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Horizon Scanning Research & Intelligence Centre

SQ HDM SLIT-tablet for house dust mite allergic asthma

NIHR HSRIC ID: 6202 ***UK PharmaScan* ID: 478177**

		Information source and date checked
Company	ALK-Abelló.	Company

POPULATION		
Indication	Allergic asthma.	Company
Subgroup	House dust mite related allergic asthma.	Company
Stage of disease	Partly controlled by a medium to high daily dose of inhaled corticosteroids (ICS).	Company
Place in Treatment	Second-line: add on therapy.	Company

INTERVENTION		
Drug name and synonyms	SQ HDM SLIT-tablet; Acarizax (MK8237; MK 8237; SCH 900237). SLIT: (sublingual allergen immunotherapy)	Company; UK PharmaScan
What other indication(s) is the drug licensed for?	SQ HDM SLIT-tablet holds Marketing Authorisation in 12 EU member states for allergic asthma. SQ HDM SLIT-tablet also holds Marketing Authorisation for allergic rhinitis.	Company
What are the licensing, launch and marketing plans for England?	In phase III clinical trials.	UK PharmaScan

OUTCOME / COMPARATOR		
Trial	NCT01433523; ALK HDM AIT vs placebo; phase III.	NCT00389363; ALK HDM SLIT vs placebo; phase II/III.
Sponsor	ALK-Abelló.	ALK-Abelló.
Status	Published.	Published
Source of information	Publication[1], abstract[2,3], trial registry[4].	Publications[5], trial registry[6].
Location	EU (incl UK).	EU (incl. UK).
Design	Randomised, placebo-controlled.	Randomised, placebo-controlled.
Participants	n=834; aged ≥18 years; clinical relevant history of house dust mite induced asthma ≥1 year; use of an appropriate dose of ICS for control of symptoms (at randomisation be in a range of budesonide 400-1200µg/day); documented reversible	n=604; aged ≥14 years; house dust mite induced asthma; mild to moderate asthma controlled with ICS 100 to 800µg/day; a clinical history mild-to-severe HDM-induced allergic rhinitis for ≥1 year; positive skin prick test to house dust mites; positive

	airway obstruction; suitable level of asthma control[1]; positive skin prick test response to Der pte and/or Der far; positive specific IgE against Der pte and/or Der far.	specific IgE to house dust mites; FEV1 ≥ 70%.
Schedule	Randomised to: oral lyophilisate ALK HDM AIT 12 DU, sublingual, once daily; oral lyophilisate ALK HDM AIT 6 DU, sublingual, once daily; or oral lyophilisate placebo, sublingual, daily. Daily ICS use was reduced to 50% for 3 months near the end of the trial and subsequently withdrawn completely for participants who did not experience an asthma exacerbation.	Randomised to: oral lyophilisate ALK HDM SLIT 1 DU, 3 DU or 6 DU, sublingual, daily or oral lyophilisate placebo, sublingual, daily. For all arms there was a pre-treatment ICS adjustment period; subjects switched to budesonide Turbuhaler; ICS dose was reduced in steps with intervals of 3-4 weeks until loss of control was provoked (an asthma control questionnaire (ACQ) score ≥1.5; ICS dose increased to previous step to regain control (ACQ score <1.5); ICS adjustment period followed by a 4-week ICS stable period; ICS adjustment process was repeated at the end of the trial.
Follow-up	Active treatment for 18 months.	Active treatment for 12 months.
Primary outcomes	Time to first moderate or severe asthma exacerbation after ICS reduction.	Reduction in ICS dose from the subject's individual baseline dose.
Secondary outcomes	Changes in immunological parameters (IgE, IgG4); frequency of asthma exacerbations following ICS reduction; overall symptom score; symptom free days; treatment emergent adverse effects (AEs). No quality of life measurement included in trial outcomes.	ICS dose; Asthma Control Questionnaire (ACQ) score; FEV1; peak expiratory flow; Quality of Life measured by Asthma Quality of Life Questionnaire (AQLQ); asthma exacerbations[2]; AEs.
Key results	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=0.045; 0.69 [95% CI, 0.50-0.96] for the 12 SQ-HDM group, P =0.03. The absolute risk differences based on the observed data (full analysis set) in the active groups vs the placebo group for the 6 SQ-HDM and 12 SQ-HDM groups respectively, 0.09 (95% CI, 0.01-0.15), 0.10 (95% CI, 0.02-0.16); no significant difference between the 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=0.17); and 0.64 [95% CI, 0.42-0.96] for the 12 SQ-HDM group, (p=0.03), and a significant increase in allergen-specific IgG4. There was no significant difference for change in asthma control questionnaire or asthma quality of life questionnaire for either dose.	For the 6 DU and placebo groups respectively: reduction in mean daily ICS dose 208µg vs. 126µg (p=0.004); discontinuation of ICS 34% vs. 21%; increase in ICS dose 8% vs. 15%; mean of individual relative reductions from baseline in ICS dose 42% vs. 15%; median values of individual relative reductions from baseline in ICS dose 50% vs 25%.

[1] FEV1 ≥ 70% of predicted value.

[2] An asthma exacerbation was defined as fulfilling one of the following criteria: need for oral corticosteroid treatment because of asthma, unscheduled visits to the trial site because of asthma, or hospitalisation because of asthma worsening.

Adverse effects (AEs)	There were no reports of severe systemic allergic reactions. The most frequent AEs 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 oedema, and throat irritation.	The most common AEs were local reactions in the mouth. The rate and severity of adverse events were higher for 3 and 6 SQ-HDM than for 1 SQ-HDM and placebo.

References

1 Virchow JC, Backer V and Kuna P. Efficacy of a house dust mite sublingual allergen immunotherapy tablet in adults with allergic asthma. A randomised trial. Journal of the American Medical Association 2016;315(16):1715-1725.

2 Virchow JC, Backer V, Kuna P, *et al.* SQ HDM SLIT-tablet is effective in the treatment of allergic asthma; results from a DBPC phase III trial (MITRA). Allergy 2014;69:183-183.

3 Hernandez D, Mosbech H, Dichmann R, *et al*. SQ HDM SLIT-tablet induces significant immunomodulatory response; results from a DBPC phase III trial (MITRA). Allergy 2014;69:186-186.

4 Clinicaltrials.gov. House dust mite treatment of asthma. The MITRA trial house dust mite treatment of asthma (MITRA). https://clinicaltrials.gov/ct2/show/NCT01433523 Accessed 17 February 2017.

5 Mosbech H, Deckelmann R, de Blay F, *et al*. Standardized quality (SQ) house dust mite sublingual immunotherapy tablet (ALK) reduces inhaled corticosteroid use while maintaining asthma control: A randomized, double-blind, placebo-controlled trial. Journal of Allergy and Clinical Immunology 2014; 134(3):568–575.

6 Clinicaltrials.gov. Efficacy and safety trial of the ALK HDM tablet in house dust mite allergic subjects. https://clinicaltrials.gov/ct2/show/NCT003893631 Accessed 17 February 2017.