Safety of Year-Round Initiation with SQ House Dust Mite Sublingual Immunotherapy Tablet

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Introduction

- Most patients with allergic rhinitis with or without conjunctivitis (AR/C) are polysensitized to more than one allergen
- Sublingual immunotherapy (SLIT) tablets for seasonal allergies have a recommended initiation of treatment several weeks before pollen season, but SQ house dust mite (HDM) SLIT-tablet may be initiated at any time of year
- In polysensitized subjects, increased exposure to pollens or other allergens could impact the safety of treatment initiation with SQ HDM SLIT-tablet

Objective

- To evaluate the safety of year-round initiation of SQ HDM SLIT-tablet (6 and 12 SQ-HDM doses)

Methods

Trial descriptions

- Five phase 2 and phase 3 randomized, double-blinded, placebo-controlled trials were conducted
  - P001 was a trial of up to 52 weeks (NCT01700192) conducted in North American subjects aged ≥12 years with HDM AR/C[1]
  - P003 was a 24-week environmental chamber trial (NCT01644617) conducted in European subjects aged ≥18 years with HDM AR/C[2]
  - MT-02 was a 52-week trial (NCT00389363) conducted in European subjects aged ≥14 years with allergic asthma[3]
  - MT-06 was a 52-week trial (NCT01454544) conducted in European subjects aged ≥18 years with HDM AR/C[4]
  - MT-04 was an 18-month trial (NCT01433523) conducted in European subjects aged ≥18 years with HDM allergic asthma and AR[5]
- Subjects received daily SQ HDM SLIT-tablet (MK-8237; Merck & Co., Inc., Kenilworth, NJ, USA/ALK, Hørsholm, Denmark; 6 or 12 SQ-HDM dose [12 SQ-HDM dose only in P001; 1, 3, or 6 SQ-HDM doses in MT-02]) or placebo
- Institutional review boards or ethics committees approved the protocols and written informed consent was obtained from the subject or subject's legal representative

Safety data collection and analysis

- In trial P001, reporting of local site reactions was solicited daily for the first ≈28 days of treatment using closed-ended questions regarding local site reactions identified by the World Allergy Organization[6]
  - AE reporting in the other four trials was unsolicited
- Data on the proportion of subjects with any AE, treatment-related AEs, local site reactions, and asthma-related AEs were pooled for the 6 and 12 SQ-HDM doses and evaluated comparing the season when treatment was initiated with the season during which the AE started (up to 2 years after initiation)
  - Seasons were winter (December-February), spring (March-May), summer (June-August), and fall (September-November)

Results

- Overall, 72% of the 3,731 subjects included in the analysis were polysensitized
- The highest reported frequencies of any AEs, treatment-related AEs, and local site reactions were consistently reported in the same season in which SLIT-tablet treatment was initiated, and decreased with treatment (**Table 1**)
- Regardless of the season in which treatment was initiated, the placebo-subtracted frequencies of treatment-related AEs were generally similar and ranged from 33% to 45% during the initiating season (**Figure 1**)
- For polysensitized and monosensitized subjects initiating in spring and summer (pollen seasons), placebo-subtracted frequencies of treatment-related AEs in spring were 46% and 44%, respectively, and in summer were 44% and 49% (**Figure 2A-B**)
- Asthma-related AE frequency was ≤7% and similar across seasons (**Table 1**)

Table 1. Summary of adverse event frequency by season of SQ HDM SLIT-tablet initiation. The first column of data displayed for each initiating group is the initiating season. Columns to the right are the subsequent seasons of treatment. Teal indicates winter initiation, green indicates spring initiation, purple indicates summer initiation, and orange indicates fall initiation. Data from one full year is shown for each initiating group.

	Winter		Spring		Summer		Fall		Winter		Spring		Summer	
Season of Initiation	SQ-HDM SLIT-tablet	Placebo	SQ-HDM SLIT-tablet	Placebo	SQ-HDM SLIT-tablet	Placebo	SQ-HDM SLIT-tablet	Placebo	SQ-HDM SLIT-tablet	Placebo	SQ-HDM SLIT-tablet	Placebo	SQ-HDM SLIT-tablet	Placebo
Winter	**N=470**	**N=539**	**N=449**	**N=533**	**N=420**	**N=511**	**N=383**	**N=461**						
TEAE, %	59	30	46	31	33	23	35	25						
TRAE, %	50	10	30	7	17	5	13	5						
Local site reactions, %	43	5	24	3	12	1	8	1						
Asthma AEs, %	3	4	7	4	4	3	1	2						
Spring			**N=695**	**N=768**	**N=608**	**N=733**	**N=563**	**N=694**	**N=539**	**N=654**				
TEAE, %			84	49	50	31	44	34	45	37				
TRAE, %			79	33	32	9	20	6	16	4				
Local site reactions, %			75	27	26	5	15	3	12	2				
Asthma AEs, %			4	2	2	3	3	3	4	3				
Summer					**N=120**	**N=121**	**N=109**	**N=113**	**N=104**	**N=103**	**N=94**	**N=94**		
TEAE, %					88	50	66	44	53	56	30	35		
TRAE, %					87	42	47	22	19	13	10	4		
Local site reactions, %					83	34	46	16	16	7	6	4		
Asthma AEs, %					2	0	1	2	2	2	1	0		
Fall							**N=97**	**N=112**	**N=95**	**N=112**	**N=91**	**N=109**	**N=89**	**N=107**
TEAE, %							54	34	45	30	28	24	21	15
TRAE, %							40	7	27	7	17	4	11	1
Local site reactions, %							33	5	18	4	11	0	8	1
Asthma AEs, %							6	5	4	5	0	4	0	4

AE, adverse event; HDM, house dust mite; SLIT, sublingual immunotherapy; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Figure 1. Placebo-subtracted frequency of treatment-related AEs by season of SQ HDM SLIT-tablet initiation. AE, adverse event; HDM, house dust mite; SLIT, sublingual immunotherapy.

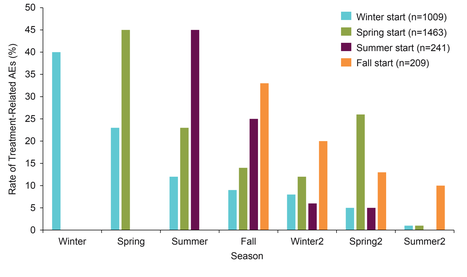
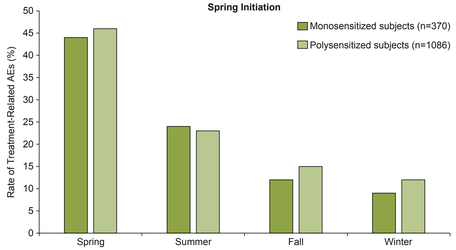
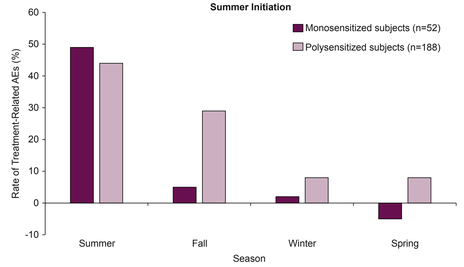


Figure 2. Placebo-subtracted frequency of treatment-related AEs among monosensitized and polysensitized subjects initiating in A) spring and B) summer. AE, adverse event; HDM, house dust mite; SLIT, sublingual immunotherapy.

A)



B)



Conclusions

- The highest AE frequency occurred within the same season in which treatment was initiated
- AEs did not appear to increase in polysensitized subjects who were initiated during pollen seasons
- The frequency of asthma-related AEs was not affected by the initiation season

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Disclosures

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