducible in the presence of omalizumab. As the assay relies on two independent antibodies binding to IgE, it is possible that the presence of omalizumab would affect the outcome.

Administration of appropriate omalizumab doses, determined using the dosing table, appears to adequately suppress free IgE below the target 50 ng/mL (7). Suppression of free IgE has also been documented in those who do not respond to omalizumab (7), but as this does not correlate with symptoms, this would suggest that IgE is not driving asthma in these cases. Reducing omalizumab doses below those specified in the dosing table is not recommended as the resulting increase in free IgE causes deterioration of asthma control (7).

To date, there is no evidence supporting the monitoring of IgE levels during omalizumab therapy. We therefore recommend that patients continue to receive omalizumab at doses determined based on baseline total IgE and body weight using the dosing table. As noted in the current dosing instructions, dose adjustments may be required if there is a significant change to the patient's bodyweight. In this case, pre-treatment IgE and the new bodyweight should be used to recalculate the dose.

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*Corresponding author: Raymond G. Slavin, M.D., Saint Louis University School of Medicine, 1402 S. Grand, St. Louis, MO 63104; USA; E-mail: slavinrg@slu.edu

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