The house dust mite SLIT-tablet is well tolerated in subjects with house dust mite allergic asthma

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Background

Several clinical trials with the house dust mite (HDM) SLIT-tablet (ALK, Denmark) have been conducted in subjects with allergic rhinitis and/or allergic asthma across Europe, North America, and Japan. Here we present the pooled safety data of the HDM SLIT-tablet in HDM allergic subjects with asthma focusing on asthma related adverse events (AEs).

Methods

Safety data from 6 phase II/III RDBPC clinical trials (MT-02, MT-04, MT-06, P001, P003, TO-203-3-1) including subjects with mild or moderate asthma were pooled and analysed comparing active treatment to placebo as well as subjects with asthma to those without (table 1). Asthma severity was defined based on ICS use at baseline and GINA[1], step 2 treatment corresponding to mild asthma and step 3 to moderate asthma. Subjects were exposed to doses of 1, 3, 6, or 12 SQ-HDM or placebo; data for the European and US approved dose of 12 SQ-HDM are presented. Asthma AEs were defined by the standardised MedDRA query (SMQ) “Asthma/Bronchospasm” (version 19.0).

Table 1: Safety data from 6 phase II/III randomised, double-blind, placebo-controlled clinical trials pooled and analysed for subjects with and without asthma

Trial ID Trial registry	Population	With asthma (N)		Without asthma (N)	
		12 SQ-HDM	Placebo	12 SQ-HDM	Placebo
MT-02/P012 EudraCT 2006-001795-20	Moderate AA + AR	-*	143	-	-
MT-04/P014** EudraCT 2010-018621-19	Moderate AA + AR	282	277	-	-
MT-06/P015 EudraCT 2011-002277-38	AR ± mild AA	153	151	166	186
P001 clinicaltrials.gov NCT01700192	AR(C) ± mild/moderate AA***	229	231	514	507
P003 EudraCT 2012-001855-38	AR(C) ± mild AA	10	9	32	32
TO-203-3-1** JapicCTI-121847	Moderate AA ± AR	277	274	-	-
Total		**951**	**1,085**	**712**	**725**

AA: allergic asthma, AR(C): allergic rhinitis (conjunctivitis), N: number of subjects in safety set
*Only doses 1, 3, and 6 SQ-HDM were in included in the trial
**Asthma exacerbations were efficacy endpoints and therefore not assessed as adverse events unless categorised as a serious event during the efficacy period
***Asthma without ICS use was classified as mild and asthma with ICS use as moderate

Conflicts of interest, presenting author:
Employee at ALK

[1]Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2017

Results

4,860 subjects were included in the trials (any treatment/dose). Of 3,209 subjects with asthma, 951 were treated with 12 SQ-HDM and 1,085 with placebo. A majority of asthma diagnoses were moderate in severity (626 12 SQ-HDM; 755 placebo).
Regardless of asthma status, the proportion of subjects who experienced AEs was numerically higher in the active group (with asthma 86%; without asthma 85%) compared to placebo (with asthma 70%; without asthma 64%) (table 2). The most common AEs were local allergic reactions in the mouth or throat, mainly mild or moderate in severity.

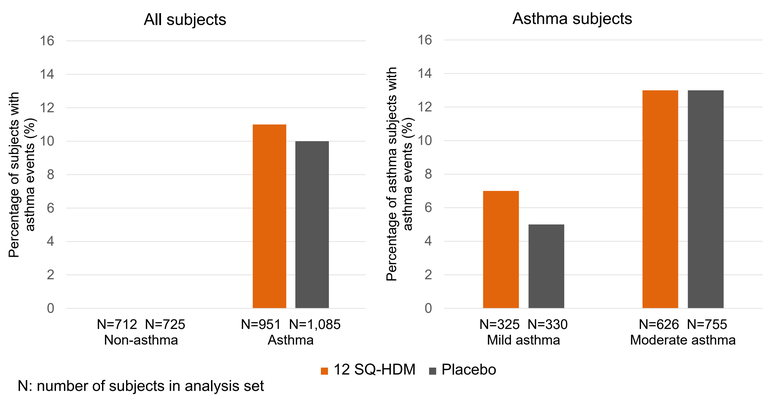
Table 2: All adverse events (percentage of subjects with events)

	With asthma		Without asthma	
%n	12 SQ-HDM (N=951)	Placebo (N=1,085)	12 SQ-HDM (N=712)	Placebo (N=725)
All events	86	70	85	64
Severity of event				
Mild	78	60	79	51
Moderate	38	29	36	29
Severe	5	4	6	6
Serious events	2	3	1	1
Adverse events leading to treatment discontinuation	8	3	7	2

N: number of subjects in analysis set, %n: percentage of subjects in treatment group of analysis set with events
Events with missing severity/seriousness grading are not shown

A numerically higher proportion of subjects with asthma (active 11%; placebo 10%) experienced asthma related AEs than subjects without (<1% both treatments), however, the frequency was similar across treatment groups (figure 1). Likewise, a higher proportion of subjects with moderate asthma experienced asthma related AEs (13% both treatments) compared to subjects with mild asthma (active 7%; placebo 5%).

Figure 1: Adverse asthma events



N: number of subjects in analysis set

Few subjects with asthma, mostly moderate in severity, discontinued treatment due to an asthma AE, regardless of treatment (active 1%; placebo <1%) (table 3).
There were few serious asthma AEs (3 on active; 3 on placebo). One of these (in the 12 SQ-HDM group) was assessed as treatment-related. The subject (with moderate asthma and a recent viral infection) experienced asthma starting on the first day of treatment; following a week with asthma worsening, the subject was hospitalised for 4 days, treated with ICS, β-agonist, and OCS, and recovered.

Table 3: Asthma events* (number and percentage of subjects with asthma events)

	With asthma		Without asthma	
n (%n)	12 SQ-HDM (N=951)	Placebo (N=1,085)	12 SQ-HDM (N=712)	Placebo (N=725)
All asthma events	104 (11)	112 (10)	2 (<1)	6 (<1)
Serious asthma events	3 (<1)	3 (<1)	-	-
Serious treatment-related asthma events	1** (<1)	-	-	-
Asthma events leading to treatment discontinuation	13 (1)	9 (<1)	-	-

N: number of subject in analysis set, n: number of subjects with events, %n: percentage of subjects in treatment group of analysis set with events
*Defined by MedDRA query (SMQ) “asthma/bronchospasm” (version 19.0)
**Following a week of asthma worsening, the subject was hospitalised, treated and recovered

Conclusion

The HDM SLIT-tablet was well tolerated in the HDM allergic asthma population. The asthma AEs were primarily associated with the presence of asthma and asthma severity rather than treatment with the HDM SLIT-tablet.