Clinical Communications

Treatment with the SQ house dust mite sublingual immunotherapy tablet may be initiated year-round

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Clinical Implications

- This study, based on pooled data from 5 phase 2/3 trials conducted in North America and Europe, indicates that treatment with the SQ house dust mite sublingual immunotherapy tablet can be safely initiated throughout winter months and during the pollen season (coseasonal initiation).

TO THE EDITOR:

Initiation of sublingual immunotherapy (SLIT) during the allergy season (coseasonal initiation) may potentially increase the risk of adverse events (AEs) in allergic individuals sensitized to more than 1 allergen (polysensitized). This concern comes from surveys analyzing the administration of subcutaneous immunotherapy with a focus on systemic allergic reactions, which suggest that injection during the height of the allergy season is an important contributing factor to near-fatal reactions.[1] Systemic allergic reactions are rare in subjects treated with SLIT[2]; however, it is uncertain whether there may be an increased risk of other types of AEs during coseasonal initiation, and most allergy immunotherapy treatment guidelines are not definitive in their recommendations. Because of the perennial nature of house dust mite (HDM) allergic disease, treatment with the SQ HDM SLIT-tablet may be initiated at any time of the year. However, because most patients with HDM allergic disease are sensitized to more than 1 allergen, increased exposure to pollen or other allergens during specific seasons may impact the safety of treatment initiation with the SQ HDM SLIT-tablet. Because most AEs reported during treatment with the SQ HDM SLIT-tablet occur during the initiation phase of the treatment,[3] the objective of this post hoc study was to evaluate the safety of year-round initiation with the SQ HDM SLIT-tablet on the basis of previously conducted trials.

Adverse events data were collected from 5 phase 2/3 trials conducted in North America and Europe[4-8] (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). The trials included 2,922 subjects receiving the HDM SLIT-tablet (dose, 12 SQ HDM) or placebo. Data on subjects with treatment-emergent AEs (TEAEs), treatment-related AEs (TRAEs), local site reactions, and asthma-related AEs were analyzed for the 12 SQ HDM SLIT-tablet (12 SQ-HDM dose) and placebo, and were grouped on the basis of when treatment was initiated and the season during which the AE started. Evaluation included 4 seasons (up to 1 year after initiation). Subjects received the SQ HDM SLIT-tablet daily during the trial period. In the P001 trial, local site reactions were documented daily during the first 28 days of treatment using questions defined by the World Allergy Organization (solicited AEs).[9] Subjects in the other trials were not asked about specific AEs (unsolicited AEs). Because the MT-02 trial did not include the 12 SQ-HDM dose, only subjects on placebo were included in the pool used for the analyses presented in this study.

The 2,922 subjects included in this study were aged 12 to 85 years with an equal distribution of males and females. Selection criteria included an FEV_1 of 70% or more (of predicted value) and no severe asthma exacerbations within the 3 months before trial enrollment, and thus only subjects with stable nonsevere asthma were included in these studies. The median serum HDM specific (*Dermatophagoides farinae* and/or *Dermatophagoides pteronyssinus*) IgE was 8.5 kU/L or more and the median HDM wheal diameter was 9.9 mm or more, indicating that subjects included in this analysis were highly sensitized toward HDM. Allergen sensitization as determined by serum specific IgE and skin prick test revealed that 72% were sensitized to HDM and other allergens (polysensitized); 69% of subjects on active treatment and 28% of subjects on placebo reported a TRAE, and at least 97% were of mild or moderate severity. One treatment-related systemic allergic reaction (moderate in severity) occurred on the first day of administration and was reported in the active group. The subject made a full recovery after discontinuation of treatment. The most frequently reported AEs were those prespecified as local application site reactions (see Table E2 in this article's Online Repository at www.jaci-inpractice.org). The highest placebo-subtracted frequencies of TEAEs, TRAEs, and local site reactions were reported in the same season in which HDM SLIT-tablet treatment was initiated, and decreased during the following seasons (Figure 1, *A-C*). Regardless of season of initiation, the placebo-subtracted frequencies of TRAEs were similar and ranged from 33% to 45% during the initiating season (Figure 1, *B*). It is important to note that while AE rates appeared to be higher for subjects initiating treatment during spring and summer (Figure 1, *A-C*), these data were based on the P001 trial in which local site reactions were solicited during this period. The data may be confounded because of a reporting bias caused by the safety data collection tool that differed from the other trials in which reporting of local site reactions was unsolicited (see the Methods section in this article's Online Repository at www.jaci-inpractice.org). The placebo-subtracted frequency of subjects with asthma-related AEs was generally low ($\leq$7%), and similar across all seasons, regardless of the season in which treatment was initiated. Thus, the frequency of subjects with asthma-related events did not appear to correlate with either treatment initiation or particular pollen seasons. However, a limitation of these analyses is the

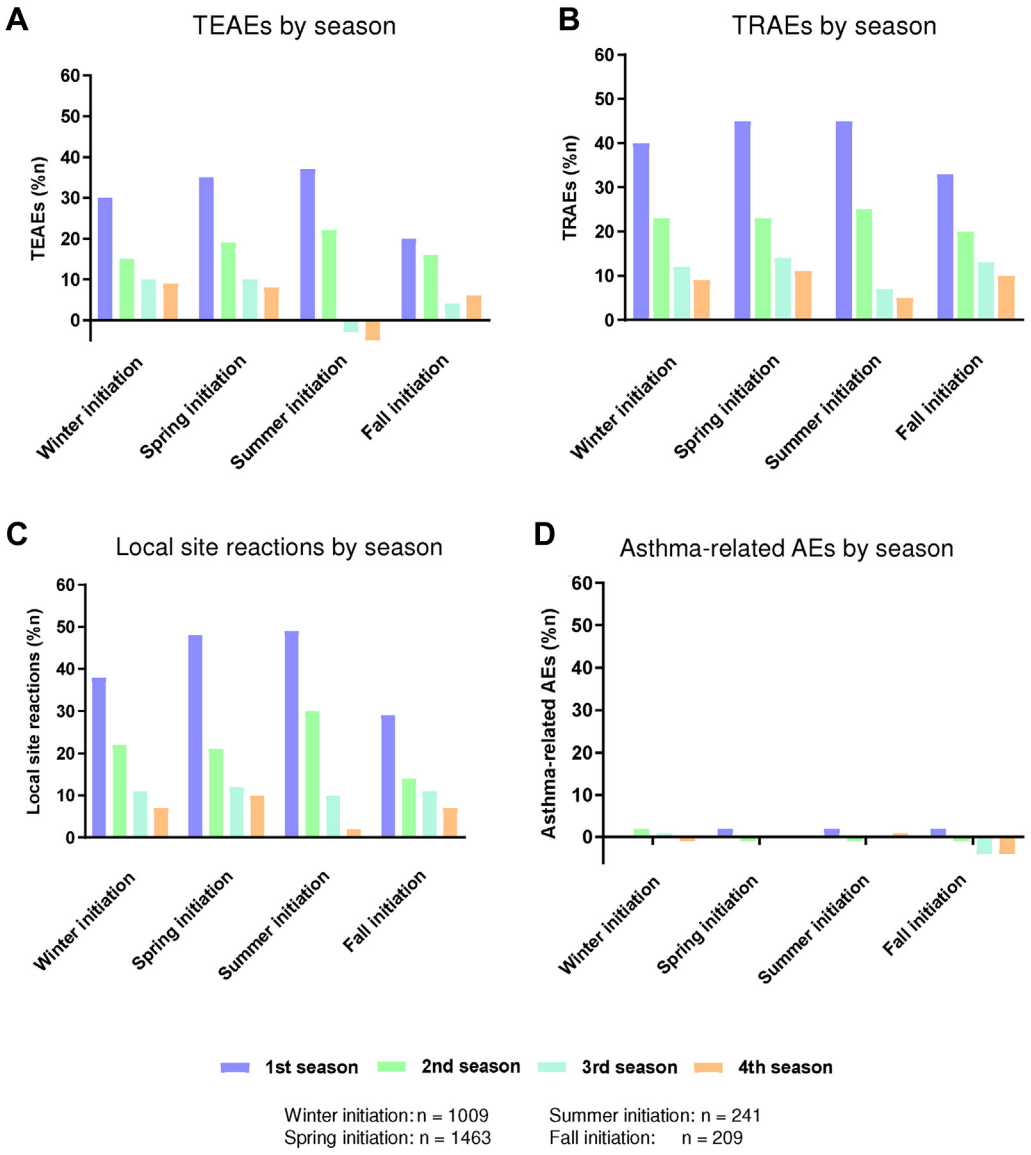

FIGURE 1. Placebo-subtracted frequencies of TEAEs (**A**), TRAEs (**B**), local site reactions (**C**), and asthma-related AEs by season (**D**).

exclusion of subjects with severe controlled asthma in the SQ HDM SLIT-tablet trials.

Because a large proportion of HDM-allergic patients are polysensitized, the safety of treatment initiation during major pollen seasons for monosensitized versus polysensitized patients is of particular interest. For polysensitized and monosensitized subjects initiating in spring or summer (major pollen seasons), the placebo-subtracted frequencies of TRAEs were 46% and 44% (spring) and 44% and 49% (summer), respectively (Figure 2, *A* and *B*). Thus, initiating treatment when pollen counts are highest does not seem to affect the rate of TRAEs for polysensitized subjects. The placebo-subtracted frequencies of subjects reporting TRAEs dropped during the following seasons, and were generally similar regardless of sensitization. For polysensitized subjects initiating treatment during the summer, there appeared to be a somewhat higher proportion reporting TRAEs in the following seasons; however, it is highly likely that this discrepancy was caused by the low number of monosensitized subjects included in this analysis (n = 52), possibly resulting in a reporting bias. No serious allergic reactions were reporting during any season.

The analyses reported in this study did not show any dependency on season of initiation in terms of frequency of subjects reporting TEAEs, TRAEs, local site reactions, or asthma-related AEs for either monosensitized or polysensitized subjects. Thus, treatment with the SQ HDM SLIT-tablet may be initiated year-round without increased risk of AEs in both monosensitized and polysensitized subjects suffering from HDM-induced allergic disease.

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