**Abstract**

The house dust mite (HDM) sublingual allergen immunotherapy (SLIT) tablet is a potential novel treatment option for HDM allergy-related asthma.

**OBJECTIVES:** To evaluate the efficacy and adverse events of the HDM SLIT tablet vs placebo for asthma exacerbations during an inhaled corticosteroid (ICS) reduction period.

**DESIGN, SETTINGS, AND PARTICIPANTS:** Double-blind, randomized, placebo-controlled trial conducted between August 2011 and April 2013 in 109 European trial sites. The trial included 834 adults with HDM allergy-related asthma not well controlled by ICS or combination products, and with HDM allergy-related rhinitis. Key exclusion criteria were FEV1 less than 70% of predicted value or hospitalization due to asthma within 3 months before randomization. Efficacy was assessed during the last 6 months of the trial when ICS was reduced by 50% for 3 months and then completely withdrawn for 3 months.

**INTERVENTIONS:** 1:1:1 randomization to once-daily treatment with placebo (n = 277) or HDM SLIT tablet (dosage groups: 6 SQ-HDM [n = 275] or 12 SQ-HDM [n = 282]) in addition to ICS and the short-acting β2-agonist salbutamol.

**MAIN OUTCOMES AND MEASURES:** Primary outcome was time to first moderate or severe asthma exacerbation during the ICS reduction period. Secondary outcomes were deterioration in asthma symptoms, change in allergen-specific immunoglobulin G4 (IgG4), change in asthma control or asthma quality-of-life questionnaires, and adverse events.

**RESULTS:** Among 834 randomized patients (mean age, 33 years [range, 17-83]; women, 48%), 693 completed the study. The 6 SQ-HDM and 12 SQ-HDM doses both significantly reduced the risk of a moderate or severe asthma exacerbation compared with placebo (hazard ratio [HR]: 0.72 [95% CI, 0.52-0.99] for the 6 SQ-HDM group, P = .045, and 0.69 [95% CI, 0.50-0.96] for the 12 SQ-HDM group, P = .03). The absolute risk differences based on the observed data (full analysis set) in the active groups vs the placebo group were 0.09 (95% CI, 0.01-0.15) for the 6 SQ-HDM group and 0.10 (95% CI, 0.02-0.16) for the 12 SQ-HDM group. There was no significant difference between the 2 active groups. Compared with placebo, there was a reduced risk of an exacerbation with deterioration in asthma symptoms (HR, 0.72 [95% CI, 0.49-1.02] for the 6 SQ-HDM group, P = .11, and 0.64 [95% CI, 0.42-0.96] for the 12 SQ-HDM group, P = .03) and a significant increase in allergen-specific IgG4. However, there was no significant difference for change in asthma control questionnaire or asthma quality-of-life questionnaire for either dose. There were no reports of severe systemic allergic reactions. The most frequent adverse events...
were mild to moderate oral pruritus (13% for the 6 SQ-HDM group, 20% for the 12 SQ-HDM group, and 3% for the placebo group), mouth edema, and throat irritation.

**CONCLUSIONS AND RELEVANCE:** Among adults with HDM allergy-related asthma not well controlled by ICS, the addition of HDM SLIT to maintenance medications improved time to first moderate or severe asthma exacerbation during ICS reduction, with an estimated absolute reduction at 6 months of 9 to 10 percentage points; the reduction was primarily due to an effect on moderate exacerbations. Treatment-related adverse events were common at both active doses. Further studies are needed to assess long-term efficacy and safety.

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