

Correspondence

Reply

To the Editor:

Marcucci et al¹ comment on some major aspects of our cross-sectional study on IgE responses to *Phleum pratense* allergenic molecules in children with hay fever and on their implication for specific immunotherapy (SIT)²: the high heterogeneity of IgE sensitization profiles and the immunologic and clinical impact of molecularly mismatched allergen- SIT.

We agree with Marcucci et al that each patient is almost “unique” in his or her molecular profile of IgE sensitization: patients grouped within the same *Phleum pratense* sensitization profile would have been further differentiated by extending our combinatorial analysis to additional molecules of pollen sources (eg, Ole e 1, Bet v 1, Par j 2, and Amb a 1).² Therefore, a molecular approach adds precision and complexity to the diagnosis of allergic diseases, and it raises new important questions. We should not ignore these questions but accept the new scientific challenge of investigating the immunologic and clinical implications of immunizing patients under well-classified mismatched conditions. Moreover, our results may contribute to the debate on the need of more flexible rules for the registration of preparations for SIT in children.³

We also agree with Marcucci et al¹ that the consequences of a mismatched immunization may be positive, instead of negative. For example, we have not excluded that an underpowered immunization could stimulate a protective immunologic response through the so-called *linked suppression* phenomenon²; similarly, we have not excluded that overpowered immunization may prevent new IgE sensitization.² However, we disagree that these “beneficial” immunologic and clinical effects are already well demonstrated. We believe that these assumptions are still interesting hypotheses deserving to be scientifically tested in properly designed clinical and immunologic trials. Actually, unwanted IgE sensitization during “overpowered” SIT has been described by Movérare et al⁴ in 2002 in patients with birch pollen allergy receiving a birch pollen extract as SIT. We guess that this phenomenon is quite infrequent in clinical practice; however, it should not be overlooked without further scientific evidence.

Last, Marcucci et al point out that the molecular preparation tested by Jutel et al⁵ showed excellent clinical results, with a 36.5% lower median average symptom score for active treatment

compared with placebo.¹ Accordingly, we have written that Jutel et al’s experimental preparation was proved safe and effective in adult patients.² On the other hand, the combined frequency of 2 more “favorable” categories (perfect match = 4%, overpowered = 32%) is 36%, that is, very similar to the 36% mentioned by Marcucci et al.¹ Moreover, IgE responses against *Phleum pratense* molecules start simple in early childhood and can become more and more complex with time.⁶ So, the quote of overpowered immunization may be higher in the case of earlier intervention. Taken together, all these studies further reinforce our opinion that a molecular approach to allergy diagnosis is a strong asset to improve our understanding of the immunologic and clinical consequences of SIT in childhood.

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