



Correspondence

Author response

We would like to thank our colleagues for the detailed reading of our review in which we focused on articles published on pediatric sublingual immunotherapy (SLIT) between 2009 and 2012.¹ The aim of our effort was to add to the understanding of the efficacy and safety of SLIT in children with allergic disease by making an integrated analysis of all lately published trials. We concluded that the evidence of efficacy of SLIT for respiratory and food allergy in children is growing and its quality improved in recent years.

However, we did not introduce further heterogeneity, because our systematic review was not aimed at estimating combined treatment effects of SLIT. We added food SLIT to the review, because we promised to deliver as complete as possible a review of latest literature. Moreover, SLIT with nonrespiratory allergens also formed part of a previous similar review.² Definitely SLIT for foods is still in an experimental phase,^{3,4} as investigators are searching for the optimal dose, schedule, and duration. Moreover, results so far are more promising for oral immunotherapy (OIT) than for SLIT. The debate concerning the induction of real tolerance is ongoing, as an important portion of the patients regain reactivity to the food in question after a certain interval of withdrawal. In 1 study we included,⁵ 50% of the high-dose OIT group passed the second food challenge after a week of nonexposure. How far these observations lay from the results of provocation testing after SLIT with aeroallergens can be disputed. Provocation testing after aeroallergen SLIT is often not improved in all subjects either, as we noted in the section on provocation testing in our review.

As for the mechanisms, both the previously mentioned milk immunotherapy trial⁵ and the peanut SLIT trial⁶ included some immunologic testing. Just as with aeroallergen SLIT,^{7,8} investigators reported a reduction in skin prick test sensitivity, an initial rise in specific immunoglobulin E followed by a reduction at 12 months and a rise in specific immunoglobulin G₄ to cow's milk and peanut, respectively. Moreover, a decrease of CD63+ basophils⁶ or a decreased expression of CD63 and CD203c⁵ potentially suggesting a state of reduced extrinsic basophil activation was reported, again, just as has been shown with SLIT.⁹ In the peanut SLIT trial, Kim et al⁶ showed further similarities with aeroallergen SLIT describing a decrease in interleukin-5 (active vs placebo: $P = .015$) and interleukin-13 (NS) and a trend toward an increase in the ratio of T regulatory cells (NS). Thus, whether and to what degree mechanisms of aeroallergen SLIT and food SLIT/OIT differ remains to be seen.

We are happy with the comments on our article that broaden the SLIT discussion, though we do not agree on all points raised by the commenters.

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