

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

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

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

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 75 (0.00%) 0 | 1 / 73 (1.37%) 1 | 0 / 74 (0.00%) 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: