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 Sinusitis With or Without the Presence of Nasal Polyps

Summary

EudraCT number	2019-000368-12
Trial protocol	GB BG
Global end of trial date	19 January 2022

Results information

Result version number	v1 (current)
This version publication date	01 April 2023
First version publication date	01 April 2023

Trial information

Trial identification

Sponsor protocol code	OPN-FLU-CS-3205

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	Global Clinical Operations, OptiNose US, Inc., john.messina@optinose.com
Scientific contact	Global Clinical Operations, 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	19 January 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 January 2022
Global end of trial reached?	Yes
Global end of trial date	19 January 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 sinusitis 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/Early Termination (ET) in the average percent of the volume opacified (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 study by 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	01 November 2018
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	Russian Federation: 24
Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	United States: 183
Country: Number of subjects enrolled	Poland: 90
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Bulgaria: 7
Country: Number of subjects enrolled	Georgia: 2
Worldwide total number of subjects	332
EEA total number of subjects	105

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)	277
From 65 to 84 years	54
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

Subjects who met eligibility criteria at screening were dispensed a single-blind kit containing 2 placebo units marked "1" and "2" for use during the 7- to 21-day. Subjects self-administered 1 spray per nostril each morning and evening. Symptoms were assessed to ensure symptom eligibility criteria and a CT scan was obtained if necessary.

Pre-assignment period milestones

Number of subjects started	556[1]
Number of subjects completed	332

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Not eligible for study treatment: 224

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: 224 subjects failed screening and were never enrolled into the study

Period 1

Period 1 title	Double-blind Treatment Phase (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)

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	Placebo	OPN-375 (186 µg BID)	OPN-375 (372 µg BID)
Started	112	111	109
Completed	96	102	101
Not completed	16	9	8
Consent withdrawn by subject	1	-	1
Adverse event, non-fatal	3	2	2
Not specified	-	2	2
Lost to follow-up	2	1	1
Lack of efficacy	9	4	2
Protocol deviation	1	-	-

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)	
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	112	111	109
Age categorical Units: Subjects			
Adults (18-64 years)	89	95	93
From 65-84 years	23	16	15
85 years and over	0	0	1
Age continuous Units: years			
arithmetic mean	49.2	48.4	49.6
standard deviation	± 15.26	± 13.85	± 13.49
Gender categorical Units: Subjects			
Female	51	47	43
Male	61	64	66
Race Units: Subjects			
White	101	99	99
American Indian or Alaska Native	0	1	0
Black or African American	6	10	4
Asian	4	1	5
Other	1	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	8	1	9
Not Hispanic or Latino	104	110	100
Previous or current diagnosis of nasal polyps Units: Subjects			
Yes	78	78	77
No	34	33	32
Number of acute sinusitis exacerbations treated with an antibiotic or oral steroids in last year Units: Subjects			
0 acute sinusitis exacerbations	50	48	49

1 acute sinusitis exacerbation	22	23	29
2 acute sinusitis exacerbations	17	15	11
3 acute sinusitis exacerbations	14	13	9
4 acute sinusitis exacerbations	5	9	9
5 acute sinusitis exacerbations	2	2	1
6 acute sinusitis exacerbations	2	0	1
7 acute sinusitis exacerbations	0	1	0
Nasal Polyp (Subgroups for Analyses in the Full Analysis Set) Units: Subjects			
Present	69	69	67
Absent	41	41	40
Not part of the Full Analysis Set	2	1	2
Prior Sinus Surgery (Subgroups for Analyses in the Full Analysis Set)			
Prior Sinus Surgery only counts any ethmoidectomy or maxillary antrostomy.			
Units: Subjects			
Yes	44	51	42
No	66	59	65
Not part of the Full Analysis Set	2	1	2
Weight Units: kilogram			
arithmetic mean	84.04	82.74	83.78
standard deviation	± 21.610	± 20.882	± 18.803

Reporting group values	Total		
Number of subjects	332		
Age categorical Units: Subjects			
Adults (18-64 years)	277		
From 65-84 years	54		
85 years and over	1		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	141		
Male	191		
Race Units: Subjects			
White	299		
American Indian or Alaska Native	1		
Black or African American	20		
Asian	10		
Other	2		
Ethnicity Units: Subjects			
Hispanic or Latino	18		
Not Hispanic or Latino	314		
Previous or current diagnosis of nasal			

polyps Units: Subjects			
Yes	233		
No	99		
Number of acute sinusitis exacerbations treated with an antibiotic or oral steroids in last year Units: Subjects			
0 acute sinusitis exacerbations	147		
1 acute sinusitis exacerbation	74		
2 acute sinusitis exacerbations	43		
3 acute sinusitis exacerbations	36		
4 acute sinusitis exacerbations	23		
5 acute sinusitis exacerbations	5		
6 acute sinusitis exacerbations	3		
7 acute sinusitis exacerbations	1		
Nasal Polyp (Subgroups for Analyses in the Full Analysis Set) Units: Subjects			
Present	205		
Absent	122		
Not part of the Full Analysis Set	5		
Prior Sinus Surgery (Subgroups for Analyses in the Full Analysis Set)			
Prior Sinus Surgery only counts any ethmoidectomy or maxillary antrostomy.			
Units: Subjects			
Yes	137		
No	190		
Not part of the Full Analysis Set	5		
Weight Units: kilogram			
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)	
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: LS = least squares. CSS = composite symptom score. -9999 = not applicable 0000 = 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	110	110	107	
Units: LS Mean Change from Baseline in CSS				
least squares mean (confidence interval 95%)				
LS Mean Change (from baseline)	-0.62 (-9999 to 0000)	-1.58 (-9999 to 0000)	-1.60 (-9999 to 0000)	
LS Mean Difference (active minus placebo)	0000 (0000 to 0000)	-0.97 (-1.41 to -0.52)	-0.98 (-1.43 to -0.54)	

Statistical analyses

Statistical analysis title	P-value versus Placebo

Statistical analysis description:

P-value versus Placebo of OPN-375 (186 µg BID) and P-value versus Placebo of OPN-375 (372 µg BID).

Inferential statistics are based on a linear mixed model for repeated measures (MMRM) including

categorical effects for previous sinus surgery, nasal polyp status, treatment, week (2, 4), treatment-by-week interaction, and continuous covariate: baseline 7-day average score, with baseline score-by-week interaction.

Comparison groups	OPN-375 (186 µg BID) v OPN-375 (372 µg BID) v Placebo
Number of subjects included in analysis	327
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM

Primary: Change from Baseline to Week 24/ET in APOV in Ethmoid and Maxillary Sinuses Combined

End point title	Change from Baseline to Week 24/ET in APOV in Ethmoid and Maxillary Sinuses Combined

End point description:

ET = early termination.
APOV = average of the percentages of opacified volume.
LS = least squares.
-9999 = not applicable.
9999 = not applicable.

End point type	Primary

End point timeframe:

Baseline to Week 24.

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	110	110	107	
Units: LS Mean Change from Baseline				
least squares mean (confidence interval 95%)				
LS Mean Change (from baseline)	-1.60 (-9999 to 9999)	-5.58 (-9999 to 9999)	-6.20 (-9999 to 9999)	
LS Mean Difference (active minus placebo)	9999 (-9999 to 9999)	-3.98 (-7.86 to -0.09)	-4.59 (-8.41 to -0.78)	

Statistical analyses

Statistical analysis title	P-value versus Placebo for OPN-375 (186 µg BID)

Statistical analysis description:

Inferential statistics are based on multiple imputation of a linear analysis of covariance (ANCOVA) model including categorical effects for nasal polyp status, previous sinus surgery, treatment, and continuous baseline value as covariate.

Comparison groups	OPN-375 (186 µg BID) v Placebo

Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.045
Method	ANCOVA

Statistical analysis title	P-value versus Placebo for OPN-375 (372 µg BID)
Comparison groups	Placebo v OPN-375 (372 µg BID)
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.018
Method	ANCOVA

Notes:

[1] - Inferential statistics are based on multiple imputation of a linear analysis of covariance (ANCOVA) model including categorical effects for nasal polyp status, previous sinus surgery, treatment, and continuous baseline value as covariate.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Pretreatment (Screening/Run-in) period to end of treatment (Week 24)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
All enrolled/randomized subjects who received at least 1 dose of placebo	
Reporting group title	OPN-375 186 µg
Reporting group description:	
All enrolled/randomized subjects who received at least 1 dose of randomized study treatment (186 µg twice daily).	
Reporting group title	OPN-375 372 µg
Reporting group description:	
All enrolled/randomized subjects who received at least 1 dose of randomized study treatment (372 µg twice daily).	

Serious adverse events	Placebo	OPN-375 186 µg	OPN-375 372 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 112 (2.68%)	1 / 111 (0.90%)	2 / 109 (1.83%)
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)			
Uterine leiomyoma			
subjects affected / exposed	1 / 112 (0.89%)	0 / 111 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 112 (0.00%)	0 / 111 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	0 / 112 (0.00%)	1 / 111 (0.90%)	0 / 109 (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
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	1 / 112 (0.89%)	0 / 111 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	1 / 112 (0.89%)	0 / 111 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Alcoholic pancreatitis			
subjects affected / exposed	0 / 112 (0.00%)	0 / 111 (0.00%)	1 / 109 (0.92%)
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	2 / 112 (1.79%)	0 / 111 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			
subjects affected / exposed	1 / 112 (0.89%)	0 / 111 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1.5 %

Non-serious adverse events	Placebo	OPN-375 186 µg	OPN-375 372 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 112 (51.79%)	57 / 111 (51.35%)	52 / 109 (47.71%)
Investigations			

Intraocular pressure increased			
subjects affected / exposed	0 / 112 (0.00%)	2 / 111 (1.80%)	0 / 109 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	3 / 112 (2.68%)	0 / 111 (0.00%)	0 / 109 (0.00%)
occurrences (all)	3	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 112 (0.00%)	2 / 111 (1.80%)	1 / 109 (0.92%)
occurrences (all)	0	2	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 112 (0.89%)	2 / 111 (1.80%)	3 / 109 (2.75%)
occurrences (all)	2	2	4
Dizziness			
subjects affected / exposed	0 / 112 (0.00%)	0 / 111 (0.00%)	3 / 109 (2.75%)
occurrences (all)	0	0	3
Parosmia			
subjects affected / exposed	1 / 112 (0.89%)	0 / 111 (0.00%)	2 / 109 (1.83%)
occurrences (all)	1	0	4
Sinus headache			
subjects affected / exposed	2 / 112 (1.79%)	0 / 111 (0.00%)	0 / 109 (0.00%)
occurrences (all)	2	0	0
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 112 (0.00%)	2 / 111 (1.80%)	0 / 109 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
Cataract nuclear			
subjects affected / exposed	0 / 112 (0.00%)	5 / 111 (4.50%)	4 / 109 (3.67%)
occurrences (all)	0	5	4
Cataract cortical			
subjects affected / exposed	1 / 112 (0.89%)	6 / 111 (5.41%)	2 / 109 (1.83%)
occurrences (all)	1	6	3
Cataract subcapsular			

subjects affected / exposed	2 / 112 (1.79%)	1 / 111 (0.90%)	1 / 109 (0.92%)
occurrences (all)	2	1	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 112 (1.79%)	1 / 111 (0.90%)	2 / 109 (1.83%)
occurrences (all)	2	1	2
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 112 (0.89%)	5 / 111 (4.50%)	13 / 109 (11.93%)
occurrences (all)	1	8	15
Asthma			
subjects affected / exposed	1 / 112 (0.89%)	5 / 111 (4.50%)	4 / 109 (3.67%)
occurrences (all)	2	6	4
Nasal polyps	Additional description: One subject reported an AE of "nasal polyps exacerbation" which was coded to the MedDRA preferred term of "nasal polyps".		
subjects affected / exposed	8 / 112 (7.14%)	4 / 111 (3.60%)	2 / 109 (1.83%)
occurrences (all)	10	4	2
Nasal congestion			
subjects affected / exposed	5 / 112 (4.46%)	1 / 111 (0.90%)	2 / 109 (1.83%)
occurrences (all)	6	1	4
Nasal mucosal erosion			
subjects affected / exposed	0 / 112 (0.00%)	2 / 111 (1.80%)	1 / 109 (0.92%)
occurrences (all)	0	2	1
Haemoptysis			
subjects affected / exposed	0 / 112 (0.00%)	2 / 111 (1.80%)	0 / 109 (0.00%)
occurrences (all)	0	3	0
Oropharyngeal pain			
subjects affected / exposed	2 / 112 (1.79%)	0 / 111 (0.00%)	1 / 109 (0.92%)
occurrences (all)	2	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 112 (0.00%)	2 / 111 (1.80%)	0 / 109 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	0 / 112 (0.00%)	0 / 111 (0.00%)	3 / 109 (2.75%)
occurrences (all)	0	0	4
Back pain			
subjects affected / exposed	0 / 112 (0.00%)	0 / 111 (0.00%)	2 / 109 (1.83%)
occurrences (all)	0	0	2
Infections and infestations			
Sinusitis			
subjects affected / exposed	9 / 112 (8.04%)	7 / 111 (6.31%)	6 / 109 (5.50%)
occurrences (all)	14	7	6
Nasopharyngitis			
subjects affected / exposed	3 / 112 (2.68%)	6 / 111 (5.41%)	3 / 109 (2.75%)
occurrences (all)	3	6	3
Acute sinusitis			
subjects affected / exposed	4 / 112 (3.57%)	5 / 111 (4.50%)	2 / 109 (1.83%)
occurrences (all)	4	6	2
COVID-19			
subjects affected / exposed	6 / 112 (5.36%)	2 / 111 (1.80%)	5 / 109 (4.59%)
occurrences (all)	6	2	5
Chronic sinusitis	Additional description: All AEs that coded to the MedDRA preferred term of "chronic sinusitis" experienced a CRS exacerbation.		
subjects affected / exposed	7 / 112 (6.25%)	5 / 111 (4.50%)	1 / 109 (0.92%)
occurrences (all)	8	5	2
Upper respiratory tract infection			
subjects affected / exposed	3 / 112 (2.68%)	3 / 111 (2.70%)	1 / 109 (0.92%)
occurrences (all)	4	3	1
Influenza			
subjects affected / exposed	0 / 112 (0.00%)	3 / 111 (2.70%)	0 / 109 (0.00%)
occurrences (all)	0	3	0
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 112 (2.68%)	1 / 111 (0.90%)	1 / 109 (0.92%)
occurrences (all)	3	1	1
Otitis media			
subjects affected / exposed	0 / 112 (0.00%)	2 / 111 (1.80%)	0 / 109 (0.00%)
occurrences (all)	0	2	0
COVID-19 pneumonia			

subjects affected / exposed occurrences (all)	2 / 112 (1.79%) 2	0 / 111 (0.00%) 0	0 / 109 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 February 2019	Required subjects to administer 2 sprays per nostril for each dose of randomized study treatment; identified the co-primary endpoint related to nasal symptoms as the CSNS ("CSS" in all reports including this CSR); extended the single-blind run-in period from 14 to 21 days; modified inclusion/exclusion criteria; added assessments of NP grading to Weeks 4, 12, and 24; added IOP >21 mmHg, nasal septal perforation, and new onset or worsening of cataracts to withdrawal criteria; and provided additional details/clarifications for primary and IAs.
05 December 2019	Modified inclusion/exclusion criteria; added a biomarker substudy (no analysis done due to low number of participating subjects); revised the 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; and added an assessment of the impact of treatment on subjects approved for surgery who no longer elect to undergo surgery.
15 June 2020	Amendments 3 (15 June 2022) and 4 (21 August 2020): Modified the protocol in reaction to the COVID-19 pandemic. Most notably, nasal endoscopy and associated polyp grading were removed from Visits 3 and 5; ocular examinations were removed; and subjects were allowed to delay the Week 24 Visit in case of COVID-19 or any upper respiratory infection and continue taking study drug until they could have the Week 24 Visit. Also, remote visits were allowed as needed and provisions were made for completing PROs remotely.
21 August 2020	Amendments 3 (15 June 2022) and 4 (21 August 2020): Modified the protocol in reaction to the COVID-19 pandemic. Most notably, nasal endoscopy and associated polyp grading were removed from Visits 3 and 5; ocular examinations were removed; and subjects were allowed to delay the Week 24 Visit in case of COVID-19 or any upper respiratory infection and continue taking study drug until they could have the Week 24 Visit. Also, remote visits were allowed as needed and provisions were made for completing PROs remotely.
23 July 2021	Modified key secondary and other secondary objectives/endpoints by moving SF-36 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; and updated sample size text.
07 January 2022	Modified key secondary and other secondary objectives/endpoints by moving SNOT-22 total score from key secondary to other secondary; moving SNOT22 and PSQI endpoints to be analyzed using pooled data from Studies 3205 and 3206 from key secondary to other secondary; and adding CSS total score and frequency of acute exacerbations of chronic sinusitis (both analyzed using pooled data from Studies 3205 and 3206) in subjects who were using a standard nasal steroid at study entry to key secondary objectives. Other changes were removal of the biomarker substudy, updates of statistical methods to reflect the changes in key and other secondary objectives/endpoints, and modifications/clarifications to poor score assignments for various endpoints in case of intercurrent events and sensitivity analyses for the APOV co-primary endpoint.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported