Clinical trial results:
A 28-day, single-armed, open-label trial to evaluate safety of the house dust mite (HDM) sublingual allergy immunotherapy (SLIT) tablet in adolescent subjects (12-17 years of age) with HDM allergic rhinitis/rhinoconjunctivitis (AR/C) with or without asthma

Summary

EudraCT number	2020-000446-34
Trial protocol	SK DE CZ
Global end of trial date	24 April 2021

Results information

Result version number	v1 (current)
This version publication date	04 November 2021
First version publication date	04 November 2021

Trial information

Trial identification

Sponsor protocol code	MT-18

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04541004
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ALK-Abelló A/S
Sponsor organisation address	Bøge Allé 6-8, Hørsholm, Denmark, DK-2970
Public contact	Global pharmacovigilance & clinical development, ALK-Abelló A/S, +45 45747576, ClinicalTrials@alk.net
Scientific contact	Global pharmacovigilance & clinical development, ALK-Abelló A/S, +45 45747576, ClinicalTrials@alk.net

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 April 2021
Global end of trial reached?	Yes
Global end of trial date	24 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the trial was to evaluate safety and tolerability of the HDM SLIT-tablet in adolescents (12-17 years of age) with 28 days of treatment.

Protection of trial subjects:

Safety surveillance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 September 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovakia: 137
Country: Number of subjects enrolled	Czechia: 87
Country: Number of subjects enrolled	Germany: 29
Worldwide total number of subjects	253
EEA total number of subjects	253

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	253
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 25 trial sites in EU (the Czech Republic, Slovakia and Germany)
First subject first visit: 23-September-2020
Last subject last visit: 19-April-2021
Last follow-up telephone call: 24-Apr-2021

Pre-assignment

Screening details:

Main selection criteria:
- Adolescents (12-17 years)
- History of allergic rhinitis/rhinoconjunctivitis to HDM of at least 1 year duration (with or without asthma) and with allergic rhinitis symptoms despite having received allergy pharmacotherapy during 1 year prior to screening
- Positive SPT against D. pteronyssinus and/or D. farinae

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	HDM SLIT-tablet arm

Arm description: -

Arm type	Experimental
Investigational medicinal product name	HDM SLIT-tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral lyophilisate
Routes of administration	Sublingual use

Dosage and administration details:

dose: 12 SQ-HDM
administration:
Prior to first IMP intake, an oropharyngeal examination had to be performed. The first intake of IMP had to be done at the clinic under medical supervision, with a subsequent observation period of at least 30 minutes.
The IMP had to be taken with dry fingers from the blister unit immediately after opening the blister and placed under the tongue, where it disperses. Swallowing had to be avoided for approximately 1 minute. Food and beverages should not have been taken for the following 5 minutes after intake of IMP. The daily dose of IMP was 1 HDM SLIT-tablet, which should have preferably been taken in the morning.

Number of subjects in period 1	HDM SLIT-tablet arm
Started	253
Completed	251
Not completed	2
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	253	253	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	253	253	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	101	101	
Male	152	152	

Subject analysis sets

Subject analysis set title	Safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received at least one dose of IMP. The safety analysis set (referred to as 'safety set') served the basis for evaluating the safety and tolerability of the HDM SLIT tablet in the trial.

Reporting group values	Safety set		
Number of subjects	253		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	253		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		

Gender categorical Units: Subjects			
Female	101		
Male	152		

End points

End points reporting groups

Reporting group title	HDM SLIT-tablet arm
Reporting group description: -	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received at least one dose of IMP. The safety analysis set (referred to as 'safety set') served the basis for evaluating the safety and tolerability of the HDM SLIT tablet in the trial.

Primary: At least 1 TEAE

End point title	At least 1 TEAE[1]

End point description:

End point type	Primary

End point timeframe:

From first IMP administration to 7 days after last IMP administration.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical analyses were performed in this trial, as this was a single-arm safety trial.

End point values	HDM SLIT-tablet arm	Safety set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	253	253		
Units: events	1940	1940		

Statistical analyses

No statistical analyses for this end point

Secondary: At least 1 solicited TEAE

End point title	At least 1 solicited TEAE

End point description:

End point type	Secondary

End point timeframe:

From first IMP administration to 7 days after last IMP administration.

End point values	HDM SLIT-tablet arm	Safety set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	253	253		
Units: events	1796	1796		

Statistical analyses

No statistical analyses for this end point

Secondary: At least 1 IMP-related AE

End point title	At least 1 IMP-related AE

End point description:

End point type	Secondary

End point timeframe:

From first IMP administration to 7 days after last IMP administration.

End point values	HDM SLIT-tablet arm	Safety set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	253	253		
Units: events	1863	1863		

Statistical analyses

No statistical analyses for this end point

Secondary: At least 1 treatment-emergent SAE

End point title	At least 1 treatment-emergent SAE

End point description:

End point type	Secondary

End point timeframe:

From first IMP administration to 7 days after last IMP administration.

End point values	HDM SLIT-tablet arm	Safety set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	253	253		
Units: events	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs were collected from first IMP intake to 7 days after end-of-trial or discontinuation.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Reporting groups	
Reporting group title	HDM SLIT-tablet group

Reporting group description: -

Serious adverse events	HDM SLIT-tablet group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 253 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	HDM SLIT-tablet group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	223 / 253 (88.14%)		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	16 / 253 (6.32%)		
occurrences (all)	24		
Ear and labyrinth disorders			
Ear pruritus			
subjects affected / exposed	101 / 253 (39.92%)		
occurrences (all)	270		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	40 / 253 (15.81%)		
occurrences (all)	77		
Diarrhoea			

subjects affected / exposed	24 / 253 (9.49%)			
occurrences (all)	30			
Enlarged uvula				
subjects affected / exposed	14 / 253 (5.53%)			
occurrences (all)	38			
Glossodynia				
subjects affected / exposed	41 / 253 (16.21%)			
occurrences (all)	87			
Lip oedema				
subjects affected / exposed	11 / 253 (4.35%)			
occurrences (all)	15			
Lip swelling				
subjects affected / exposed	40 / 253 (15.81%)			
occurrences (all)	89			
Mouth swelling				
subjects affected / exposed	14 / 253 (5.53%)			
occurrences (all)	32			
Mouth ulceration				
subjects affected / exposed	38 / 253 (15.02%)			
occurrences (all)	68			
Nausea				
subjects affected / exposed	40 / 253 (15.81%)			
occurrences (all)	83			
Oedema mouth				
subjects affected / exposed	21 / 253 (8.30%)			
occurrences (all)	35			
Oral pain				
subjects affected / exposed	10 / 253 (3.95%)			
occurrences (all)	19			
Oral pruritus				
subjects affected / exposed	169 / 253 (66.80%)			
occurrences (all)	421			
Swollen tongue				
subjects affected / exposed	29 / 253 (11.46%)			
occurrences (all)	51			
Tongue eruption				

subjects affected / exposed	6 / 253 (2.37%)		
occurrences (all)	16		
Tongue ulceration			
subjects affected / exposed	42 / 253 (16.60%)		
occurrences (all)	79		
Vomiting			
subjects affected / exposed	6 / 253 (2.37%)		
occurrences (all)	9		
Respiratory, thoracic and mediastinal disorders			
Pharyngeal paraesthesia			
subjects affected / exposed	17 / 253 (6.72%)		
occurrences (all)	34		
Pharyngeal swelling			
subjects affected / exposed	33 / 253 (13.04%)		
occurrences (all)	59		
Throat irritation			
subjects affected / exposed	132 / 253 (52.17%)		
occurrences (all)	323		
Infections and infestations			
Rhinitis			
subjects affected / exposed	6 / 253 (2.37%)		
occurrences (all)	10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 April 2020	In this amendment, a section including COVID-19 related risks in context of the trial was inserted, and the mould allergen (Cladosporium herbarum) was removed from the SPT. The first amendment was made before FSFV and as such did not impact the conduct of the trial. This amendment applied to all countries.
14 September 2020	In this amendment, new wording for an inclusion criterion (I3) was adapted. This change intended to clarify that the medical history of HDM allergic rhinitis/rhinoconjunctivitis referred to patients with a moderate to severe medical history of HDM allergic rhinitis/rhinoconjunctivitis, to align with the approved indication in Germany. In addition, a minor revision was included to specify the guidance for re-screening procedures. This amendment applied to Germany only, and was based on feedback from Paul-Ehrlich Institut (PEI). There were no changes affecting subject information and assent forms and the amendment did not impact the conduct of the trial.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported