Clinical trial results:
A 24-Week Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study Evaluating the Efficacy and Safety of Intranasal Administration of 186 and 372 g of OPN-375 Twice a Day (BID) in Subjects with Chronic Rhinoinusitis Without the Presence of Nasal Polyps

Summary

EudraCT number	2019-000648-86
Trial protocol	GB CZ PL ES BG RO
Global end of trial date	04 May 2022

Results information

Result version number	v1 (current)
This version publication date	25 May 2023
First version publication date	25 May 2023

Trial information

Trial identification

Sponsor protocol code	OPN-FLU-CS-3206

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 110089

Notes:

Sponsors

Sponsor organisation name	OptiNose US, Inc.
Sponsor organisation address	1020 Stony Hill Road, Suite 300, Yardley, PA, United States, 19067
Public contact	John Messina, Sr. VP Global Clinical Research and Medical Affairs, OptiNose US, Inc., john.messina@optinose.com
Scientific contact	John Messina, Sr. VP Global Clinical Research and Medical Affairs, OptiNose US, Inc., john.messina@optinose.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	04 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 May 2022
Global end of trial reached?	Yes
Global end of trial date	04 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to compare the efficacy of intranasal administration of twice-daily doses of 186 and 372 µg of OPN-375 (fluticasone propionate) with placebo in subjects with chronic rhinosinusitis (CRS) using the following co-primary endpoints:
• change from baseline in symptoms as measured by a composite score of nasal symptoms (CSNS): congestion, facial pain or pressure sensation, and nasal discharge (anterior and/or posterior) at the end of Week 4
and
• change from baseline to Week 24/ET in the average percent of the opacified volume (APOV) in the ethmoid and maxillary sinuses

Protection of trial subjects:

Subjects will be informed that they are free to withdraw from study treatment and/or the study at any time at their own request without prejudice to their future medical care, or that they may be withdrawn at any time at the discretion of the investigator or Sponsor for safety, nonadherence to protocol requirements, or administrative reasons (eg, termination of the study ty Sponsor). Subjects wishing to withdraw from study treatment will be strongly encouraged to continue in the study and have all scheduled study procedures performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2019
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	United States: 22
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Georgia: 23
Country: Number of subjects enrolled	Poland: 103
Country: Number of subjects enrolled	Romania: 24
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Bulgaria: 16
Country: Number of subjects enrolled	Czechia: 18
Worldwide total number of subjects	223
EEA total number of subjects	171

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)	196
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was carried out in subjects with chronic sinusitis without nasal polyps.

Pre-assignment

Screening details:

Subjects who met screening eligibility criteria at Visit 1 (Screening) entered a 7- to 21-day, singleblind, placebo, run-in period to ensure symptom eligibility criteria were met, and (if meeting symptom criteria) to have CT verification of eligibility.

Pre-assignment period milestones

Number of subjects started	475[1]
Number of subjects completed	222

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failed: 1
Reason: Number of subjects	Not eligible: 252

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 253 subjects failed the eligibility verification phase and were never enrolled into the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo nasal spray, 1 or 2 sprays per nostril twice daily

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

1 or 2 sprays per nostril twice daily

Arm title	OPN-375 (186 µg BID)

Arm description:

OPN-375 1 spray per nostril (186 µg) twice daily (BID).

One subject was randomized in error (inadvertently registered as randomized; misrandomized) by the study site in the interactive web response system that was supposed to be “screen failed.” The error was recognized at the time of the misrandomization and the subject never received any investigational product and was therefore not treated. This subject is presented as "screen failed" in the preassignment period details and has not been included as part of the study results. This subject was not included in the baseline or any of the results tables.

Arm type	Experimental
Investigational medicinal product name	OPN-375
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

1 spray per nostril (186 µg per dose)

Arm title	OPN-375 (372 µg BID)

Arm description:

OPN-375 2 sprays per nostril (372 µg) twice daily (BID)

Arm type	Experimental
Investigational medicinal product name	OPN-375
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

2 sprays per nostril (372 µg per dose)

Number of subjects in period 1[2]	Placebo	OPN-375 (186 µg BID)	OPN-375 (372 µg BID)
Started	75	73	74
Completed	69	70	71
Not completed	6	3	3
Consent withdrawn by subject	1	1	1
Adverse event, non-fatal	2	1	1
Lost to follow-up	1	-	-
Lack of efficacy	2	1	-
Protocol deviation	-	-	1

Notes:

[2] - 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: One subject was randomized in error (inadvertently registered as randomized; misrandomized) by the study site in the interactive web response system that was supposed to be “screen failed.” The error was recognized at the time of the misrandomization and the subject never received any investigational product. This subject is presented as "screen failed" in the preassignment period details and has not been included as part of the study results but is included in the worldwide number enrolled.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo nasal spray, 1 or 2 sprays per nostril twice daily	
Reporting group title	OPN-375 (186 µg BID)
Reporting group description:	
OPN-375 1 spray per nostril (186 µg) twice daily (BID). One subject was randomized in error (inadvertently registered as randomized; misrandomized) by the study site in the interactive web response system that was supposed to be "screen failed." The error was recognized at the time of the misrandomization and the subject never received any investigational product and was therefore not treated. This subject is presented as "screen failed" in the preassignment period details and has not been included as part of the study results. This subject was not included in the baseline or any of the results tables.	
Reporting group title	OPN-375 (372 µg BID)
Reporting group description:	
OPN-375 2 sprays per nostril (372 µg) twice daily (BID)	

Reporting group values	Placebo	OPN-375 (186 µg BID)	OPN-375 (372 µg BID)
Number of subjects	75	73	74
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)	67	62	66
From 65-84 years	8	11	8
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	48.7	47.1	49.4
standard deviation	± 12.34	± 13.75	± 13.53
Gender categorical Units: Subjects			
Female	32	40	39
Male	43	33	35
Race Units: Subjects			
White	74	72	73
Black or African American	1	1	0
Other	0	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	1	2	0

Not Hispanic or Latino	74	71	74
Previous or current diagnosis of nasal polyps Units: Subjects			
Yes	16	9	18
No	59	64	56
Diagnosed with aspirin esacerbated respiratory disease (AERD) Units: Subjects			
Yes	2	1	0
No	73	72	74
Diagnosed with environmental allergies Units: Subjects			
Yes	23	24	22
No	52	49	52
Currently receiving immunotherapy for environmental allergies (denominator = subjects diagnosed with			
Currently receiving immunotherapy for environmental allergies (denominator = subjects diagnosed with environmental allergies) Not applicable = subjects not diagnosed with environmental allergies			
Units: Subjects			
Yes	1	3	2
No	24	23	21
Not applicable	50	47	51
Number of acute exacerbations of chronic sinusitis with an antibiotic or oral steriod last year Units: Subjects			
0 acute sinusitis exacerbations	34	36	34
1 acute sinusitis exacerbations	20	17	19
2 acute sinusitis exacerbations	11	10	10
3 acute sinusitis exacerbations	5	5	6
4 acute sinusitis exacerbations	3	1	3
5 acute sinusitis exacerbations	1	4	1
6 acute sinusitis exacerbations	0	0	1
7 acute sinusitis exacerbations	0	0	0
8 acute sinusitis exacerbations	1	0	0
Prior Sinus Surgery (Subgroups for Analyses in the Full Analysis Set)			
Prior Sinus Surgery only counts any ethmoidectomy or maxillary antrostomy.			
Units: Subjects			
Yes	27	25	26
No	48	47	47
Not applicable	0	1	1
Weight Units: kilograms			
arithmetic mean	77.90	75.66	82.07
standard deviation	± 16.860	± 14.935	± 20.451

Reporting group values	Total		
Number of subjects	222		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	195		
From 65-84 years	27		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	111		
Male	111		
Race Units: Subjects			
White	219		
Black or African American	2		
Other	1		
Ethnicity Units: Subjects			
Hispanic or Latino	3		
Not Hispanic or Latino	219		
Previous or current diagnosis of nasal polyps Units: Subjects			
Yes	43		
No	179		
Diagnosed with aspirin esacerbated respiratory disease (AERD) Units: Subjects			
Yes	3		
No	219		
Diagnosed with environmental allergies Units: Subjects			
Yes	69		
No	153		
Currently receiving immunotherapy for environmental allergies (denominator = subjects diagnosed with			
Currently receiving immunotherapy for environmental allergies (denominator = subjects diagnosed with environmental allergies) Not applicable = subjects not diagnosed with environmental allergies			
Units: Subjects			
Yes	6		
No	68		

