Safety profile of grass, ragweed, and house dust mite sublingual immunotherapy tablets in children and adolescents

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Introduction

- Allergy immunotherapy (AIT) is the only disease-modifying treatment for allergic rhinitis and/or conjunctivitis (AR/C)[1]
- In children, AIT has the added benefit of preventing the onset of asthma symptoms and asthma medication use[2-4]
- The convenience of at-home administration and injection-free administration may make sublingual immunotherapy (SLIT)-tablets preferred by children (5-11 y), adolescents (12-17 y), and their caregivers[5]
- The grass and ragweed SLIT-tablets are approved for ages 5+ years, and the house dust mite (HDM) SLIT-tablet is approved for ages 12+ years for the treatment of AR/C
- A robust analysis of the safety of SLIT-tablets in children and adolescents supports SLIT-tablets as a well tolerated alternative to subcutaneous immunotherapy

Objective

- To evaluate the safety of grass, ragweed, and HDM SLIT-tablets for AR/C in children and adolescents across the clinical development program

Methods

- Data for the analysis are from 9 grass, 1 ragweed, and 2 HDM randomized, double-blind, placebo-controlled trials
- Seriousness, severity, and the possible relationship to treatment for all adverse events (AEs) were assessed by investigators
  - Serious AEs: events that caused death or were life-threatening, that resulted in persistent or significant disability/incapacity or inpatient hospitalization, or that were judged to be medical important
  - Mild AEs: easily tolerated and did not disrupt daily activities
  - Moderate AEs: causing interference with daily activities
  - Severe AEs: incapacitating, resulting in inability to do normal activities
- Data from each SLIT-tablet were pooled to determine the incidence of treatment-related AEs (TRAEs)
- The presence of known SLIT AEs was actively solicited and captured in an online daily diary in the ragweed trial and 1 HDM trial

Results

- Across the trials, the majority of subjects were males, an average of 27% had asthma, and an average of 78% were polysensitized (**Table 1**)
- The proportion of pediatric subjects with TRAEs was 59% with grass SLIT-tablet, 66% with ragweed SLIT-tablet, and 79% with HDM SLIT-tablet (**Figure 1**)
- Across all 3 SLIT-tablets, most TRAEs were local application site reactions; the most common were oral pruritus, throat irritation, and ear pruritus (**Figure 1**)
- Nearly all (≥98%) TRAEs were assessed as mild or moderate in severity
- Less than 3% of subjects had TRAEs assessed as severe and less than 1% had serious TRAEs (**Figure 2**)
  - There were no deaths or life-threatening events
- Discontinuation rates due to AEs were 7% with grass SLIT-tablet, 4% with ragweed SLIT-tablet, and 5% with HDM SLIT-tablet
- There were no reports of treatment-related anaphylaxis with any of the SLIT-tablets

Table 1. Demographic characteristics of the pooled populations*

	Grass Trials†		Ragweed Trial†		HDM Trials†	
Characteristic	SLIT-Tablet 2800 BAU Dose n=923	Placebo n=895	SLIT-Tablet 12 Amb a 1-U Dose n=512	Placebo n=510	SLIT-Tablet 12 SQ-HDM Dose n=201	Placebo n=194
Age, mean y (SD)	10.2 (3.1)	10.5 (3.1)	12.1 (3.2)	12.2 (3.1)	14.3 (1.6)	14.5 (1.7)
5–11 y, n (%)‡	629 (68)	576 (64)	206 (40)	204 (40)	-	-
12–17 y, n (%)	294 (32)	319 (36)	306 (60)	306 (60)	201 (100)	194 (100)
Male, n (%)	603 (65)	568 (63)	324 (63)	319 (63)	120 (60)	106 (55)
Race, n (%)						
Asian	19 (2)	8 (<1)	4 (1)	6 (1)	112 (56)	106 (55)
Black	33 (4)	22 (2)	18 (4)	14 (3)	12 (6)	6 (3)
Multiracial or other	32 (3)	22 (2)	17 (3)	13 (2)	12 (6)	12 (6)
White	839 (91)	843 (94)	473 (92)	477 (94)	65 (32)	70 (36)
Subjects with asthma, n (%)	164 (18)	146 (16)	219 (43)	217 (43)	39 (19)	40 (21)
Subjects polysensitized, n (%)	724 (79)	700 (78)	405 (79)	389 (76)	156 (78)	149 (77)

HDM, house dust mite; SD, standard deviation; SLIT, sublingual immunotherapy.
*All subjects as treated for the grass and HDM trials and all randomized subjects for the ragweed trial.
†Data are from 9 grass trials (GT-09, GT-10, GT-11, GT-12, P05239, P08067, GT-19, GT-21, GT-23), 1 ragweed trial (P008), and 2 HDM trials (P001, TO-203-3-2).
‡2 children were age 4 years at screening.

Figure 1. Treatment-related AEs reported in ≥5% of subjects across trials

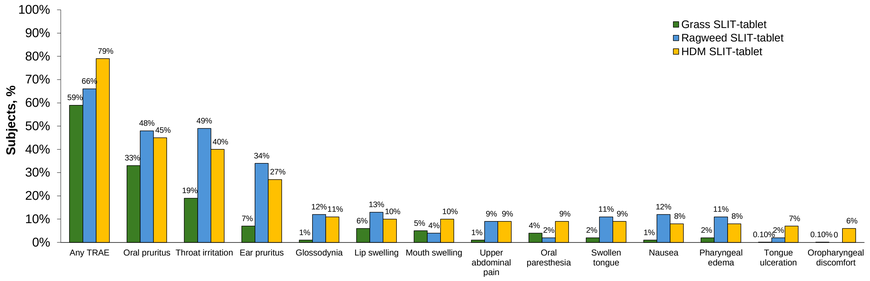
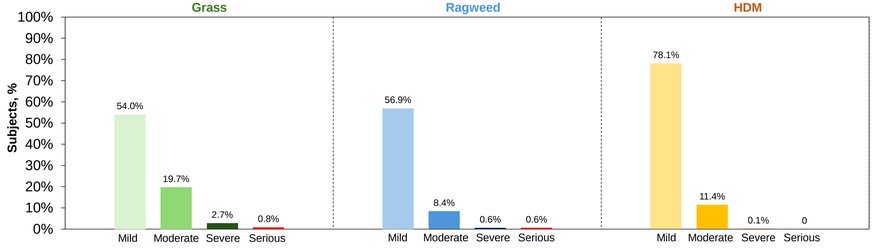


Figure 2. Frequency of subjects reporting treatment-related AEs by severity and seriousness across trials



References

1. Cox L, et al. *J Allergy Clin Immunol.* 2011;127(1 Suppl):S1-55.
2. Jacobsen L, et al. *Allergy.* 2007;62(8):943-948.
3. Marogna M, et al. *J Allergy Clin Immunol.* 2010;126(5):969-975.
4. Valovirta E, et al. *J Allergy Clin Immunol.* 2018;141:529-538.
5. Rance K, et al. *Ann Allergy Asthma Immunol.* 2023;131(5):S27.

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Conclusions

Although AEs are common, reactions are mild to moderate and rarely lead to discontinuation. Hence, SLIT-tablets are well tolerated by children and adolescents with AR/C.