

Allergic burden and response to dupilumab



To the Editor:

The *post hoc* analysis of Corren et al¹ looked at the response to dupilumab according to the criteria for allergic asthma based on eligibility for omalizumab, namely, a total serum IgE level of greater than or equal to 30 IU/mL and 1 or more perennial aeroallergen-specific IgE level of greater than or equal to 0.35 kU/L at baseline. The inference made here is that dupilumab works equally well in both allergic and nonallergic asthma. Pointedly, only 41% of the so-called nonallergic group had no history of allergic rhinitis and also tested negative for any aeroallergens. We feel these artificial criteria for allergic asthma may have blunted the ability to predict whether an increased atopic burden is associated with a differential response to dupilumab.

For example, in our regional multidisciplinary severe asthma meeting, we would not consider a specific IgE of say 0.4 kU/L along with a total IgE of say 40 IU/mL as being indicative of a prominent allergic phenotype. Hence, we would be interested to see a more appropriate breakdown for exacerbation reduction and improvement in FEV₁ for dupilumab versus placebo according to baseline total and specific IgE quintiles for the entire cohort or even as a continuous variable. In addition, it would be worth evaluating the response in those patients with 1, 2, 3, 4, 5, or more positive aeroallergen-specific IgE either perennial or seasonal. In other words, this would help to elucidate whether there is a significant putative relationship between increasing levels of nonspecific and specific atopy in predicting the response to dupilumab. It would also be meaningful to know whether increasing levels of atopy per se interact with type 2 inflammatory markers such as fractional exhaled nitric oxide and blood eosinophils. This would help clinicians better identify a particular phenotype that is likely to respond to dupilumab in a real-life setting.

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Conflicts of interest: B. Lipworth reports grants and personal fees from Regeneron, Sanofi, Mylan, and Teva; grants, personal fees, and nonfinancial support from AstraZeneca; other fees from GlaxoSmithKline; personal fees from Novartis during the conduct of the study and from Lupin, Glenmark, Vectura, and Cipla, outside the submitted work; grants, personal fees, and other fees from Boehringer Ingelheim; and that his son is an employee of AstraZeneca. R. Chan has nothing to disclose. C. Kuo reports personal fees from Pfizer, AstraZeneca, and Chiesi, outside the submitted work.

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- Corren J, Castro M, O'Riordan T, Hanania NA, Pavord ID, Quirce S, et al. Dupilumab efficacy in patients with uncontrolled, moderate-to-severe allergic asthma. *J Allergy Clin Immunol Pract* 2020;8:516-26.

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Reply



To the Editor:

We appreciate the correspondence from Lipworth et al¹ regarding our recent publication in *The Journal of Allergy and Clinical Immunology: In Practice* titled "Dupilumab efficacy in patients with uncontrolled, moderate-to-severe allergic asthma."² The diagnostic criteria used to define the allergic group in the article reflects clinical practice in the United States (minimum threshold of 30 IU of total IgE and specific IgE of 0.35 IU for perennial aeroallergens), with the exception of not having an upper limit of 700 IU for total serum IgE (because dupilumab therapy in adults is not weight based). There are limitations to this definition, which are acknowledged in the discussion section.

We welcome Lipworth et al's¹ suggestions for additional analyses in the allergic subgroup and assure them that we are working on many of these and other related analyses, with plans to publish the outcomes in the near future, with the caveat that small numbers for some of the subgroups may not have adequate statistical power.

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Multiple drug hypersensitivity syndrome (MDH) should not be diagnosed by drug provocation tests



To the Editor:

The recent paper of Landry et al¹ summarizes the frequency and characteristics of multiple drug hypersensitivity syndrome (MDH) based on clinical data of 45 patients. The observation of MDH goes back to some short letters of Sullivan et al,² and has later been addressed and refined by Pichler et al in various reports.^{3,4} It soon became clear that the term MDH is used for clinically and mechanistically different diseases and that it is important to make a distinction to drug-induced intolerance reactions from clearly immune-mediated MDH.^{3,4} Therefore, we proposed to speak of MDH only if an immune-mediated mechanism was proven—either by skin testing or by *in vitro* tests, clearly distinguishing it from multiple drug intolerance reactions or flare-up reactions.^{3,4}

The retrospective study of Landry et al reaches the diagnosis of MDH by using either skin tests (in 44.5%, n = 20) and drug