Not applicable	148		
Number of acute exacerbations of chronic sinusitis with an antibiotic or oral steriod last year Units: Subjects			
0 acute sinusitis exacerbations	104		
1 acute sinusitis exacerbations	56		
2 acute sinusitis exacerbations	31		
3 acute sinusitis exacerbations	16		
4 acute sinusitis exacerbations	7		
5 acute sinusitis exacerbations	6		
6 acute sinusitis exacerbations	1		
7 acute sinusitis exacerbations	0		
8 acute sinusitis exacerbations	1		
Prior Sinus Surgery (Subgroups for Analyses in the Full Analysis Set)			
Prior Sinus Surgery only counts any ethmoidectomy or maxillary antrostomy.			
Units: Subjects			
Yes	78		
No	142		
Not applicable	2		
Weight Units: kilograms arithmetic mean standard deviation	 -		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo nasal spray, 1 or 2 sprays per nostril twice daily	
Reporting group title	OPN-375 (186 µg BID)
Reporting group description:	
OPN-375 1 spray per nostril (186 µg) twice daily (BID). One subject was randomized in error (inadvertently registered as randomized; misrandomized) by the study site in the interactive web response system that was supposed to be "screen failed." The error was recognized at the time of the misrandomization and the subject never received any investigational product and was therefore not treated. This subject is presented as "screen failed" in the preassignment period details and has not been included as part of the study results. This subject was not included in the baseline or any of the results tables.	
Reporting group title	OPN-375 (372 µg BID)
Reporting group description:	
OPN-375 2 sprays per nostril (372 µg) twice daily (BID)	

Primary: Change from Baseline to Week 4 in the 7-Day Average of Instantaneous Morning Composite Symptom Score

End point title	Change from Baseline to Week 4 in the 7-Day Average of Instantaneous Morning Composite Symptom Score
End point description:	
Change from baseline to the end of Week 4 in average total instantaneous morning (AM) scores (evaluation of symptom severity immediately preceding the time of scoring in the morning) of a composite symptom score (CSS): nasal congestion, facial pain or pressure sensation, and nasal discharge (anterior and/or posterior). LS = least squares CSS = composite symptom score -9999/9999= not applicable	
End point type	Primary
End point timeframe:	
Baseline to Week 4	

End point values	Placebo	OPN-375 (186 µg BID)	OPN-375 (372 µg BID)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72	72	71	
Units: LS mean change from baseline in CSS				
least squares mean (confidence interval 95%)				
LS Mean Change (from baseline)	-0.81 (-9999 to 9999)	-1.54 (-9999 to 9999)	-1.74 (-9999 to 9999)	
LS Mean Difference (active minus placebo)	9999 (-9999 to 9999)	-0.73 (-1.29 to -0.17)	-0.93 (-1.49 to -0.37)	

Statistical analyses

Statistical analysis title	OPN-375 (186 µg BID) versus Placebo
Comparison groups	OPN-375 (186 µg BID) v Placebo
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	Mixed models analysis

Statistical analysis title	OPN-375 (372 µg BID) versus Placebo
Comparison groups	Placebo v OPN-375 (372 µg BID)
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Mixed models analysis

Primary: Change from Baseline to Week 24/early termination in average of the percentages of opacified volume in Ethmoid and Maxillary Sinuses Combined

End point title	Change from Baseline to Week 24/early termination in average of the percentages of opacified volume in Ethmoid and Maxillary Sinuses Combined

End point description:

Change from Baseline to Week 24/early termination in average of the percentages of opacified volume in Ethmoid and Maxillary Sinuses Combined (Full Analysis Set – Primary Estimand)

LS = least squares
-9999/9999 = not applicable

End point type	Primary

End point timeframe:

Baseline to Week 24 or early termination

End point values	Placebo	OPN-375 (186 µg BID)	OPN-375 (372 µg BID)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	66	70	69	
Units: LS mean change from baseline				
least squares mean (confidence interval 95%)				
LS Mean Change (from baseline)	1.19 (-9999 to 9999)	-7.00 (-9999 to 9999)	-5.14 (-9999 to 9999)	
LS Mean Difference (active minus placebo)	9999 (-9999 to 9999)	-8.19 (-12.93 to -3.45)	-6.33 (-11.08 to -1.58)	

Statistical analyses

Statistical analysis title	OPN-375 (186 µg BID) versus placebo
Comparison groups	Placebo v OPN-375 (186 µg BID)
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA

Statistical analysis title	OPN-375 (372 µg BID) versus placebo
Comparison groups	Placebo v OPN-375 (372 µg BID)
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	ANCOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

.Period of observation for collection of AEs extended from time the subject gave informed consent until completion of the double-blind treatment period or an early termination visit. Serious AEs were reported through 30 days after

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo nasal spray, 1 or 2 sprays per nostril twice daily

Reporting group title	OPN-375 186 µg

Reporting group description:

OPN-375 1 spray per nostril (186 µg) twice daily (BID). Adverse events are provided for the safety analysis set.

Reporting group title	OPN-375 372 µg

Reporting group description:

OPN-375 2 sprays per nostril (372 µg) twice daily (BID)

Serious adverse events	Placebo	OPN-375 186 µg	OPN-375 372 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	4 / 74 (5.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	OPN-375 186 µg	OPN-375 372 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 75 (41.33%)	24 / 73 (32.88%)	43 / 74 (58.11%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	2 / 74 (2.70%)
occurrences (all)	3	0	2
Chest discomfort			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Fatigue			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 75 (0.00%)	4 / 73 (5.48%)	7 / 74 (9.46%)
occurrences (all)	0	4	16
Asthma			
subjects affected / exposed	4 / 75 (5.33%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	4	0	2
Cough			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	2	0	1
Dyspnoea			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	1	0	1
Rhinalgia			
subjects affected / exposed	1 / 75 (1.33%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	1	1	0
Rhinitis allergic			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Interstitial lung disease			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Nasal mucosal erosion			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Nasal polyps			
subjects affected / exposed	4 / 75 (5.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	4	0	0
Nasal septum ulceration			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			

subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	3 / 74 (4.05%)
occurrences (all)	1	0	3
Insomnia			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	1 / 74 (1.35%)
occurrences (all)	0	1	1
Anxiety			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Persistent depressive disorder			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	2	0	0
Investigations			
Intraocular pressure increased			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	1 / 74 (1.35%)
occurrences (all)	0	1	1
Blood pressure increased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Foot fracture			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Vaccination complication			

subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	2	0	0
Congenital, familial and genetic disorders			
Block vertebra			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Chronic coronary syndrome			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 75 (8.00%)	2 / 73 (2.74%)	7 / 74 (9.46%)
occurrences (all)	8	2	11
Sinus headache			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Anosmia			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Cataract cortical			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	1	0	1
Cataract nuclear			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	2	0	1
Conjunctival haemorrhage			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Eye irritation			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Eye allergy			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Toothache			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Madarosis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Spinal osteoarthritis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Arthralgia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	1	0	1
Back pain			
subjects affected / exposed	2 / 75 (2.67%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	2	0	1
Myalgia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	1	0	1
Osteoarthritis			

subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 75 (2.67%)	3 / 73 (4.11%)	7 / 74 (9.46%)
occurrences (all)	2	3	7
Nasopharyngitis			
subjects affected / exposed	5 / 75 (6.67%)	3 / 73 (4.11%)	4 / 74 (5.41%)
occurrences (all)	6	3	5
Chronic sinusitis			
subjects affected / exposed	5 / 75 (6.67%)	1 / 73 (1.37%)	3 / 74 (4.05%)
occurrences (all)	5	2	3
Upper respiratory tract infection			
subjects affected / exposed	2 / 75 (2.67%)	2 / 73 (2.74%)	1 / 74 (1.35%)
occurrences (all)	2	2	1
Influenza			
subjects affected / exposed	0 / 75 (0.00%)	2 / 73 (2.74%)	0 / 74 (0.00%)
occurrences (all)	0	3	0
Sinusitis			
subjects affected / exposed	3 / 75 (4.00%)	0 / 73 (0.00%)	2 / 74 (2.70%)
occurrences (all)	8	0	2
Urinary tract infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Acute sinusitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Lyme disease			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 74 (0.00%)
occurrences (all)	0	1	0

Herpes zoster			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Laryngopharyngitis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Hyperglycaemia			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 July 2020	Amendment 1: Added a biomarker substudy; modified inclusion/exclusion criteria; added "cobicistat" to examples of CYP3A4 inhibitors; modified the protocol in reaction to the Coronavirus Disease 2019 (COVID-19) pandemic; changed physical examination at screening from full to brief; clarified that urine pregnancy test was required at each visit; revised an endpoint related to sinus volume occupied by disease from evaluating "each" maxillary and ethmoid sinus occupied by disease to evaluating the "worst" maxillary and "worst" ethmoid sinus; added an assessment of the impact of treatment on subjects approved for surgery who no longer elect to undergo surgery; limited ocular assessments to visual acuity, cataract assessment, and IOP assessment (later removed for pandemic reasons); and removed receipt of systemic corticosteroids (oral or parenteral) as a reason for withdrawing a subject from the study.
28 August 2020	Amendment 2: Removed ocular assessments; removed "Early Termination (ET)" from objectives and endpoints; modified exclusion criteria; updated statistical analyses; clarified concomitant medication vs rescue medications.
15 October 2021	Amendment 3: Modified key secondary and other secondary objectives/endpoints by moving SF36v2 MCS and PCS endpoints from key secondary to other secondary; added key secondary objectives/endpoints to be analyzed using pooled data from Studies 3205 and 3206; added "Early Termination (ET)" back to the objectives and endpoints; and updated sample size based on results from an IA of Study 3205.

Notes:

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.

Not applicable.

Notes: