Advancing paediatric allergy care: key findings from the largest trial of house dust mite sublingual immunotherapy-tablets in children

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Allergic rhinitis and rhinoconjunctivitis (AR/C) caused by house dust mites (HDM) significantly burden children's daily lives.[1] Despite allergen reduction and pharmacotherapy, many children experience substantial symptoms and impaired quality of life,[2] highlighting the need for disease-modifying treatments like allergen immunotherapy (AIT). In this issue, Schuster et al.[3] present compelling results from the largest double-blind, placebo-controlled trial of SQ HDM sublingual immunotherapy (SLIT)-tablets or placebo for one year in children aged 5–11 years (n = 1460) with physician-diagnosed HDM AR/C from 95 sites across Europe and North America. The primary outcome was the Total Combined Rhinitis Score during the final 8 weeks of treatment, where a 22% reduction was demonstrated with the HDM SLIT-tablet compared to placebo (absolute difference, 1.0, 95% CI: 0.5–1.4; $p < 0.0001$), which exceeds the minimal clinically important difference of 15%.[4]

Improvements were also observed in symptom severity, medication use, and quality of life, with relative reductions exceeding 22% across all rhinitis-related domains. These findings suggest that even in the presence of pharmacotherapy, the addition of HDM SLIT-tablets has a clinically important impact by alleviating symptoms and improving daily functioning. Importantly, there were no cases of severe anaphylaxis and systemic allergic reactions only occurred in three (0.41%) in the HDM SLIT-group and in two (0.27%) in the placebo group, demonstrating the safety of HDM SLIT-tablets. In contrast, a meta-analysis of HDM subcutaneous immunotherapy (SCIT) in children showed a higher prevalence of systemic allergic reactions.[5] The study addresses critical gaps in paediatric AIT research, especially for younger children. Previous studies have shown efficacy of HDM SLIT-tablets in adults and adolescents, but data for children under 12 years are sparse. This trial strengthens the evidence base and provides clinicians with robust data to support integration of HDM SLIT-tablets into routine care for children unresponsive to conventional pharmacotherapy.

Further, the findings align with broader evidence that AIT can modify disease progression.[6] For children, this is particularly relevant, as early interventions may prevent the progression of AR/C to asthma.[7] But is there evidence to conclude that SLIT AIT treatment of AR/C in children can prevent development of asthma? To date, the only randomized, double-blind, placebo-controlled trial in children designed to explore this question, is the Grazax Asthma Prevention (GAP) trial that recruited 812 children aged 5–12 years with grass pollen AR/C without a history of concurrent asthma.[8] The study showed no significant protective effect of grass SLIT on asthma debut, however, there were improvements in relevant measures such as asthma symptoms and medication use. In the study by Schuster et al,[3] improvements in asthma-related parameters were noted, but the study was neither powered to assess outcomes for comorbid asthma nor for the subsequent development of asthma. The asthma daily symptom score was significantly reduced in the HDM SLIT-tablet group compared to placebo (absolute difference, 0.1, 95% CI: 0.0–0.2; $p = 0.026$) and nocturnal awakenings requiring short-acting beta-agonist were reduced in the HDM SLIT-tablet group compared to placebo (0.5% vs. 0.8%, OR 0.6, 95% CI: 0.4–1.0; $p = 0.028$), suggesting that while HDM SLIT-tablets may provide some benefits for asthma symptoms, the magnitude of these effects may not be clinically important for the child. Future studies powered on asthma endpoints are needed to clarify the potential benefits of HDM SLIT-tablets for primary and secondary prevention of asthma in children.

Another unanswered question is whether HDM SLIT-tablets induce sustained unresponsiveness? While the study confirms benefits over a one-year treatment course, longer-term follow-ups are necessary to evaluate whether these effects persist after therapy cessation. Additionally, investigating biomarkers predictive of

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treatment response could help identify which children are most likely to benefit, further personalizing allergy care. Finally, it would be beneficial to examine how SLIT efficacy compares with other AIT modalities, such as SCIT, in paediatric populations.

Other clinically relevant questions are how many children achieved complete symptom resolution and/or could halt pharmacotherapy? Although the study reported clinically important improvements in symptom scores, the proportion of children experiencing total relief of symptoms and/or halting pharmacotherapy was not explicitly stated. This would provide valuable insights for parents and clinicians considering treatment options.

Finally, it is unanswered whether there is an age-related treatment effect? Given the inclusion of a wide age range of 5–11 years, it remains unclear whether younger children benefit more than older children, which was observed on asthma outcomes in the GAP trial.[8] Future studies should investigate whether early intervention yields larger treatment effects, potentially capitalizing on the immunological plasticity of younger children.

In conclusion, this landmark trial confirms the efficacy and safety of HDM SLIT-tablets in children with HDM AR/C, offering hope for children and families burdened by HDM allergy and date for improving treatment guidelines. As we look forward, expanding research into long-term outcomes, asthma-specific benefits, and predictive biomarkers will be essential to fully harness the potential of SLIT-tablets in paediatric allergy care.

Contributors

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Declaration of interests

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