

Can Xolair Be Used in Nonallergic Asthmatic?

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Each month we present highlights from the Ask the Expert section of the American Academy of Allergy, Asthma & Immunology (AAAAI) Web site written by the Ask the Expert editors. For more questions and answers, visit www.aaaai.org/ask-the-expert.aspx.

Question:

Can Xolair be used in nonallergic asthmatic?

Answer:

Thank you for your question. I forwarded it to Dr Thomas B. Casale, Professor of Medicine and Director of Clinical Research Center at the University of South Florida and a leading investigator of biologic therapy of airway disease. Dr. Casale's response is below.

"Yes, omalizumab has been used in trials for nonallergic asthma. A study in 2013 demonstrated a reduction in exacerbations in nonallergic asthma, similar to the reduction reported in allergic asthma.¹ This was a small study of 41 patients because it was a proof-of-concept study. The exacerbation rate trended downward during the 16 weeks but did not meet statistical significance. The high-affinity IgE receptors were decreased on both blood basophils and plasmacytoid dendritic cells, the primary outcome of the study. In addition, forced expiratory volume in 1 second (FEV1) increased 250 mL.

The PROSPERO study of omalizumab had a subset of subjects with features of both asthma and chronic obstructive pulmonary disease (COPD), also termed asthma COPD overlap (ACO), which also showed a benefit.² PROSPERO was a "real

world" study of the use of omalizumab in a clinical setting. The decision to initiate therapy was dependent on the individual, treating physician, and there was no randomization or control group. Most of these subjects had asthma with allergy.³ However, the PROSPERO study included subjects with asthma who smoked at least 10 pack years and had an FEV1/forced vital capacity less than 0.7 or a medical history positive for both asthma and COPD.² Fifty-nine of the 737 patients met the first criteria, 56 the second, and 20 both. Subjects with ACO had the same reduction in exacerbations as subjects with asthma. Finally, the inner city asthma studies looked at school age children with initiation of omalizumab in the summer before school.^{4,5} These exacerbations are due to viral infections, and omalizumab reduced the exacerbations. Furthermore, there is evidence that viral airway infections are affected by IgE or high-affinity IgE receptors.⁶ Infections are likely to be important in allergic asthma, nonallergic asthma, and COPD."

In summary, the original approval for omalizumab focused on subjects with persistent asthma and specific IgE to perennial allergens. Additional studies show omalizumab therapy to have benefit in patients without allergy, with COPD features, or with viral rather than allergic exacerbations. The mechanism of action is not fully understood, but there appears to be an interaction between IgE, IgE receptors, nonallergic respiratory disease, and infectious exacerbations of asthma. Additional studies of the effectiveness of omalizumab in nonallergic asthmatic patients would be desirable to more definitely answer the question.

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Conflicts of interest: D. K. Ledford is employed by the University of South Florida College of Medicine and the Veterans Administration; has provided expert witness testimony for Wicker, Smith, O'Hara, McCoy, Ford regarding asthma death, for Shook Hardy Bacon regarding drug allergy, for Saieva and Stine regarding metal allergy; has received consultancy fees from Genentech and AstraZeneca; has received speaker fees from TEVA, Boehringer Ingelheim, AstraZeneca, Genentech, and Novartis; has received research support from AstraZeneca; is on the Editorial Board for *Annals of Allergy Asthma and Immunology*; is Co-editor of *Asthma: Comorbidities, Coexisting Conditions, & Differential Diagnosis*; is Editor for *Allergens and Allergen Immunotherapy*; is Volume Editor for the *Encyclopedia of Allergy, Immunology and Vaccines*; and is Co-editor of *Asthma and Allergy Basics* (UpToDate). T. B. Casale has received research support and consultancy fees from Novartis and Genentech; and has received fees for Data Monitoring Board from Novartis.

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