

CORRESPONDENCE

Inferring clinical relevance of Der p 23 from the restricted effect on treatment outcomes after tablet allergy immunotherapy

To the Editor,

We read with interest your paper entitled: "Limited impact of Der p 23 IgE on treatment outcomes in tablet allergy immunotherapy phase III study" by Stranz and coworkers.¹ An accurate knowledge of the house dust mites (HDM) allergens in the patient's environment is decisive in the prescription of effective allergen immunotherapy (AIT). HDM polysensitization is frequent under subtropical humid weather conditions, with a serodominant Der p 23 found over 80% of patients with respiratory allergy (Figure 1).²

Although the relative values of RNA expression render only an estimate of the trend in allergen abundance, suggesting that the immune response to Der p 23 is not proportional to its abundance,³ this allergen not only has the potential to induce robust hypersensitivity reactions by provocation challenging and basophil degranulation,⁴ but also shows as a clinical biomarker involved in recent real-life asthma trials.⁵

The retrospective post hoc observation of a missing association between the clinical efficacy of AIT and sensitization to individual mite allergens in a cohort of HDM allergic asthma patients should be cautiously interpreted. In the aforementioned investigation, the HDM (sublingual immunotherapy) SLIT tablet contains standardized extract from *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, with a 1:1:1:1 ratio of the major allergens—Group 1 and Group 2 allergens—of HDM and their corresponding biological activity expressed in the unit SQ-HDM. The proposed intervention protocol included a 1:1 randomization to once-daily treatment with either placebo or 12 SQ-HDM SLIT tablet. Although not commercially available nowadays, an additional

subset of patients treated with a represented and standardized source of Der p 23—quantified in SQ-HDM units, not limited to a molar-scale determination—seems essential to a preferred assessment of the clinical and immunological outcomes of this allergen upon uncontrolled asthma. Furthermore, IgG4 is not the unique mechanism—concurrent with the induction of Treg cells—linked to the clinical efficacy of allergen immunotherapy, the greater dose-dependent increases observed in allergen-specific IgG4 to *D pteronyssinus* for Der p 1 and Der p 2 compared to the Der p 23-specific IgG4 responses, suggests that although Der p 23 might be a weak IgG4 inducer, and may be underrepresented in the intended HDM SLIT tablet, could alternatively prime an increase in Treg cells more than other tolerogenic immune mechanism.

In this regard, former post hoc analysis, by Chen and coworkers, confirmed that HDM allergoid extracts inducing IgG antibodies, mainly to Der p 1 and Der p 2, were only clinically beneficial—after 47 weeks of treatment—for patients sensitized to Der p 1 and/or Der p 2, but not for those with a sensitization to other HDM allergens present in more than 40% of the patients (ie, Der p 23, Der p 5, Der p 4, Der p 7, and Der p 21).⁶ Regrettably, these results are difficult to correlate among therapeutic extracts, as the variations in the biological activity amid allergen extracts and manufacturers are dependent on the origin of the source material, the extraction and reconstitution process (based on arbitrary in-house reference standards) and further to this, AIT bearing a complete HDM standardized allergen profile, is not available at present.

Personalized medicine, dealing with broadly heterogeneous molecular-allergen profiles, is today a paradigm for current and future AIT,

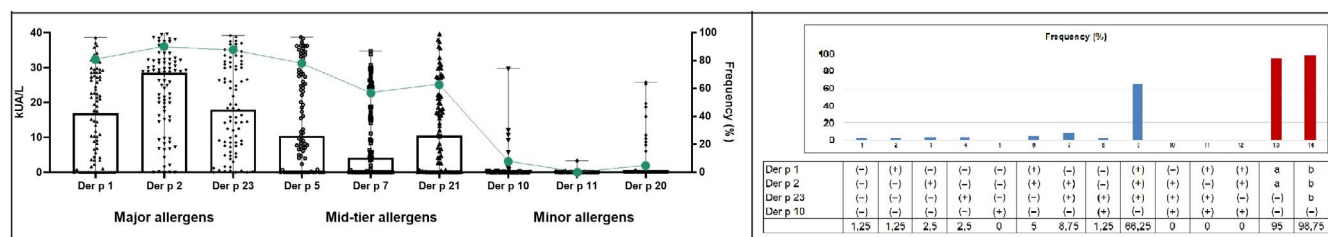


FIGURE 1 A, Sensitization frequencies—median and range—of allergen-specific IgE concentration (KUA/L); B, IgE sensitization frequencies (%) in allergic moderate-to-severe persistent asthma. Most frequently associated sIgE HDM profiles are shown, a: Der p 1 and/or Der p 2; b: Der p 1 and/or Der p 2 and/or Der p 23 (n = 45). Modified from González-Pérez et al J Allergy Clin Immunol 2020, Vol 145, Issue 2, AB11

moving away from the “one size fits all” perspective. The development of new models, including economically affordable molecular extracts and/or hybrid allergens, is warranted to better manage patients' health and target therapies to achieve the best outcomes in IgE-mediated allergic disease.

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Nothing to disclose.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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