

Correspondence

Reply

To the Editor:

We thank Lipworth for his letter¹ commenting on our recent publication showing efficacy of the SQ house dust mite (HDM) sublingual immunotherapy tablet (SLIT-tablet) in subjects with moderate to severe HDM-induced allergic rhinitis.² Lipworth notes that the results are promising but questions the clinical relevance of the difference in the primary end point (total combined rhinitis score [TCRS]) based on the lower bounds of the 95% CI. Lipworth makes reference to a publication that uses an anchor-and distribution-based approach to derive a minimal clinically important difference (MCID) in rhinitis to be a difference of 0.55 (no 95% CI provided) in total nasal symptom score.³ This is based on analysis of data from 9 allergy pharmacotherapy trials with a total of 226 subjects. This MCID cannot be applied directly to the results of our trial for a number of reasons. None of the studies included in the referenced publication was an allergy immunotherapy trial; most of the studies (6 of 9) enrolled patients with intermittent allergic rhinitis rather than persistent allergy, and none of the studies used the TCRS. Furthermore, our trial allowed use of rescue medications, which is in contrast to the pharmacotherapy trials included in the referenced publication, making comparisons difficult. It is common practice to focus on the estimated mean difference from placebo when comparing to MCID (which for the 12 SQ-HDM dose in our trial was 1.22) rather than the 95% CI.

Lipworth also argues that there were no clinically relevant improvements in the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) in our trial. However, we did see a statistically significant reduction in RQLQ with the 12 SQ-HDM dose compared with placebo (not corrected for rescue medication use, which was significantly greater in the placebo group).

To date, there is no consensus regarding the optimal methodology to set the MCID for TCRS in allergy immunotherapy trials in perennial allergic rhinitis. The Committee for Medicinal Products for Human Use of the European Medicines Agency has therefore omitted to provide fixed values for the definition of a clinically relevant difference in the primary end point between test and control population, but rather ask the investigators to

predefine and justify their specific approach handling end points in allergy immunotherapy trials.⁴ An MCID for within-patient changes in RQLQ has been suggested,⁵ but not for between-group comparisons. We welcome any further efforts in this area.

Last, we want to emphasize that our trial on efficacy and safety of the SQ HDM SLIT-tablet was conducted in subjects with moderate to severe persistent allergic rhinitis, despite being treated with allergy pharmacotherapy. Thus, the improvements seen in our trial should be seen as add-on to what can be achieved by standard of care allergy pharmacotherapy.

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