Clinical trial results:
A randomized, double-blind, placebo-controlled study to determine tolerability and safety of different dosages of SUBLIVAC FIX Mite mixture in patients with allergic rhinitis / rhinoconjunctivitis caused by house dust mites.

Summary

EudraCT number	2014-002047-18
Trial protocol	DE
Global end of trial date	19 November 2015

Results information

Result version number	v1 (current)
This version publication date	25 January 2017
First version publication date	25 January 2017

Trial information

Trial identification

Sponsor protocol code	SM/0044

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02345278
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	HAL Allergy
Sponsor organisation address	J.H. Oortweg 15-17, Leiden, Netherlands, NL-2333 CH
Public contact	Head of Clinical Development & Pharmacovigilance, HAL Allergy, + 31 881959000, pjdkam@hal-allergy.com
Scientific contact	Head of Clinical Development & Pharmacovigilance, HAL Allergy, + 31 881959000, pjdkam@hal-allergy.com

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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 July 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 November 2015
Global end of trial reached?	Yes
Global end of trial date	19 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Determination of the tolerability and safety by local and systemic reactions of different SUBLIVAC FIX Mite mixture dosages during 1 month of treatment in patients with HDM induced allergic rhinitis/rhinoconjunctivitis in comparison with placebo

Protection of trial subjects:

First dosing of each patient was performed at the investigational site under supervision of the investigator. Adding higher dose groups was done using a staggered design, following safety evaluation by a Data Safety Monitoring Board (DSMB). Accordingly the 50,000 AUN/ml treatment group was started following safety evaluation of the first 10 days treatment period of 12 patients on 25,000 AUN/ml. Similarly 100,000 AUN/ml was started following evaluation of the first 10 days treatment with 50,000 AUN/ml in 12 patients. In addition safety was evaluated in a blinded fashion at weekly intervals during the entire treatment phase of the study.

Background therapy:

No background therapy was used

Evidence for comparator:

No active comparator was used

Actual start date of recruitment	30 April 2015
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	Germany: 81
Worldwide total number of subjects	81
EEA total number of subjects	81

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)	0
Adults (18-64 years)	81
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment took place from May to August 2015.

Pre-assignment

Screening details:

Male/female patients, 18-60 years of age with house dust mites allergy as assessed by: 1. Presence of allergic rhinitis or rhinoconjunctivitis induced by HDM for at least 1 year, 2. Positive SPT to HDM D. pter or D. far, 3. Allergen specific serum IgE (ssIgE) level in serum for HDM D. pter or D. far (> 0.7 U/ml).

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

The randomisation code list was stored in a sealed envelope in the department of Clinical Data Management of the CRO in a locked cupboard. The data manager responsible for creation and release of the randomisation list was not involved in this study until after data base lock and routine unblinding. A copy of the randomisation list was stored at a study independent person of the sponsor responsible for labelling and packing of the trial material, in order to warrant allocation concealment.

Arms

Are arms mutually exclusive?	Yes
Arm title	IMP-Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	SUBLIVAC FIX Mites placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal drops
Routes of administration	Sublingual use

Dosage and administration details:

Up dosing phase: 1 drop on 1st day, 2nd day 2 drops, till 5 drops on 5th day. Maintenance phase: maintenance dose of 5 drops (daily) started from 6th day

Arm title	IMP 10,000

Arm description: -

Arm type	Experimental
Investigational medicinal product name	SUBLIVAC FIX Mites 10,000AUN/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal solution
Routes of administration	Sublingual use

Dosage and administration details:

Up dosing phase: 1 drop on 1st day, 2nd day 2 drops, till 5 drops on 5th day. Maintenance phase: maintenance dose of 5 drops (daily) started from 6th day

Arm title	IMP 25,000

Arm description: -

Arm type	Experimental

Investigational medicinal product name	SUBLIVAC FIX Mites 25,000 AUN/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal drops
Routes of administration	Sublingual use

Dosage and administration details:

Up dosing phase: 1 drop on 1st day, 2nd day 2 drops, till 5 drops on 5th day. Maintenance phase: maintenance dose of 5 drops (daily) started from 6th day

Arm title	IMP-50,000

Arm description: -

Arm type	Experimental
Investigational medicinal product name	SUBLIVAC FIX Mites 50,000 AUN/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal drops
Routes of administration	Sublingual use

Dosage and administration details:

Up dosing phase: 1 drop on 1st day, 2nd day 2 drops, till 5 drops on 5th day. Maintenance phase: maintenance dose of 5 drops (daily) started from 6th day

Arm title	IMP-100,000

Arm description: -

Arm type	Experimental
Investigational medicinal product name	SUBLIVAC FIX Mites 100,000 AUN/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal drops
Routes of administration	Sublingual use

Dosage and administration details:

Up dosing phase: 1 drop on 1st day, 2nd day 2 drops, till 5 drops on 5th day. Maintenance phase: maintenance dose of 5 drops (daily) started from 6th day

Number of subjects in period 1	IMP-Placebo	IMP 10,000	IMP 25,000
Started	16	16	16
Completed	16	16	16
Not completed	0	0	0
Adverse event, non-fatal	-	-	-
Pregnancy	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	IMP-50,000	IMP-100,000
Started	17	16
Completed	14	14
Not completed	3	2
Adverse event, non-fatal	1	1
Pregnancy	1	-
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	IMP-Placebo
Reporting group description: -	
Reporting group title	IMP 10,000
Reporting group description: -	
Reporting group title	IMP 25,000
Reporting group description: -	
Reporting group title	IMP-50,000
Reporting group description: -	
Reporting group title	IMP-100,000
Reporting group description: -	

Reporting group values	IMP-Placebo	IMP 10,000	IMP 25,000
Number of subjects	16	16	16
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	16	16	16
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	31.13	28.13	37.44
full range (min-max)	19 to 53	18 to 49	27 to 60
Gender categorical Units: Subjects			
Female	8	8	6
Male	8	8	10

Reporting group values	IMP-50,000	IMP-100,000	Total
Number of subjects	17	16	81
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0

Adults (18-64 years)	17	16	81
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	35.53	31.63	
full range (min-max)	22 to 50	18 to 50	-
Gender categorical			
Units: Subjects			
Female	10	6	38
Male	7	10	43

End points

End points reporting groups

Reporting group title	IMP-Placebo
Reporting group description: -	
Reporting group title	IMP 10,000
Reporting group description: -	
Reporting group title	IMP 25,000
Reporting group description: -	
Reporting group title	IMP-50,000
Reporting group description: -	
Reporting group title	IMP-100,000
Reporting group description: -	

Primary: Occurrence and severity of local reactions of different doses of SUBLIVAC Fix Mites compared to placebo

End point title	Occurrence and severity of local reactions of different doses of SUBLIVAC Fix Mites compared to placebo[1]

End point description:

Occurrence and severity were assessed on basis of all local reactions observed during the treatment period of one month (from start till end of study). These reactions were selected from all treatment emergent adverse events considering their presentation (local and systemic). Results are presented by number of patients with at least one local reaction, per treatment group. For this endpoint descriptive statistics were used.

End point type	Primary

End point timeframe:

The first month of treatment, i.e. the total treatment period of the study

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: Only descriptive statistics were performed.

End point values	IMP-Placebo	IMP 10,000	IMP 25,000	IMP-50,000
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	16	16	17
Units: number of patients				
Mild	4	8	6	6
Moderate	0	0	0	0
Severe	0	0	0	0

End point values	IMP-100,000			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: number of patients				
Mild	6			
Moderate	1			
Severe	0			

Statistical analyses

No statistical analyses for this end point

Primary: Occurrence and severity of systemic reactions of different doses of SUBLIVAC Fix Mites compared to placebo

End point title	Occurrence and severity of systemic reactions of different doses of SUBLIVAC Fix Mites compared to placebo[2]

End point description:

Occurrence and severity were assessed on basis of all systemic reactions observed during the treatment period of one month (from start till end of study). These reactions were selected from all treatment emergent adverse events considering their presentation (local and systemic). Results are presented by number of patients with at least one local reaction, per treatment group. For this endpoint descriptive statistics were used.

End point type	Primary

End point timeframe:

The first month of treatment, i.e. the total treatment period of the study.

Notes:

[2] - 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: Only descriptive statistics were performed.

End point values	IMP-Placebo	IMP 10,000	IMP 25,000	IMP-50,000
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	16	16	17
Units: number of patients				
Mild	3	5	1	2
Moderate	2	1	0	1
Severe	0	0	0	0

End point values	IMP-100,000			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: number of patients				
Mild	3			
Moderate	0			
Severe	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Treatment Emergent Adverse Events have been reported from start to the end of treatment period

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	IMP-Placebo
Reporting group description: -	
Reporting group title	IMP-10,000
Reporting group description: -	
Reporting group title	IMP-25,000
Reporting group description: -	
Reporting group title	IMP-50,000
Reporting group description: -	
Reporting group title	IMP-100,000
Reporting group description: -	

Serious adverse events	IMP-Placebo	IMP-10,000	IMP-25,000
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Carpal tunnel syndrome	Additional description: Patient was hospitalized and underwent surgery because of bilateral carpal tunnel syndrome		
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	IMP-50,000	IMP-100,000	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Carpal tunnel syndrome	Additional description: Patient was hospitalized and underwent surgery because of bilateral carpal tunnel syndrome		

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	IMP-Placebo	IMP-10,000	IMP-25,000
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 16 (50.00%)	11 / 16 (68.75%)	9 / 16 (56.25%)
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Administration site reaction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	2 / 16 (12.50%)	3 / 16 (18.75%)	1 / 16 (6.25%)
occurrences (all)	3	6	1
Dyspnoea exertional			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nasal discomfort			

subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nasal obstruction			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Nasal oedema			
subjects affected / exposed	2 / 16 (12.50%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	9	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pharyngeal oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 16 (6.25%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	1	2	2
Sneezing			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Throat irritation			
subjects affected / exposed	0 / 16 (0.00%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	0	7	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 16 (6.25%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	1	5	1
Paraesthesia			
subjects affected / exposed	2 / 16 (12.50%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Sinus headache			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Lymph node pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pruritus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Vertigo			
subjects affected / exposed	0 / 16 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
Eye pruritus			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Gastric disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Glossitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia oral			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	2 / 16 (12.50%)
occurrences (all)	2	0	7
Lip swelling			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Oedema mouth			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Oral discomfort			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Oral pruritus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Paraesthesia oral			
subjects affected / exposed	3 / 16 (18.75%)	4 / 16 (25.00%)	3 / 16 (18.75%)
occurrences (all)	3	6	5
Swollen tongue			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	4 / 16 (25.00%)
occurrences (all)	0	0	5

Tongue pruritus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	5	0
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	3 / 16 (18.75%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	5	1	0
Rash			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Urticaria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 16 (12.50%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	2	1	1
Tonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Non-serious adverse events	IMP-50,000	IMP-100,000	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 17 (64.71%)	10 / 16 (62.50%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			

Administration site reaction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	3	1	
Dyspnoea exertional			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Nasal discomfort			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Nasal obstruction			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nasal oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Pharyngeal oedema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			

subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Sneezing			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Throat irritation			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Blood bilirubin increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	3 / 17 (17.65%)	1 / 16 (6.25%)	
occurrences (all)	5	1	
Paraesthesia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	

Sinus headache			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Lymph node pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pruritus			
subjects affected / exposed	0 / 17 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Vertigo			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Eye disorders			
Eye pruritus			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Gastric disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Glossitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	5	
Hypoaesthesia oral			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	20	
Lip swelling			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	6	

Nausea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Oedema mouth			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Oral discomfort			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Oral pruritus			
subjects affected / exposed	0 / 17 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	10	
Paraesthesia oral			
subjects affected / exposed	0 / 17 (0.00%)	3 / 16 (18.75%)	
occurrences (all)	0	3	
Swollen tongue			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Tongue pruritus			
subjects affected / exposed	3 / 17 (17.65%)	0 / 16 (0.00%)	
occurrences (all)	7	0	
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			

Gastrointestinal infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	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

None reported