Clinical trial results:
A Phase IIa, Randomised, Double-blind, Placebo-controlled Study to Evaluate the Efficacy, Safety and Tolerability of 3% LTX-109 compared to Placebo for nasal decolonisation of Staphylococcus aureus

Summary

EudraCT number	2022-001938-11
Trial protocol	SE
Global end of trial date	24 October 2022

Results information

Result version number	v1 (current)
This version publication date	13 September 2023
First version publication date	13 September 2023

Trial information

Trial identification

Sponsor protocol code	C22-109-08

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Pharma Holdings AS
Sponsor organisation address	Killengreensgate 8, postbox 1288, Tromsø, Norway, NO-9263
Public contact	Johnny Ryvoll, VP projects, Pharma Holdings AS, ryvoll@pharmaholdings.no
Scientific contact	Johnny Ryvoll, VP projects, Pharma Holdings AS, ryvoll@pharmaholdings.no

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	24 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 October 2022
Global end of trial reached?	Yes
Global end of trial date	24 October 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of LTX-109 (3%) gel in an intensive dosing regimen to anterior nares in healthy volunteers who have persistent carriage of S. aureus.

Protection of trial subjects:

The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and are compliant with the ICH GCP E6 (R2) guidance, the EU Clinical Trials Directive 2001/20/EC, and applicable local regulatory requirements. It was the responsibility of the Investigator/authorised associate to give each potential study subject adequate verbal and written information before any study specific assessments were performed. The information included the objectives and the procedures of the study as well as any risks or inconvenience involved. It was emphasised that participation in the study was voluntary and that the subject could withdraw from participation at any time and for any reason, without any prejudice. All subjects were given the opportunity to ask questions about the study and were given sufficient time to consider participation before signing the Informed consent form (ICF). Before performing any study-related procedures, the ICF had to be signed by the subject and by the person who conducted the informed consent discussion. A copy of the subject information including the signed ICF was provided to the subject. The ICF process was carried out in 2 steps. At the first screening visit (Visit 1), the subject was provided with the written study information and was informed about the study. The subjects signed an ICF for nasal swab for the first MSSA verification. At Visit 1 the first nasal swab was performed in line with Inclusion criterion No 3 but no other criteria were checked. A positive result of the first nasal swab at Visit 1 had to be available prior to Visit 2. Subjects who tested positive for S. aureus at Visit 1 were asked to come back for comprehensive information about the study and subsequent signing of the full ICF covering their participation in the remaining part of the study. Following the subjects' signing of second ICF, all eligibility criteria were checked at Visit 2 and verified at Visit 3 prior to dosing.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 August 2022
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	Sweden: 27
Worldwide total number of subjects	27
EEA total number of subjects	27

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)	27
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from CTC's database of healthy volunteers, as well as from strategic marketing campaigns. Advertisements in social media and other media (newspapers, internet, radio, local distribution of flyers et c.) were used to reach the target audience.

Pre-assignment

Screening details:

A total of 153 subjects were screened and 27 were randomised and dosed in the study. Most non-randomised subjects (n=113) were screening failures, most commonly due to not being persistent nasal carriers of S. aureus (MSSA) (n=104). Twelve subjects withdrew consent prior to randomisation and 1 subject was lost to follow-up.

Period 1

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

Blinding implementation details:

This was a double-blind study. The allocation of treatments was not disclosed until clean file had been declared and the database had been locked. LTX-109 and the placebo were identical in appearance.

Arms

Are arms mutually exclusive?	Yes
Arm title	LTX-109 3% Cohort 1

Arm description:

On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4).
This arm represents LTX-109 3% Cohort 1.

Arm type	Experimental
Investigational medicinal product name	LTX-109 3%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Day 1: all subjects were dosed 4 times, during an intensive dosing regimen for 4 ½-hours (every 1 ½ hours at 0, 1 ½, 3 and 4 ½hours). Before the first application of IMP, the nose was cleansed with sodium chloride (0.9 % NaCl). On each dosing occasion, a large drop (diameter approx., 8 to 9 mm corresponding to approx. 250 µL) of the assigned treatment (LTX-109 or placebo) was applied into each nostril and distributed to cover the whole area of the nostril by a qualified healthcare professional. It was important that the volume was large enough to cover the whole inner area of the nose. A nasal bandage was used to prevent the liquid from leaking. The subjects lied in an approximately 30-degree supine position during the application. After application of the IMP to both nostrils, the nostrils were gently squeezed together and were gently massaged. Subjects had to remain in the 30-degree supine position for 5 minutes after each IMP application.

Arm title	Placebo Cohort 1

Arm description:

On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4).
This arm represents Placebo Cohort 1.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Day 1: all subjects were dosed 4 times, during an intensive dosing regimen for 4 ½-hours (every 1 ½ hours at 0, 1 ½, 3 and 4 ½hours). Before the first application of IMP, the nose was cleansed with sodium chloride (0.9 % NaCl). On each dosing occasion, a large drop (diameter approx., 8 to 9 mm corresponding to approx. 250 µL) of the assigned treatment (LTX-109 or placebo) was applied into each nostril and distributed to cover the whole area of the nostril by a qualified healthcare professional. It was important that the volume was large enough to cover the whole inner area of the nose. A nasal bandage was used to prevent the liquid from leaking. The subjects lied in an approximately 30-degree supine position during the application. After application of the IMP to both nostrils, the nostrils were gently squeezed together and were gently massaged. Subjects had to remain in the 30-degree supine position for 5 minutes after each IMP application.

Arm title	LTX-109 3% Cohort 2

Arm description:

On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4).
This arm represents LTX-109 3% Cohort 2.

Arm type	Experimental
Investigational medicinal product name	LTX-109 3%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Day 1: all subjects were dosed 4 times, during an intensive dosing regimen for 4 ½-hours (every 1 ½ hours at 0, 1 ½, 3 and 4 ½hours). Before the first application of IMP, the nose was cleansed with sodium chloride (0.9 % NaCl). On each dosing occasion, a large drop (diameter approx., 8 to 9 mm corresponding to approx. 250 µL) of the assigned treatment (LTX-109 or placebo) was applied into each nostril and distributed to cover the whole area of the nostril by a qualified healthcare professional. It was important that the volume was large enough to cover the whole inner area of the nose. A nasal bandage was used to prevent the liquid from leaking. The subjects lied in an approximately 30-degree supine position during the application. After application of the IMP to both nostrils, the nostrils were gently squeezed together and were gently massaged. Subjects had to remain in the 30-degree supine position for 5 minutes after each IMP application.

Arm title	Placebo Cohort 2

Arm description:

On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4).
This arm represents Placebo Cohort 2.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Day 1: all subjects were dosed 4 times, during an intensive dosing regimen for 4 ½-hours (every 1 ½ hours at 0, 1 ½, 3 and 4 ½hours). Before the first application of IMP, the nose was cleansed with sodium chloride (0.9 % NaCl). On each dosing occasion, a large drop (diameter approx., 8 to 9 mm corresponding to approx. 250 µL) of the assigned treatment (LTX-109 or placebo) was applied into each nostril and distributed to cover the whole area of the nostril by a qualified healthcare professional. It was important that the volume was large enough to cover the whole inner area of the nose. A nasal bandage was used to prevent the liquid from leaking. The subjects lied in an approximately 30-degree supine position during the application. After application of the IMP to both nostrils, the nostrils were

gently squeezed together and were gently massaged. Subjects had to remain in the 30-degree supine position for 5 minutes after each IMP application.

Number of subjects in period 1	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2
Started	9	5	9
Completed	9	5	9

Number of subjects in period 1	Placebo Cohort 2
Started	4
Completed	4

Baseline characteristics

Reporting groups	
Reporting group title	LTX-109 3% Cohort 1
Reporting group description:	
On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4). This arm represents LTX-109 3% Cohort 1.	
Reporting group title	Placebo Cohort 1
Reporting group description:	
On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4). This arm represents Placebo Cohort 1.	
Reporting group title	LTX-109 3% Cohort 2
Reporting group description:	
On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4). This arm represents LTX-109 3% Cohort 2.	
Reporting group title	Placebo Cohort 2
Reporting group description:	
On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4). This arm represents Placebo Cohort 2.	

Reporting group values	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2
Number of subjects	9	5	9
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)	9	5	9
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	30.89	39.20	31.67
standard deviation	± 12.22	± 13.10	± 12.21
Gender categorical Units: Subjects			
Female	2	3	6
Male	7	2	3

Reporting group values	Placebo Cohort 2	Total	

Number of subjects	4	27	
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)	0	0	
Adults (18-64 years)	4	27	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	36.75		
standard deviation	± 9.430	-	
Gender categorical Units: Subjects			
Female	4	15	
Male	0	12	

End points

End points reporting groups

Reporting group title	LTX-109 3% Cohort 1

Reporting group description:

On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4).
This arm represents LTX-109 3% Cohort 1.

Reporting group title	Placebo Cohort 1

Reporting group description:

On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4).
This arm represents Placebo Cohort 1.

Reporting group title	LTX-109 3% Cohort 2

Reporting group description:

On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4).
This arm represents LTX-109 3% Cohort 2.

Reporting group title	Placebo Cohort 2

Reporting group description:

On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4).
This arm represents Placebo Cohort 2.

Subject analysis set title	LTX-109 3%
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4). This subject analysis set represents the active treatment groups receiving LTX-109.

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4). This subject analysis set represents the groups receiving placebo treatment.

Primary: Number of subjects on LTX-109 vs placebo with complete bacterial eradication period lasting for 6 hours – the Operation Window

End point title	Number of subjects on LTX-109 vs placebo with complete bacterial eradication period lasting for 6 hours – the Operation Window

End point description:

Eradication of bacteria is defined as non-presence of S. aureus (MSSA) in quantitative cultures (<5 CFU/mL). Non persistent MSSA carriers are not included in the analysis (e.g., subjects with no growth of S.aureus at time 0 are omitted from the analysis). Subjects need to be eradicated at both 6 and 12 hours to be defined as "Yes".

End point type	Primary

End point timeframe:

From 6 to 12 hours after start of treatment, corresponding to the "Operation Window".

End point values	LTX-109 3%	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	9		
Units: Number of subjects				
Yes	2	1		
No	14	8		

Statistical analyses

Statistical analysis title	Difference between LTX-109 and placebo

Statistical analysis description:

The number of subjects on LTX-109 versus placebo with bacterial eradication period lasting for 6 hours, from 6 to 12 hours after start of treatment (the OW) was analysed using Fisher's exact test. The significance level of the test was targeted at 0.0500. There was no statistically significant difference in the number of subjects with complete eradication during the Operation Window between the treatment groups.

Comparison groups	LTX-109 3% v Placebo
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Secondary: Number of subjects on LTX-109 vs placebo with bacterial eradication at 4 ½, 6 and 12 hours after start of treatment

End point title	Number of subjects on LTX-109 vs placebo with bacterial eradication at 4 ½, 6 and 12 hours after start of treatment

End point description:

Eradication of bacteria is defined as non-presence of S. aureus (MSSA) in quantitative cultures (<5 CFU/mL). Non persistent MSSA carriers are not included in the analysis (e.g., subjects with no growth of S.aureus at time 0 are omitted from the analysis).

End point type	Secondary

End point timeframe:

At 4 ½, 6 and 12 hours after start of treatment.

End point values	LTX-109 3%	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	9		
Units: Number of subjects				
Visit 3, Day 1, TIME POINT: 4H 30MIN - Yes	7	1		

Visit 3, Day 1, TIME POINT: 4H 30MIN - No	9	8		
Visit 3, Day 1, TIME POINT: 6H - Yes	5	2		
Visit 3, Day 1, TIME POINT: 6H - No	11	7		
Visit 3, Day 1, TIME POINT: 12H - Yes	4	1		
Visit 3, Day 1, TIME POINT: 12H - No	12	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change in colony forming units/mL (CFU/mL) from baseline to 4 ½, 6 and 12 hours after start of treatment (Relative change from baseline)

End point title	Percentage change in colony forming units/mL (CFU/mL) from baseline to 4 ½, 6 and 12 hours after start of treatment (Relative change from baseline)

End point description:

Eradication of bacteria is defined as non-presence of S. aureus (MSSA) in quantitative cultures (<5 CFU/mL). Non persistent MSSA carriers are not included in the analysis (e.g., subjects with no growth of S.aureus at time 0 are omitted from the analysis).

End point type	Secondary

End point timeframe:

At pre-dose (baseline) and at 4 1/2, 6 and 12 hours after start of treatment.

End point values	LTX-109 3%	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	9		
Units: percent				
arithmetic mean (standard deviation)				
Visit 3, Day 1, TIMEPOINT: 4H 30MIN	-93.8 (± 13.6)	4600 (± 13600)		
Visit 3, Day 1, TIMEPOINT: 6H	-97.6 (± 5.76)	208 (± 62048)		
Visit 3, Day 1, TIMEPOINT: 12H	-77.1 (± 69.2)	71.2 (± 460)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects on LTX-109 versus placebo with bacterial eradication period lasting for 48 hours, from 6 to 54 hours after start of treatment (the "48 hours Eradication Window")

End point title	Number of subjects on LTX-109 versus placebo with bacterial eradication period lasting for 48 hours, from 6 to 54 hours after start of treatment (the "48 hours Eradication Window")

End point description:

Eradication of bacteria is defined as non-presence of S. aureus (MSSA) in quantitative cultures (<5 CFU/mL). Non persistent MSSA carriers are not included in the analysis (e.g., subjects with no growth of

S.aureus at time 0 are omitted from the analysis). Subjects need to be eradicated at all timepoints from 6 to 54 hours to be defined as "Yes".

End point type	Secondary

End point timeframe:

From 6 to 54 hours after start of treatment (the "48 hours Eradication Window").

End point values	LTX-109 3%	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	9		
Units: Number of subjects				
Yes	0	1		
No	16	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence and frequency of adverse events (AEs)

End point title	Occurrence and frequency of adverse events (AEs)

End point description:

The grading of the severity/intensity of AEs followed the common terminology criteria for AEs (CTCAE) v5.0. AEs were assessed as unlikely, possibly or probably related to the IMP.

End point type	Secondary

End point timeframe:

AEs (including SAEs) were collected from the start of IMP administration until the end-of-study visit.

End point values	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	5	9	4
Units: Number of subjects				
Any AE	8	4	6	2
Any SAE	0	0	0	0
Any AE leading to withdrawal from study	0	0	0	0
Any AE leading to death	0	0	0	0
Causality to IMP - Unlikely Related	7	2	2	1
Causality to IMP - Possibly Related	1	2	3	1
Causality to IMP - Probably Related	5	2	3	1
Causality to Hibiscrub - Unlikely Related	7	4	6	2
Causality to Hibiscrub - Possibly Related	0	1	0	0
Causality to Hibiscrub - Probably Related	1	0	1	0
Severity - Mild	8	4	6	2
Severity - Moderate	4	0	0	0

Severity - Severe	0	0	0	0
Severity - Life-Threatening	0	0	0	0
Severity - Death	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically significant (CS) changes in laboratory parameters

End point title	Clinically significant (CS) changes in laboratory parameters

End point description:

Safety laboratory values were specified and documented as normal, abnormal not clinically significant, or abnormal clinically significant. Abnormal values assessed as clinically significant were reported as AEs. If an abnormal value was associated with corresponding clinical signs or symptoms, the sign/symptom had to be reported as the AE.

End point type	Secondary

End point timeframe:

Blood samples for the analysis of clinical chemistry and haematology were collected through venepuncture or an indwelling venous catheter at screening, pre-dose Day 1 (baseline), 54 hours after first dose and at the end-of-study visit Day 7.

End point values	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	5	9	4
Units: Number of CS abnormal findings	0	2	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically significant (CS) changes in vital signs

End point title	Clinically significant (CS) changes in vital signs

End point description:

Systolic and diastolic blood pressure and pulse were measured in supine position after 10 minutes of rest. Any vital signs outside of normal ranges were specified and documented as clinically significant or not clinically significant. Abnormal post-IMP administration findings assessed as clinically significant were reported as AEs.

End point type	Secondary

End point timeframe:

Vital signs (blood pressure and pulse) were measured at screening, pre-dose Day 1 (baseline) at 24 hours and 54 hours after first dose and at the end-of-study visit on Day 7.

End point values	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	5	9	4
Units: Number of CS abnormal findings	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically significant (CS) changes in physical examination findings

End point title	Clinically significant (CS) changes in physical examination findings

End point description:

A complete physical examination included assessments of the head, eyes, ears, nose, throat, skin, thyroid, neurological, lungs, cardiovascular, abdomen (liver and spleen), lymph nodes and extremities. Any abnormalities were specified and documented as clinically significant or not clinically significant. Abnormal post-IMP administration findings assessed by the Investigator as clinically significant were reported as AEs.

End point type	Secondary

End point timeframe:

A physical examination was performed at screening and at the end-of-study visit on Day 7 (Visit 5).

End point values	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	5	9	4
Units: Number of CS abnormal findings	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Local tolerability assessed by qualified health care professional: Erythema

End point title	Local tolerability assessed by qualified health care professional: Erythema

End point description:

Local erythema was assessed in left and right nostril and graded using a 4-graded scale (1 none/2 mild/3 moderate/4 severe).

End point type	Secondary

End point timeframe:

Day 1 (pre-dose and at 1 ½ h, 4 ½ h, 6 h, 12 h post first dose), Day 3 (54 h post first dose) and at end-of-study visit Day 7.

End point values	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[1]	5	9	4
Units: Number of subjects				
LEFT: Visit 3, Day 1, PRE-DOSE - NONE	8	5	9	4
LEFT: Visit 3, Day 1, PRE-DOSE - MILD	1	0	0	0
LEFT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN - NONE	9	5	9	4
LEFT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN - NONE	9	5	9	4
LEFT: Visit 3, Day 1, TIMEPOINT: 6H - NONE	9	5	8	4
LEFT: Visit 3, Day 1, TIMEPOINT: 6H - MILD	0	0	1	0
LEFT: Visit 3, Day 1, TIMEPOINT: 12H - NONE	7	5	7	4
LEFT: Visit 3, Day 1, TIMEPOINT: 12H - MILD	2	0	1	0
LEFT: Visit 3, Day 1, TIMEPOINT: 12H - MODERATE	0	0	1	0
LEFT: Visit 4, Day 3, TIMEPOINT: 54H - NONE	8	5	8	4
LEFT: Visit 4, Day 3, TIMEPOINT: 54H - MILD	0	0	1	0
LEFT: Visit 5, Day 7, END OF STUDY - NONE	9	5	9	4
RIGHT: Visit 3, Day 1, PRE-DOSE - NONE	9	5	9	4
RIGHT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN - NONE	9	5	9	4
RIGHT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN - NONE	9	5	9	4
RIGHT: Visit 3, Day 1, TIMEPOINT: 6H - NONE	9	5	8	4
RIGHT: Visit 3, Day 1, TIMEPOINT: 6H - MILD	0	0	1	0
RIGHT: Visit 3, Day 1, TIMEPOINT: 12H - NONE	9	4	7	3
RIGHT: Visit 3, Day 1, TIMEPOINT: 12H - MILD	0	1	2	1
RIGHT: Visit 4, Day 3, TIMEPOINT: 54H - NONE	7	5	6	4
RIGHT: Visit 4, Day 3, TIMEPOINT: 54H - MILD	1	0	3	0
RIGHT: Visit 5, Day 7, END OF STUDY - NONE	9	3	8	4
RIGHT: Visit 5, Day 7, END OF STUDY - MILD	0	2	1	0

Notes:

[1] - Subjects at Visit 4, Day 3, TIMEPOINT: 54H = 8

Statistical analyses

No statistical analyses for this end point

Secondary: Local tolerability assessed by qualified health care professional: Swelling

End point title	Local tolerability assessed by qualified health care professional: Swelling

End point description:

Local swelling was assessed in left and right nostril and graded using a 4-graded scale (1 none/2 mild/3 moderate/4 severe).

End point type	Secondary

End point timeframe:

Day 1 (pre-dose and at 1 ½ h, 4 ½ h, 6 h, 12 h post first dose), Day 3 (54 h post first dose) and at end-of-study visit Day 7.

End point values	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[2]	5	9	4
Units: Number of subjects				
LEFT: Visit 3, Day 1, PRE-DOSE - NONE	9	5	8	4
LEFT: Visit 3, Day 1, PRE-DOSE - MILD	0	0	1	0
LEFT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN - NONE	9	5	6	4
LEFT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN - MILD	0	0	2	0
LEFT: Visit 3, Day 1, TIMEPOINT: 1H30MIN- MODERATE	0	0	1	0
LEFT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN - NONE	8	5	4	4
LEFT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN - MILD	1	0	4	0
LEFT: Visit 3, Day 1, TIMEPOINT: 4H30MIN- MODERATE	0	0	1	0
LEFT: Visit 3, Day 1, TIMEPOINT: 6H - NONE	6	5	5	2
LEFT: Visit 3, Day 1, TIMEPOINT: 6H - MILD	2	0	3	2
LEFT: Visit 3, Day 1, TIMEPOINT: 6H - MODERATE	1	0	0	0
LEFT: Visit 3, Day 1, TIMEPOINT: 6H - SEVERE	0	0	1	0
LEFT: Visit 3, Day 1, TIMEPOINT: 12H - NONE	7	5	6	4
LEFT: Visit 3, Day 1, TIMEPOINT: 12H - MILD	2	0	3	0
LEFT: Visit 4, Day 3, TIMEPOINT: 54H - NONE	8	5	8	3
LEFT: Visit 4, Day 3, TIMEPOINT: 54H - MILD	0	0	1	1
LEFT: Visit 5, Day 7, END OF STUDY - NONE	9	5	8	4
LEFT: Visit 5, Day 7, END OF STUDY - MILD	0	0	1	0
RIGHT: Visit 3, Day 1, PRE-DOSE - NONE	8	4	8	2

RIGHT: Visit 3, Day 1, PRE-DOSE - MILD	1	1	1	2
RIGHT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN - NONE	8	4	8	2
RIGHT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN - MILD	1	1	1	2
RIGHT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN - NONE	7	3	7	3
RIGHT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN - MILD	2	1	2	1
RIGHT: Visit 3,Day 1, TIMEPOINT: 4H30MIN- MODERATE	0	1	0	0
RIGHT: Visit 3, Day 1, TIMEPOINT: 6H - NONE	5	2	4	2
RIGHT: Visit 3, Day 1, TIMEPOINT: 6H - MILD	4	2	4	2
RIGHT: Visit 3, Day 1, TIMEPOINT: 6H - MODERATE	0	1	1	0
RIGHT: Visit 3, Day 1, TIMEPOINT: 12H - NONE	7	5	7	4
RIGHT: Visit 3, Day 1, TIMEPOINT: 12H - MILD	2	0	2	0
RIGHT: Visit 4, Day 3, TIMEPOINT: 54H - NONE	7	5	8	4
RIGHT: Visit 4, Day 3, TIMEPOINT: 54H - MILD	1	0	0	0
RIGHT: Visit 4, Day 3, TIMEPOINT: 54H - MODERATE	0	0	1	0
RIGHT: Visit 5, Day 7, END OF STUDY - NONE	7	5	8	4
RIGHT: Visit 5, Day 7, END OF STUDY - MILD	2	0	1	0

Notes:

[2] - Subjects at Visit 4, Day 3, TIMEPOINT: 54H = 8

Statistical analyses

No statistical analyses for this end point

Secondary: Local tolerability assessed by qualified health care professional: Lesions

End point title	Local tolerability assessed by qualified health care professional: Lesions

End point description:

Local lesions were assessed in left and right nostril and graded using a 4-graded scale (1 none/2 mild/3 moderate/4 severe).

End point type	Secondary

End point timeframe:

Day 1 (pre-dose and at 1 ½ h, 4 ½ h, 6 h, 12 h post first dose), Day 3 (54 h post first dose) and at end-of-study visit Day 7.

End point values	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[3]	5	9	4
Units: Number of subjects				
LEFT: Visit 3, Day 1, PRE-DOSE - NONE	9	5	9	4
LEFT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN - NONE	8	5	8	4
LEFT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN - MILD	1	0	1	0
LEFT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN - NONE	8	5	8	4
LEFT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN - MILD	1	0	1	0
LEFT: Visit 3, Day 1, TIMEPOINT: 6H - NONE	8	5	9	4
LEFT: Visit 3, Day 1, TIMEPOINT: 6H - MILD	1	0	0	0
LEFT: Visit 3, Day 1, TIMEPOINT: 12H - NONE	9	4	8	4
LEFT: Visit 3, Day 1, TIMEPOINT: 12H - MILD	0	1	0	0
LEFT: Visit 3, Day 1, TIMEPOINT: 12H - MODERATE	0	0	1	0
LEFT: Visit 4, Day 3, TIMEPOINT: 54H - NONE	8	5	9	4
LEFT: Visit 5, Day 7, END OF STUDY - NONE	9	5	9	4
RIGHT: Visit 3, Day 1, PRE-DOSE - NONE	9	5	9	4
RIGHT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN - NONE	9	4	9	4
RIGHT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN - MILD	0	1	0	0
RIGHT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN - NONE	9	4	9	4
RIGHT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN - MILD	0	1	0	0
RIGHT: Visit 3, Day 1, TIMEPOINT: 6H - NONE	9	3	9	4
RIGHT: Visit 3, Day 1, TIMEPOINT: 6H - MILD	0	2	0	0
RIGHT: Visit 3, Day 1, TIMEPOINT: 12H - NONE	8	4	9	4
RIGHT: Visit 3, Day 1, TIMEPOINT: 12H - MILD	1	1	0	0
RIGHT: Visit 4, Day 3, TIMEPOINT: 54H - NONE	7	5	9	4
RIGHT: Visit 4, Day 3, TIMEPOINT: 54H - MILD	1	0	0	0
RIGHT: Visit 5, Day 7, END OF STUDY - NONE	9	5	9	4

Notes:

[3] - Subjects at Visit 4, Day 3, TIMEPOINT: 54H = 8

Statistical analyses

No statistical analyses for this end point

Secondary: Local tolerability assessed by subject: Pruritus (Absolute change from baseline)

End point title	Local tolerability assessed by subject: Pruritus (Absolute change from baseline)

End point description:

Each nostril was evaluated separately using a Visual analogue scale (VAS).

End point type	Secondary

End point timeframe:

Day 1 (pre-dose and at 1 ½ hours, 4 ½ hours, 6 hours and 12 hours post first dose), Day 3 (54 hours post first dose) and at the end-of-study visit Day 7.

End point values	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[4]	5	9	4
Units: (VAS) (mm)				
arithmetic mean (standard error)				
LEFT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN	14.7 (± 18.1)	1.2 (± 2.7)	4.7 (± 10.3)	-11.8 (± 16.5)
LEFT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN	6.7 (± 19.5)	11.8 (± 26.4)	17.3 (± 21.5)	-4.3 (± 27.6)
LEFT: Visit 3, Day 1, TIMEPOINT: 6H	13.2 (± 30.6)	0.0 (± 0.0)	1.9 (± 5.7)	-11.0 (± 18.3)
LEFT: Visit 3, Day 1, TIMEPOINT: 12H	9.6 (± 20.8)	0.0 (± 0.0)	1.0 (± 2.0)	-12.5 (± 16.6)
LEFT: Visit 4, Day 3, TIMEPOINT: 54H	0.4 (± 2.0)	0.0 (± 0.0)	0.7 (± 2.0)	-11.8 (± 16.5)
LEFT: Visit 5, Day 7, END OF STUDY	-2.2 (± 7.2)	0.0 (± 0.0)	0.0 (± 0.0)	-12.5 (± 16.6)
RIGHT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN	10.9 (± 16.4)	0.0 (± 0.0)	1.3 (± 2.7)	-11.5 (± 17.8)
RIGHT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN	16.6 (± 19.7)	0.0 (± 0.0)	14.3 (± 21.5)	-11.3 (± 18.0)
RIGHT: Visit 3, Day 1, TIMEPOINT: 6H	12.0 (± 21.5)	0.0 (± 0.0)	1.6 (± 3.1)	-12.5 (± 17.3)
RIGHT: Visit 3, Day 1, TIMEPOINT: 12H	11.3 (± 15.8)	0.0 (± 0.0)	-1.1 (± 9.7)	-12.5 (± 17.3)
RIGHT: Visit 4, Day 3, TIMEPOINT: 54H	-3.0 (± 8.5)	0.0 (± 0.0)	-2.8 (± 8.3)	-11.8 (± 17.6)
RIGHT: Visit 5, Day 7, END OF STUDY	-7.0 (± 15.4)	0.0 (± 0.0)	-2.8 (± 8.3)	-12.5 (± 17.3)

Notes:

[4] - Subjects at Visit 4, Day 3, TIMEPOINT: 54H = 8

Statistical analyses

No statistical analyses for this end point

Secondary: Local tolerability assessed by subject: Discomfort (Absolute change from baseline)

End point title	Local tolerability assessed by subject: Discomfort (Absolute change from baseline)

End point description:

Each nostril was evaluated separately using a VAS.

End point type	Secondary

End point timeframe:

Day 1 (pre-dose and at 1 ½ hours, 4 ½ hours, 6 hours and 12 hours post first dose), Day 3 (54 hours post first dose) and at the end-of-study visit Day 7.

End point values	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[5]	5	9	4
Units: (VAS) (mm)				
arithmetic mean (standard deviation)				
LEFT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN	32.6 (± 25.2)	-2.2 (± 4.9)	30.9 (± 22.3)	23.5 (± 37.0)
LEFT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN	36.9 (± 37.8)	8.6 (± 27.7)	42.1 (± 26.7)	18.8 (± 26.4)
LEFT: Visit 3, Day 1, TIMEPOINT: 6H	32.0 (± 38.5)	-2.0 (± 6.9)	8.4 (± 15.4)	-0.8 (± 1.5)
LEFT: Visit 3, Day 1, TIMEPOINT: 12H	22.6 (± 29.1)	-1.2 (± 5.9)	0.6 (± 9.2)	-0.8 (± 1.5)
LEFT: Visit 4, Day 3, TIMEPOINT: 54H	16.4 (± 23.9)	-2.6 (± 5.8)	-4.0 (± 7.3)	0.0 (± 0.0)
LEFT: Visit 5, Day 7, END OF STUDY	5.7 (± 18.2)	-3.2 (± 7.2)	-4.2 (± 7.2)	-0.8 (± 1.5)
RIGHT: Visit 3, Day 1, TIMEPOINT: 1H 30MIN	34.1 (± 22.3)	0.0 (± 0.0)	25.9 (± 19.9)	15.3 (± 21.0)
RIGHT: Visit 3, Day 1, TIMEPOINT: 4H 30MIN	40.0 (± 38.3)	4.0 (± 8.9)	44.9 (± 27.6)	12.3 (± 18.1)
RIGHT: Visit 3, Day 1, TIMEPOINT: 6H	33.9 (± 39.8)	0.0 (± 0.0)	8.6 (± 11.4)	-0.8 (± 1.5)
RIGHT: Visit 3, Day 1, TIMEPOINT: 12H	27.4 (± 36.5)	0.6 (± 1.3)	3.3 (± 12.8)	8.3 (± 18.6)
RIGHT: Visit 4, Day 3, TIMEPOINT: 54H	12.3 (± 24.3)	0.0 (± 0.0)	-2.3 (± 7.0)	0.0 (± 0.0)
RIGHT: Visit 5, Day 7, END OF STUDY	3.7 (± 20.3)	0.0 (± 0.0)	-2.3 (± 7.0)	-0.8 (± 1.5)

Notes:

[5] - Subjects at Visit 4, Day 3, TIMEPOINT: 54H = 8

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs (including SAEs) were collected from the start of IMP administration until the end-of-study visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	LTX-109 3% Cohort 1

Reporting group description:

On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4).
This arm represents LTX-109 3% Cohort 1.

Reporting group title	Placebo Cohort 1

Reporting group description:

On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4).
This arm represents Placebo Cohort 1.

Reporting group title	LTX-109 3% Cohort 2

Reporting group description:

On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4).
This arm represents LTX-109 3% Cohort 2.

Reporting group title	Placebo Cohort 2

Reporting group description:

On Day 1, subjects were randomised in a 2:1 ratio to receive either LTX-109 (n=18) or placebo (n=9). Cohort (1 [8 doses] or 2 [6 doses]) was used as a stratification variable to preserve the 2:1 treatment randomisation ratio in each cohort (LTX-109 n=9 or placebo n=5/4).
This arm represents Placebo Cohort 2.

Serious adverse events	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Placebo Cohort 2		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	LTX-109 3% Cohort 1	Placebo Cohort 1	LTX-109 3% Cohort 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 9 (88.89%)	4 / 5 (80.00%)	6 / 9 (66.67%)
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	4 / 9 (44.44%)	2 / 5 (40.00%)	1 / 9 (11.11%)
occurrences (all)	5	2	1
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	4 / 9 (44.44%)	2 / 5 (40.00%)	4 / 9 (44.44%)
occurrences (all)	9	2	6
Fatigue			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Central serous chorioretinopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Eye irritation			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Visual impairment			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Lip blister			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Oral pruritus			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Dry throat			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Nasal congestion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Nasal discomfort			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Paranasal sinus discomfort			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Sinus pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Placebo Cohort 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)		

Vascular disorders Flushing subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1 0 / 4 (0.00%) 0		
General disorders and administration site conditions Application site pain subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 2 0 / 4 (0.00%) 0		
Eye disorders Central serous chorioretinopathy subjects affected / exposed occurrences (all) Eye irritation subjects affected / exposed occurrences (all) Visual impairment subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		
Gastrointestinal disorders Dyspepsia subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all) Lip blister	 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Oral pruritus			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dry throat			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Nasal discomfort			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Paranasal sinus discomfort			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Sinus pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Throat irritation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			

Dry skin subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Rash subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Rhinitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 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