Clinical trial results:
A multicentre, randomized, open label clinical trial for the safety evaluation of a short dose escalation scheme using one strength for allergen immunotherapy with an aluminium-hydroxide adsorbed native allergen preparation of house dust mite allergens in adult and adolescent patients with moderate to severe allergic rhinitis or rhinoconjunctivitis with or without asthma

Summary

EudraCT number	2020-004328-41
Trial protocol	DE PL
Global end of trial date	14 July 2022

Results information

Result version number	v1 (current)
This version publication date	12 March 2023
First version publication date	12 March 2023

Trial information

Trial identification

Sponsor protocol code	AL0001nh

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Allergopharma GmbH & Co. KG
Sponsor organisation address	Hermann-Körner-Straße 52, Reinbek, Germany, 21465
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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	25 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 July 2022
Global end of trial reached?	Yes
Global end of trial date	14 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this therapeutic phase II trial was to evaluate the safety and tolerability of an accelerated high dose escalation scheme with one strength for allergen immunotherapy with NHD D.p./D.f. 50%/50% compared to the standard escalation scheme involving 3 strengths. Adults and adolescents with rhinitis or rhinoconjunctivitis triggered by house dust mite allergens, with or without allergic asthma on a well controlled level, were enrolled. The trial consisted of a dose escalation phase (T1 to T6) for the accelerated dose escalation (One Strength) or (T1 to T14) for the standard dose escalation (Standard).
Maintenance treatment phase T7-T8 (One Strength) and T15-T16 (Standard), and a follow-up phase of 14-28 days after the last IMP (final visit [FV]). The whole treatment duration (escalation + maintenance phase) lasted for approx. 16 weeks and 24 weeks, respectively, for the two treatment groups. Data are presented as subgroups: Adults and adolescents per treatment group.

Protection of trial subjects:

The trial was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with the International Conference on Harmonization of technical requirements for registration of pharmaceuticals for human use (ICH) guidance for Good Clinical Practice (GCP) and the applicable regulatory requirements. Data Safety Monitoring Board (DSMB) was in place throughout the trial; DSMB consisted of 3 independent physicians, experienced in the field of allergy. The primary function of the DSMB was to ensure the subjects' safety. At the beginning of the trial, only adult patients were included. After 15 adult patients of the One Strength group completed their dose escalation phase and reached the maximum tolerated dose, the DSMB assessed safety and tolerability of the One Strength dose escalation and concluded on an acceptable safety profile for adults with no objections against the enrollment of adolescent patients. Only after this favorable opinion of the DSMB, enrollment and randomization of adolescents was started. During the further course of the trial, the DSMB team reviewed an update of the safety data from all treated patients. After each administration of the IMP, each patient in the study was kept under supervision of a qualified and trained investigator for at least 120 min. Safety evaluation during supervision after IMP administration consisted of: FEV1, Systolic BP, Diastolic BP, Heart rate (Pulse rate), Respiratory rate. Other than routine care, no specific measures were implemented for the protection of trial subjects.

Background therapy:

There was no background therapy planned in this trial. Concomitant medication was defined as any medication other than the IMP that was taken during the clinical trial. Any relevant medication taken before entering the clinical trial was considered as "previous medication". All anti-allergic medication administered in the last 2 years and other medication used during the last 6 weeks prior to enrollment to the trial had to be documented at the screening visit. Medication against rhinitis and rhinoconjunctivitis was permitted, but had to be documented as concomitant medication. Patients with bronchial asthma who required regular basic treatment of their allergic asthma were treated as recommended by GINA (GINA, 2020) to control their asthma. Any asthma medication had to be documented as concomitant medication. Restricted medication and nonpermitted medications were clearly defined in the trial protocol.

Evidence for comparator:

There was no comparator used in this trial. Abbreviations used in this document: AE=Adverse event AIT=Allergen immunotherapy BP=Blood pressure bpm=Beats per minute D.f. = Dermatophagoides farinae D.p. = Dermatophagoides pteronyssinus DSMB=Data Safety Monitoring Board FEV1=Forced expiratory volume in 1 second GINA=Global Initiative for Asthma ICF=Informed consent form IgE = Immunoglobulin E IgG=Immunoglobulin G kU/L=kilo Units per Litre IMP=Investigational medicinal product IS=Injection site MedDRA=Medical Dictionary for Regulatory Activities RBC=Red blood cells T=Treatment (as in T1 =Treatment visit 1, etc.) TEAE=Treatment-emergent adverse event TU=Therapeutic units WAO=World Allergy Organization y=year

Actual start date of recruitment	24 June 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 176
Country: Number of subjects enrolled	Germany: 8
Worldwide total number of subjects	184
EEA total number of subjects	184

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)	83
Adults (18-64 years)	101
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall, 184 male and female patients (11 to ≤ 65 y) were screened for eligibility; of these, 143 were randomised to treatment according to the exclusion and inclusion criteria and 142 were actually treated with IMP (75 patients in the One Strength group and 67 patients in the Standard group).

Pre-assignment

Screening details:

Trial patients (outpatients) were included if they were suffering from immunoglobulin (Ig)E-mediated moderate to severe allergic rhinitis or rhinoconjunctivitis, with or without allergic asthma, triggered by house dust mite (HDM) allergens documented by skin prick test (SPT) wheal for HDM and specific IgE value of ≥ 0.70 kU/L to HDM.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	One Strength

Arm description:

Patients randomized to the 'One Strength' dose escalation scheme received 6 injections with one strength of the IMP (strength 3: 5,000 therapeutic units [TU]/mL), followed by 2 injections with the maximum recommended dose (5,000 TU). Duration of the treatment was approximately 16 weeks.

Arm type	Experimental
Investigational medicinal product name	Novo-Helisen Depot house dust mite mixture allergen preparation [NHD (D.p./D.f.)]
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

IMP is an aluminum hydroxide-adsorbed allergen preparation of house dust mites (D.p.:D.f. /50:50% by volume). IMP was available in 3 concentrations (strength 1: 50 TU/mL; 2: 500 TU/mL; 3: 5,000 TU/mL). In the One Strength group, only strength 3 (5,000 TU/mL) was used. IMP was administered subcutaneously in the upper arm. Doses were escalated once every 7 days in 6 steps in the One Strength group: (250; 500; 1,000; 2,000; 3,000; 5,000 TU). Maintenance 2 weeks after last dose: 5,000 TU, then 4 weeks after last dose: 5,000 TU. Patients had to demonstrate an FEV1 of at least 70% of predicted normal ranges before injection, otherwise no injection was to be given and the visit was rescheduled. If the FEV1 decreased after injection compared with the value measured before injection, the investigator checked whether an AE occurred that needed documentation and medical treatment. In this group, 80.0% of patients reached the 1st IMP injection of the maintenance phase without dose adjustment.

Arm title	Standard

Arm description:

Patients randomized to the 'Standard' dose escalation scheme received 14 injections with 3 different strengths of the IMP (strength 1: 50 TU/mL; 2: 500 TU/mL; 3: 5,000 TU/mL), followed by 2 injections with the maximum recommended dose (5,000 TU). Duration of the treatment was approximately 24 weeks.

Arm type	Active comparator

Investigational medicinal product name	Novo-Helisen Depot house dust mite mixture allergen preparation [NHD (D.p./D.f.)]
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

IMP is an aluminum hydroxide-adsorbed allergen preparation of house dust mites (D.p.:D.f. /50:50% by volume). IMP was available in 3 concentrations (1: 50 TU/mL; 2: 500 TU/mL; 3: 5,000 TU/mL). In the Standard group, all strengths were used. IMP was administered subcutaneously in the upper arm. Doses were escalated once every 7 days in 14 steps in the Standard group: (5; 10; 20; 40; 50; 100; 200; 400; 500; 1,000; 2,000; 3,000; 4,000; 5,000 TU). Maintenance 2 weeks after last dose: 5,000 TU, then 4 weeks after last dose: 5,000 TU. Patients had to demonstrate an FEV1 of at least 70% of predicted normal ranges before injection, otherwise no injection was to be given and the visit was rescheduled. If the FEV1 decreased after injection compared with the value measured before injection, the investigator checked whether an AE occurred that needed documentation and medical treatment. In this group, 85.1% of patients reached the 1st IMP injection of the maintenance phase without dose adjustment

Number of subjects in period 1[1]	One Strength	Standard
Started	75	67
Completed	70	62
Not completed	5	5
Consent withdrawn by subject	-	2
Adverse event, non-fatal	4	2
Lost to follow-up	-	1
Sponsor/DSMB decision	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of patients enrolled worldwide includes screening failures (i.e. patients that signed the informed consent form, but were not randomized; N=41) and patients that were randomized, but never treated (N= 1).
The number of patients in the baseline period equals the number of patients who were actually treated with IMP (= number of patients in the safety set, which was used for all analyses of this trial).

Baseline characteristics

Reporting groups	
Reporting group title	One Strength
Reporting group description:	
Patients randomized to the 'One Strength' dose escalation scheme received 6 injections with one strength of the IMP (strength 3: 5,000 therapeutic units [TU]/mL), followed by 2 injections with the maximum recommended dose (5,000 TU). Duration of the treatment was approximately 16 weeks.	
Reporting group title	Standard
Reporting group description:	
Patients randomized to the 'Standard' dose escalation scheme received 14 injections with 3 different strengths of the IMP (strength 1: 50 TU/mL; 2: 500 TU/mL; 3: 5,000 TU/mL), followed by 2 injections with the maximum recommended dose (5,000 TU). Duration of the treatment was approximately 24 weeks.	

Reporting group values	One Strength	Standard	Total
Number of subjects	75	67	142
Age categorical Units: Subjects			
Adolescents (12 to < 18 y)	33	30	63
Adults (18 to ≤ 65 y)	42	37	79
Age continuous Units: years			
arithmetic mean	25.1	23.9	
standard deviation	± 13.3	± 11.3	-
Gender categorical Units: Subjects			
Female	39	27	66
Male	36	40	76
Ethnic group Units: Subjects			
White	75	67	142

Subject analysis sets	
Subject analysis set title	Adults (18 to ≤ 65 y) One Strength
Subject analysis set type	Safety analysis
Subject analysis set description:	
Adults (18 to ≤ 65 y), randomized to and treated according to One Strength dose escaltion scheme	
Subject analysis set title	Adults (18 to ≤ 65 y) Standard
Subject analysis set type	Safety analysis
Subject analysis set description:	
Adults (18 to ≤ 65 y), randomized to and treated according to Standard dose escaltion scheme	
Subject analysis set title	Adolescents (12 to < 18 y) One Strength
Subject analysis set type	Safety analysis
Subject analysis set description:	
Adolescents (12 to < 18 y) randomized to and treated according to the One Strength dose escalation scheme	
Subject analysis set title	Adolescents (12 to < 18 y) Standard
Subject analysis set type	Safety analysis

Subject analysis set description:

Adolescents (12 to < 18 y) randomized to and treated according to the Standard dose escalation scheme

Reporting group values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength
Number of subjects	42	37	33
Age categorical Units: Subjects			
Adolescents (12 to < 18 y)	0	0	33
Adults (18 to ≤ 65 y)	42	37	0
Age continuous Units: years			
arithmetic mean	33.4	31.5	14.5
standard deviation	± 12.4	± 10.2	± 1.8
Gender categorical Units: Subjects			
Female	25	18	14
Male	17	19	19
Ethnic group Units: Subjects			
White	42	37	33

Reporting group values	Adolescents (12 to < 18 y) Standard		
Number of subjects	30		
Age categorical Units: Subjects			
Adolescents (12 to < 18 y)	30		
Adults (18 to ≤ 65 y)	0		
Age continuous Units: years			
arithmetic mean	14.7		
standard deviation	± 1.6		
Gender categorical Units: Subjects			
Female	9		
Male	21		
Ethnic group Units: Subjects			
White	30		

End points

End points reporting groups

Reporting group title	One Strength

Reporting group description:

Patients randomized to the 'One Strength' dose escalation scheme received 6 injections with one strength of the IMP (strength 3: 5,000 therapeutic units [TU]/mL), followed by 2 injections with the maximum recommended dose (5,000 TU). Duration of the treatment was approximately 16 weeks.

Reporting group title	Standard

Reporting group description:

Patients randomized to the 'Standard' dose escalation scheme received 14 injections with 3 different strengths of the IMP (strength 1: 50 TU/mL; 2: 500 TU/mL; 3: 5,000 TU/mL), followed by 2 injections with the maximum recommended dose (5,000 TU). Duration of the treatment was approximately 24 weeks.

Subject analysis set title	Adults (18 to ≤ 65 y) One Strength
Subject analysis set type	Safety analysis

Subject analysis set description:

Adults (18 to ≤ 65 y), randomized to and treated according to One Strength dose escaltion scheme

Subject analysis set title	Adults (18 to ≤ 65 y) Standard
Subject analysis set type	Safety analysis

Subject analysis set description:

Adults (18 to ≤ 65 y), randomized to and treated according to Standard dose escaltion scheme

Subject analysis set title	Adolescents (12 to < 18 y) One Strength
Subject analysis set type	Safety analysis

Subject analysis set description:

Adolescents (12 to < 18 y) randomized to and treated according to the One Strength dose escalation scheme

Subject analysis set title	Adolescents (12 to < 18 y) Standard
Subject analysis set type	Safety analysis

Subject analysis set description:

Adolescents (12 to < 18 y) randomized to and treated according to the Standard dose escalation scheme

Primary: 1_Treament emergent adverse events - Overall

End point title	1_Treament emergent adverse events - Overall[1]

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which did not necessarily have a causal relationship with this treatment. An AE could be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an IMP, whether or not related to the IMP. A treatment emergent adverse event (TEAE) was defined as any AE that started or worsened after the first use of trial medication until 30 days after the last IMP administration or trial-related procedure. Results in the table below summarize the number of patients affected by a TEAE; the number of the respective events (n) is also shown. The TEAEs (as System Organ Class and as Preferred Term) are listed under the section 'Adverse events'.

End point type	Primary

End point timeframe:

Between the signature date of the ICF and the final visit, until approx. 30 days after the last IMP administration or trial-related procedure. Approx. 16 weeks for patients in One Strength and 24 weeks for patients in Standard treatment group

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: This was a safety-focused trial. No statistical analysis was performed. Results were evaluated descriptively.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[2]	37[3]	33[4]	30[5]
Units: Patients with at least one event				
1_Patients with TEAE	23	21	18	12
2_Patients with serious TEAE	1	0	2	0
3_Patients with TEAEs related to IMP	19	10	10	5
4_Patients with TEAE leading to discontinuation	2	1	2	1

Notes:

[2] - Safety analysis set was used for all treatment groups
1_n=211 2_n=1 3_n=132 4_n=2

[3] - 1_n=142 2_n=0 3_n=73 4_n=1

[4] - 1_n=84 2_n=2 3_n=41 4_n=2

[5] - 1_n=46 2_n=0 3_n=7 4_n=1

Statistical analyses

No statistical analyses for this end point

Primary: 2_Treatment emergent adverse events - Maximum intensity

End point title	2_Treatment emergent adverse events - Maximum intensity[6]

End point description:

A treatment emergent adverse event (TEAE) was defined as any AE that started or worsened after the first use of trial medication until 30 days after the last IMP administration or trial-related procedure. The intensity of the TEAE was assessed by the the investigator. Mild=Transient symptoms, no interference with the patient's daily activities. Moderate=Marked symptoms, moderate interference with the patient's daily activities. Severe=Considerable interference with the patient's daily activities.

End point type	Primary

End point timeframe:

Between the signature date of the ICF and the final visit, until approx. 30 days after the last IMP administration or trial-related procedure.

Notes:

[6] - 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: This was a safety-focused trial. No statistical analysis was performed. Results were evaluated descriptively.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[7]	37	33	30
Units: Patients with maximum event intensity				
Mild	17	17	10	5
Moderate	6	4	5	6
Severe	0	0	3	1

Notes:

[7] - Safety analysis set was used for all treatment groups

Statistical analyses

No statistical analyses for this end point

Primary: 3_Treatment emergent adverse events - Causal Relationship (IMP-related)

End point title	3_Treatment emergent adverse events - Causal Relationship (IMP-related)[8]

End point description:

TEAEs - causal relationship to IMP. Results in the table below show the number of subjects with at least one TEAE related to IMP, as assessed by the investigator. The number of the respective events (n) is also shown. The actual number of TEAEs are listed under the section 'Adverse events'. Most of the related TEAEs were mild in intensity in both treatment groups (>95% adults and >75% adolescent). Related TEAEs experienced by more than 2 patients per age group were: Injection site (IS) swelling, IS erythema, IS pruritus, IS pain, IS oedema, Hypersensitivity and Arthralgia.

End point type	Primary

End point timeframe:

Between the signature date of the ICF and the final visit, until approx. 30 days after the last IMP administration or trial-related procedure.

Notes:

[8] - 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: This was a safety-focused trial. No statistical analysis was performed. Results were evaluated descriptively.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[9]	37[10]	33[11]	30[12]
Units: Patients with at least one event				
1_Patients with TEAEs related to IMP	19	10	10	5
2_Patients with serious TEAEs related to IMP	1	0	2	0

Notes:

[9] - Safety analysis set was used for all treatment groups
1_n=132 2_n=1

[10] - 1_n=73 2_n=0

[11] - 1_n=41 2_n=2

[12] - 1_n=7 2_n=0

Statistical analyses

No statistical analyses for this end point

Secondary: 4_Treatment emergent adverse events - Systemic allergic reactions related to IMP according to WAO

End point title	4_Treatment emergent adverse events - Systemic allergic reactions related to IMP according to WAO

End point description:

Systemic allergic reaction related to IMP: TEAE were graded by the investigator according to the WAO grading system, which is based on the organ systems involved and the severity of the reaction. Dose reductions for systemic reactions acc. to WAO : • Grade 1: reduction by 1 dose step of the last applied dose. • Grade 2: reduction by 2 dose steps of the last applied dose. • Grade 3: patient must have been withdrawn from the trial. For WAO Grade 1 and WAO Grade 2: if the 1st dose reduction was not tolerated, a 2nd dose reduction by 1 dose step of the last applied dose was administered. All 19 systemic allergic reactions were assessed by the investigator as IMP-related. Adults: Hypersensitivity, Rhinorrhoea, Cough, FEV1 decreased, Dizziness, Dermatitis atopic, Urticaria; Adolescents: Anaphylactic reaction, Hypersensitivity, FEV1 decreased, Dyspnoea, Erythema. Intensity: mild: 9, moderate: 7, severe: 3. 3 systemic allergic reaction were serious adverse events (adults: 1; adolescents: 2).

End point type	Secondary

End point timeframe:

Between the signature date of the ICF and the final visit, until approx. 30 days after the last IMP administration or trial-related procedure.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[13]	37	33	30
Units: Systemic TEAEs related to IMP				
Grade 1	5	5	2	1
Grade 2	3	0	1	1
Grade 3	0	0	1	0

Notes:

[13] - Safety analysis set was used for all treatment groups

Statistical analyses

No statistical analyses for this end point

Secondary: 5_Treatment emergent adverse events - Local reactions related to IMP

End point title	5_Treatment emergent adverse events - Local reactions related to IMP

End point description:

Treatment-emergent adverse event - Local reactions. Results in the table below summarize the number of subjects affected by TEAEs 'local reactions', that were assessed by the investigators as related to the IMP. The number of the respective events (n) is also shown. Local reactions related to IMP were:
Adults: Injection site (IS) erythema, IS oedema, IS pain, IS pruritus, IS swelling, IS induration, IS papule, IS warmth, Arthralgia, Pain in extremity, Fine moter skill dysfunction;
Adolescents: IS erythema, IS pain, IS pruritus, IS swelling, IS oedema, IS rash, Arthralgia, Pain in extremity, Peripheral swelling.

End point type	Secondary

End point timeframe:

Between the signature date of the ICF and the final visit, until approx. 30 days after the last IMP administration or trial-related procedure.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[14]	37[15]	33[16]	30[17]
Units: Patients with at least one event	19	9	8	4

Notes:

[14] - Safety analysis set was used for all treatment groups n=114

[15] - n=65

[16] - n=35

[17] - n=5

Statistical analyses

No statistical analyses for this end point

Secondary: 6_Numer of patients reaching the maintenance period without dose adjustment due to TEAE

End point title	6_Numer of patients reaching the maintenance period without dose adjustment due to TEAE

End point description:

Number of patients reaching the maintenance period without dose adjustment due to TEAE. The start of the maintenance period was defined as the second injection of the maximum tolerated dose of IMP (5,000 TU = M1). Patients not reaching the maintenance period without dose adjustments due to other reasons (such as visit window deviations) are not respected here.

End point type	Secondary

End point timeframe:

Between the signature date of the ICF and the final visit, until approx. 30 days after the last IMP administration or trial-related procedure.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[18]	37	33	30
Units: Number of patients	35	36	29	28

Notes:

[18] - Safety analysis set was used for all treatment groups

Statistical analyses

No statistical analyses for this end point

Secondary: 7_Vital signs - Heart rate (Pulse rate)

End point title	7_Vital signs - Heart rate (Pulse rate)

End point description:

Vital signs (BP, heart rate, resp. rate) were assessed at: screening, during treatment visits / any unscheduled visit, and at the final visit. Vital signs are summarized by a representative parameter Heart rate (Pulse rate). Results are shown as the change from pre- to 30 min post administration of IMP on the first- (T1), last (regular) dose escalation visit (T6/T14), and last maintenance visit (T8/T16 = M2). The number of patients missing at each visit is also shown.

End point type	Secondary

End point timeframe:

At IMP treatment visits (dose escalation and maintenance phase): before and 30/120 min after administration.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[19]	37[20]	33[21]	30[22]
Units: bpm				
median (full range (min-max))				

T1 First escalation dose	-2.0 (-18 to 10)	-2.0 (-14 to 10)	-1.0 (-7 to 12)	-2.0 (-14 to 4)
T6/T14 Last escalation dose	-2.5 (-15 to 11)	0.0 (-9 to 6)	-1.0 (-10 to 20)	-0.5 (-8 to 19)
M2 Last maintenance dose	-1.0 (-11 to 2)	-1.0 (-12 to 10)	-1.0 (-8 to 4)	0.0 (-26.0 to 6)

Notes:

[19] - Safety analysis set was used for all treatment groups
missings: T6=2; M2=3

[20] - missings: T14=4; M2=4

[21] - missings: T6=1; M2=2

[22] - missings: M2=1

Statistical analyses

No statistical analyses for this end point

Secondary: 8_Lung function test - FEV1

End point title	8_Lung function test - FEV1

End point description:

Subjects had to demonstrate FEV1 of at least 70% of predicted normal ranges before IMP injection, otherwise no injection was given and the visit was rescheduled. If the FEV1 decreased after injection compared to the value measured before injection, the investigator checked if an AE had to be documented and adequate medical treatment initiated. An FEV1 decrease of ≥ 20% after injection as compared to the value measured before injection, was documented as an AE. Results shown are representative for the study visits at the first escalation dose visit (T1), at the last (regular) dose escalation dose (T6/T14), and at the last maintenance dose visit (T8/T16 = M2); before and 30 min after injection of IMP. The number of patients missing at each visit is also shown. Neither for adults nor for adolescents systematic differences were detected between groups.

End point type	Secondary

End point timeframe:

At IMP treatment visits (dose escalation and maintenance phase): before and 30/120 min after administration.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[23]	37[24]	33[25]	30[26]
Units: measured values (L/s)				
arithmetic mean (standard deviation)				
T1 First escalation dose, before IMP	3.435 (± 0.763)	3.591 (± 0.721)	3.515 (± 0.812)	3.596 (± 0.918)
T1 First escalation dose, 30 min after IMP	3.381 (± 0.773)	3.590 (± 0.706)	3.563 (± 0.817)	3.582 (± 0.957)
T6/T14 Last escalation dose, before IMP	3.453 (± 0.732)	3.517 (± 0.824)	3.599 (± 0.821)	3.671 (± 0.855)
T6/T14 Last escalation dose, 30 min after IMP	3.440 (± 0.745)	3.512 (± 0.820)	3.593 (± 0.857)	3.641 (± 0.826)
M2 Last maintenance dose, before IMP	3.547 (± 0.734)	3.584 (± 0.813)	3.726 (± 0.866)	3.726 (± 0.841)
M2 Last maintenance dose, 30 min after IMP	3.479 (± 0.716)	3.577 (± 0.834)	3.700 (± 0.876)	3.717 (± 0.885)

Notes:

[23] - missings: T6=2; M2=3

[24] - missings: T14=4; M2=4

[25] - missings: T6=1; M2=2

[26] - missings: M2=1

Statistical analyses

No statistical analyses for this end point

Secondary: 9a_Tolerability: Likert scale at Final Visit - Investigator

End point title	9a_Tolerability: Likert scale at Final Visit - Investigator

End point description:

Assessment of the overall tolerability by the investigator using a 5-point Likert scale. Likert scale score system: 1=Very bad; 2=Bad; 3=Average; 4=Good; 5=Very good. Table below shows the number of patients in each tolerability category of the Likert scale, as assessed by the investigator. The majority of investigators (> 95%) assessed tolerability as 'good' or 'very good'. All patients with assessment 'bad' or 'average' prematurely terminated the trial due to IMP-related TEAEs.

End point type	Secondary

End point timeframe:

Tolerability assessment of the entire trial period at Final Visit.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[27]	37	33	30
Units: Number of patients				
Missing	0	2	0	0
Very Bad	0	0	0	0
Bad	2	0	0	0
Average	0	0	2	1
Good	5	3	0	0
Very Good	35	32	31	29

Notes:

[27] - Safety analysis set was used for all treatment groups

Statistical analyses

No statistical analyses for this end point

Secondary: 9b_Tolerability: Likert scale at Final Visit - Patient

End point title	9b_Tolerability: Likert scale at Final Visit - Patient

End point description:

Assessment of the overall tolerability by the patient using a 5-point Likert scale. Likert scale score system: 1=Very bad; 2=Bad; 3=Average; 4=Good; 5=Very good. Table below shows the number of patients in each tolerability category of the Likert scale, as assessed by the patient. The majority of patients (> 95%) assessed tolerability as 'good' or 'very good'. All patients with assessment 'very bad', 'bad' or 'average' prematurely terminated the trial due to IMP-related TEAEs.

End point type	Secondary

End point timeframe:

Tolerability assessment of the entire trial period at Final Visit.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[28]	37	33	30
Units: Number of patients				
Missing	0	2	0	0
Very Bad	1	0	0	1
Bad	1	1	0	0
Average	0	0	2	0
Good	6	4	2	5
Very Good	34	30	29	24

Notes:

[28] - Safety analysis set was used for all treatment groups

Statistical analyses

No statistical analyses for this end point

Secondary: 10a_Treatment emergent adverse events related to IMP (all) - Time to onset

End point title	10a_Treatment emergent adverse events related to IMP (all) - Time to onset

End point description:

Results show time to onset of all IMP-related TEAEs.

End point type	Secondary

End point timeframe:

Between the signature date of the ICF and the final visit, until approx. 30 days after the last IMP administration or trial-related procedure.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[29]	37	33	30
Units: TEAEs realated to IMP				
Overall	132	73	41	7
≤ 30 min	15	7	12	3
> 30 min ≤ 6 h	88	51	10	3
> 6 h ≤ 24 h	19	13	14	1
> 24 h	10	2	5	0

Notes:

[29] - Safety analysis set was used for all treatment groups

Statistical analyses

No statistical analyses for this end point

Secondary: 10b_Treatment emergent adverse events related to IMP (systemic) - Time to onset

End point title	10b_Treatment emergent adverse events related to IMP (systemic) - Time to onset

End point description:

Results show time to onset of all systemic IMP-related TEAEs.

End point type	Secondary

End point timeframe:

Between the signature date of the ICF and the final visit, until approx. 30 days after the last IMP administration or trial-related procedure.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[30]	37	33	30
Units: TEAEs related to IMP				
Overall	8	5	4	2
≤ 30 min	1	2	4	1
> 30 min ≤ 6 h	5	1	0	1
> 6 h ≤ 24 h	2	1	0	0
> 24 h	0	1	0	0

Notes:

[30] - Safety analysis set was used for all treatment groups

Statistical analyses

No statistical analyses for this end point

Secondary: 10c_Treatment emergent adverse events related to IMP (local) - Time to onset

End point title	10c_Treatment emergent adverse events related to IMP (local) - Time to onset

End point description:

Results show time to onset of all local IMP-related TEAEs.

End point type	Secondary

End point timeframe:

Between the signature date of the ICF and the final visit, until approx. 30 days after the last IMP administration or trial-related procedure.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[31]	37	33	30
Units: TEAEs related to IMP				
Overall	114	65	35	5
≤ 30 min	14	3	8	2
> 30 min ≤ 6 h	74	49	9	2
> 6 h ≤ 24 h	17	12	13	1
> 24 h	9	1	5	0

Notes:

[31] - Safety analysis set was used for all treatment groups

Statistical analyses

No statistical analyses for this end point

Other pre-specified: 11_Immunological profile (specific IgG4 against house dust mites)

End point title	11_Immunological profile (specific IgG4 against house dust mites)

End point description:

According to the study inclusion criteria, all patients had IgE-mediated allergic rhinitis or rhinoconjunctivitis (with or without allergic asthma), triggered by house dust mite allergens. Changes in the immunological profile of specific IgG4 against house dust mites provide valuable information and evidence for the immunogenic activity of the active preparation. Changes in IgG4 were analyzed as an exploratory parameter. The results (shown as changes from baseline) indicate that for all patients (adults and adolescents), during the course of the trial, the median IgG4 levels against Dermatophagoides pteronyssinus (D.p.) and Dermatophagoides farinae (D.f.) increased notably over time in both treatment groups [p-values for all patients (adults and adolescents) < 0.0001]. The number of subjects contributing to the data is also shown (N).

End point type	Other pre-specified

End point timeframe:

To determine the immunological profile, blood was taken at screening (baseline) and the final visit/premature termination of the study.

End point values	Adults (18 to ≤ 65 y) One Strength	Adults (18 to ≤ 65 y) Standard	Adolescents (12 to < 18 y) One Strength	Adolescents (12 to < 18 y) Standard
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42[32]	37[33]	33[34]	30[35]
Units: mg/L				
median (full range (min-max))				
D.p.	1.130 (-0.07 to 11.52)	1.700 (-0.20 to 6.60)	1.720 (0.23 to 19.67)	1.425 (-0.03 to 5.82)
D.f.	1.190 (-0.02 to 6.22)	1.750 (0.23 to 6.48)	2.240 (0.13 to 17.91)	1.900 (0.02 to 5.97)

Notes:

[32] - Safety analysis set was used for all treatment groups
D.p.: N= 40; D.f.: N=42

[33] - D.p.: N= 33; D.f.: N=34

[34] - D.p.: N= 33; D.f.: N=33

[35] - D.p.: N= 30; D.f.: N=30

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Between the signature date of the ICF and the final visit, until approx. 30 days after the last IMP administration or trial-related procedure.

Adverse event reporting additional description:

Results are shown for the safety analysis set and show treatment emergent adverse event (TEAE): any AE that started or worsened after first use of IMP until 30 days after last use of IMP or trial-related procedure. For further clarification of AEs see 'Description' section for end point 1. Frequency threshold (≥2%) was set for each age-group.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Adults (18 to ≤65 y) One Strength

Reporting group description:

Adults (18 to ≤65 y), randomized to and treated according to the One Strength dose escalation scheme.

Reporting group title	Adults (18 to ≤65 y) Standard

Reporting group description:

Adults (18 to ≤65 y), randomized to and treated according to the Standard dose escalation scheme.

Reporting group title	Adolescents (12 to <18 y) One Strength

Reporting group description:

Adolescents (12 to <18 y), randomized to and treated according to the One Strength dose escalation scheme.

Reporting group title	Adolescents (12 to <18 y) Standard

Reporting group description:

Adolescents (12 to <18 y), randomized to and treated according to the Standard dose escalation scheme.

Serious adverse events	Adults (18 to ≤65 y) One Strength	Adults (18 to ≤65 y) Standard	Adolescents (12 to <18 y) One Strength
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 42 (2.38%)	0 / 37 (0.00%)	2 / 33 (6.06%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 42 (2.38%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic reaction			

subjects affected / exposed	0 / 42 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 42 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Adolescents (12 to <18 y) Standard		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaphylactic reaction			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Adults (18 to ≤65 y) One Strength	Adults (18 to ≤65 y) Standard	Adolescents (12 to <18 y) One Strength
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 42 (54.76%)	21 / 37 (56.76%)	18 / 33 (54.55%)

Nervous system disorders			
Headache			
subjects affected / exposed	10 / 42 (23.81%)	11 / 37 (29.73%)	8 / 33 (24.24%)
occurrences (all)	29	20	16
Dizziness			
subjects affected / exposed	0 / 42 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	5 / 42 (11.90%)	4 / 37 (10.81%)	3 / 33 (9.09%)
occurrences (all)	6	13	8
Injection site pain			
subjects affected / exposed	9 / 42 (21.43%)	4 / 37 (10.81%)	1 / 33 (3.03%)
occurrences (all)	22	14	1
Injection site pruritus			
subjects affected / exposed	6 / 42 (14.29%)	4 / 37 (10.81%)	3 / 33 (9.09%)
occurrences (all)	32	17	8
Injection site swelling			
subjects affected / exposed	11 / 42 (26.19%)	7 / 37 (18.92%)	6 / 33 (18.18%)
occurrences (all)	40	18	14
Injection site oedema			
subjects affected / exposed	4 / 42 (9.52%)	1 / 37 (2.70%)	1 / 33 (3.03%)
occurrences (all)	8	1	2
Pyrexia			
subjects affected / exposed	0 / 42 (0.00%)	3 / 37 (8.11%)	1 / 33 (3.03%)
occurrences (all)	0	4	1
Fatigue			
subjects affected / exposed	2 / 42 (4.76%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	4 / 42 (9.52%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences (all)	4	0	1
Eye disorders			
Eye pruritus			

subjects affected / exposed	1 / 42 (2.38%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	4	2	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 42 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	1 / 42 (2.38%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 42 (0.00%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 42 (2.38%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences (all)	7	2	1
Dyspnoea			
subjects affected / exposed	0 / 42 (0.00%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences (all)	0	2	1
Oropharyngeal pain			
subjects affected / exposed	1 / 42 (2.38%)	3 / 37 (8.11%)	1 / 33 (3.03%)
occurrences (all)	2	3	2
Rhinorrhoea			
subjects affected / exposed	2 / 42 (4.76%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences (all)	5	1	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 42 (2.38%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
Urticaria			
subjects affected / exposed	1 / 42 (2.38%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	2 / 42 (4.76%)	1 / 37 (2.70%)	2 / 33 (6.06%)
occurrences (all)	2	1	2
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 42 (7.14%)	1 / 37 (2.70%)	1 / 33 (3.03%)
occurrences (all)	5	1	1
Bronchitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 42 (2.38%)	2 / 37 (5.41%)	3 / 33 (9.09%)
occurrences (all)	2	3	3
Oral herpes			
subjects affected / exposed	0 / 42 (0.00%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	5 / 42 (11.90%)	1 / 37 (2.70%)	1 / 33 (3.03%)
occurrences (all)	14	1	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 42 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Otitis media			
subjects affected / exposed	0 / 42 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	3

Non-serious adverse events	Adolescents (12 to <18 y) Standard		

Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 30 (40.00%)		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	 4 / 30 (13.33%) 4 0 / 30 (0.00%) 0		
General disorders and administration site conditions Injection site erythema subjects affected / exposed occurrences (all) Injection site pain subjects affected / exposed occurrences (all) Injection site pruritus subjects affected / exposed occurrences (all) Injection site swelling subjects affected / exposed occurrences (all) Injection site oedema subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1 0 / 30 (0.00%) 0 0 / 30 (0.00%) 0 1 / 30 (3.33%) 1 0 / 30 (0.00%) 0 2 / 30 (6.67%) 2 0 / 30 (0.00%) 0		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1		
Eye disorders			

Eye pruritus subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	 2 / 30 (6.67%) 10 0 / 30 (0.00%) 0		
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all)	 0 / 30 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	 0 / 30 (0.00%) 0 0 / 30 (0.00%) 0 2 / 30 (6.67%) 2 1 / 30 (3.33%) 1		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	 0 / 30 (0.00%) 0 0 / 30 (0.00%) 0		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Bronchitis			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Rhinitis			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
COVID-19			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported.

Notes: