



Clinical trial results:

Efficacy and safety of acetylcysteine for the treatment of acute uncomplicated rhinosinusitis: a prospective, randomized, double-blind, placebo-controlled trial

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2019-000060-20 |
| Trial protocol | DE BG |
| Global end of trial date | 20 April 2021 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 05 November 2021 |
| First version publication date | 05 November 2021 |

Trial information

Trial identification

| | |
|-----------------------|--------------------------|
| Sponsor protocol code | 2018-08-EFT-1 / C1018001 |
|-----------------------|--------------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04123405 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.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 | 20 April 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 April 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to assess the efficacy of three different total daily doses of the investigational medicinal product containing 600 mg acetylcysteine per effervescent tablet compared to placebo for the treatment of acute uncomplicated rhinosinusitis.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use <https://www.novctrd.com/CtrdWeb/home.nov> for complete trial results

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 22 October 2020 |
| 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 | Bulgaria: 284 |
| Country: Number of subjects enrolled | Germany: 55 |
| Country: Number of subjects enrolled | Moldova, Republic of: 334 |
| Country: Number of subjects enrolled | Russian Federation: 271 |
| Worldwide total number of subjects | 944 |
| EEA total number of subjects | 339 |

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 | 0 |

| | |
|---------------------------|-----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 17 |
| Adults (18-64 years) | 879 |
| From 65 to 84 years | 48 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled from 42 clinical centers located in Bulgaria, Germany, Moldova and Russia.

Pre-assignment

Screening details:

Participants were randomized in 1:1:1:1 ratio

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (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 | Group A: 600 mg acetylcysteine |

Arm description:

one tablet test product plus three tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily)

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | acetylcysteine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Effervescent tablet |
| Routes of administration | Oral use |

Dosage and administration details:

one tablet test product plus three tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily)

| | |
|------------------|---------------------------------|
| Arm title | Group B: 1200 mg acetylcysteine |
|------------------|---------------------------------|

Arm description:

two tablets test product plus two tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily)

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | acetylcysteine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Effervescent tablet |
| Routes of administration | Oral use |

Dosage and administration details:

two tablets test product plus two tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily)

| | |
|------------------|---------------------------------|
| Arm title | Group C: 2400 mg acetylcysteine |
|------------------|---------------------------------|

Arm description:

four tablets test product per day (taken as two tablets dissolved in a glass of water, twice daily)

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|---------------------|
| Investigational medicinal product name | acetylcysteine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Effervescent tablet |
| Routes of administration | Oral use |

Dosage and administration details:

four tablets test product per day (taken as two tablets dissolved in a glass of water, twice daily)

| | |
|------------------|------------------|
| Arm title | Group D: Placebo |
|------------------|------------------|

Arm description:

four tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily).

| | |
|--|---------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Effervescent tablet |
| Routes of administration | Oral use |

Dosage and administration details:

four tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily)

| Number of subjects in period 1 | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine |
|---------------------------------------|--------------------------------|---------------------------------|---------------------------------|
| Started | 235 | 238 | 238 |
| Full Analysis set | 235 | 236 | 238 |
| Safety Set | 235 | 238 | 238 |
| Completed | 231 | 231 | 235 |
| Not completed | 4 | 7 | 3 |
| Exclusion criteria met | 1 | 2 | - |
| Contact to subject lost | - | - | - |
| Consent withdrawn by subject | 1 | 3 | - |
| Adverse event, non-fatal | 1 | 2 | 3 |
| screening failure | 1 | - | - |

| Number of subjects in period 1 | Group D: Placebo |
|---------------------------------------|------------------|
| Started | 233 |
| Full Analysis set | 230 |
| Safety Set | 233 |
| Completed | 225 |
| Not completed | 8 |
| Exclusion criteria met | 2 |
| Contact to subject lost | 1 |
| Consent withdrawn by subject | 2 |
| Adverse event, non-fatal | 3 |
| screening failure | - |

Baseline characteristics

Reporting groups

| | |
|--|---------------------------------|
| Reporting group title | Group A: 600 mg acetylcysteine |
| Reporting group description: one tablet test product plus three tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily) | |
| Reporting group title | Group B: 1200 mg acetylcysteine |
| Reporting group description: two tablets test product plus two tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily) | |
| Reporting group title | Group C: 2400 mg acetylcysteine |
| Reporting group description: four tablets test product per day (taken as two tablets dissolved in a glass of water, twice daily) | |
| Reporting group title | Group D: Placebo |
| Reporting group description: four tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily). | |

| Reporting group values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine |
|--|--------------------------------|---------------------------------|---------------------------------|
| Number of subjects | 235 | 238 | 238 |
| 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) | 6 | 5 | 3 |
| Adults (18-64 years) | 219 | 222 | 224 |
| From 65-84 years | 10 | 11 | 11 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 41.0 | 40.7 | 41.3 |
| standard deviation | ± 13.8 | ± 13.6 | ± 13.1 |
| Sex: Female, Male Units: Participants | | | |
| Female | 128 | 142 | 145 |
| Male | 107 | 96 | 93 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Caucasian | 230 | 235 | 232 |
| Asian | 4 | 2 | 5 |
| Unknown | 1 | 1 | 1 |

| Reporting group values | Group D: Placebo | Total | |
|------------------------|------------------|-------|--|
| Number of subjects | 233 | 944 | |

| | | | |
|---|--------|-----|--|
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 3 | 17 | |
| Adults (18-64 years) | 214 | 879 | |
| From 65-84 years | 16 | 48 | |
| 85 years and over | 0 | 0 | |
| Age Continuous Units: Years | | | |
| arithmetic mean | 41.1 | | |
| standard deviation | ± 14.0 | - | |
| Sex: Female, Male Units: Participants | | | |
| Female | 141 | 556 | |
| Male | 92 | 388 | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Caucasian | 231 | 928 | |
| Asian | 2 | 13 | |
| Unknown | 0 | 3 | |

End points

End points reporting groups

| | |
|--|---------------------------------|
| Reporting group title | Group A: 600 mg acetylcysteine |
| Reporting group description: one tablet test product plus three tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily) | |
| Reporting group title | Group B: 1200 mg acetylcysteine |
| Reporting group description: two tablets test product plus two tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily) | |
| Reporting group title | Group C: 2400 mg acetylcysteine |
| Reporting group description: four tablets test product per day (taken as two tablets dissolved in a glass of water, twice daily) | |
| Reporting group title | Group D: Placebo |
| Reporting group description: four tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily). | |

Primary: Mean change from baseline in the daily Major Symptom Score (MSS) over the entire treatment period, Full Analysis Set

| | |
|--|---|
| End point title | Mean change from baseline in the daily Major Symptom Score (MSS) over the entire treatment period, Full Analysis Set ^[1] |
| End point description: The MSS combines the 5 most relevant symptoms of rhinosinusitis based on expert clinician recommendations (rhinorrhea/ anterior discharge, postnasal drip, nasal congestion, headache, and facial pain/pressure). The patient rated the severity of each of the five symptoms of the MSS using a four-point rating scale of increasing severity (0 = none/not present, 1 = mild, 2 = moderate, 3 = severe). The MSS is then the sum of single ratings with a possible range from 0 to 15. Mean change from baseline in the daily Major Symptom Score (MSS) over the entire treatment period was calculated as the average total score from Day 2 to 15 compared to Baseline (Day 1). Negative change from baseline means improvement. | |
| End point type | Primary |
| End point timeframe: Baseline (Day 1), Day 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 and 15 | |
| Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No statistical analyses were performed for this endpoint | |

| End point values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine | Group D: Placebo |
|--------------------------------------|--------------------------------|---------------------------------|---------------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 235 | 236 | 238 | 230 |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | -4.8213 (± 1.98247) | -4.7394 (± 1.99090) | -4.7758 (± 1.96938) | -5.0180 (± 1.98262) |

Statistical analyses

No statistical analyses for this end point

Primary: Mean change from baseline in the daily Major Symptom Score (MSS) over the entire treatment period, Per-Protocol Set

| | |
|-----------------|--|
| End point title | Mean change from baseline in the daily Major Symptom Score (MSS) over the entire treatment period, Per-Protocol Set ^[2] |
|-----------------|--|

End point description:

The MSS combines the 5 most relevant symptoms of rhinosinusitis based on expert clinician recommendations (rhinorrhea/ anterior discharge, postnasal drip, nasal congestion, headache, and facial pain/pressure). The patient rated the severity of each of the five symptoms of the MSS using a four-point rating scale of increasing severity (0 = none/not present, 1 = mild, 2 = moderate, 3 = severe). The MSS is then the sum of single ratings with a possible range from 0 to 15.

Mean change from baseline in the daily Major Symptom Score (MSS) over the entire treatment period was calculated as the average total score from Day 2 to 15 compared to Baseline (Day 1). Negative change from baseline means improvement.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline (Day 1), Day 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 and 15

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were performed for this endpoint

| End point values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine | Group D: Placebo |
|--------------------------------------|--------------------------------|---------------------------------|---------------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 213 | 215 | 212 | 207 |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | -4.9085 (± 1.92431) | -4.8688 (± 1.84448) | -4.8002 (± 1.90569) | -5.1256 (± 1.95072) |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to onset of action, Full Analysis Set

| | |
|-----------------|---|
| End point title | Time to onset of action, Full Analysis Set ^[3] |
|-----------------|---|

End point description:

Time to onset of action was defined as first day of active treatment on which MSS showed statistically significant (p value<0.05) improvement from placebo. There was no statistically significant improvement of the drug from placebo on any day

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Day 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 and 15

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There was no statistically significant improvement of the drug from placebo on any day

| End point values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine | |
|-----------------------------|--------------------------------|---------------------------------|---------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 235 | 236 | 238 | |
| Units: Days | 999 | 999 | 999 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to onset of action, Per-Protocol Set

| | |
|--|--|
| End point title | Time to onset of action, Per-Protocol Set ^[4] |
| End point description: Time to onset of action was defined as first day of active treatment on which MSS showed statistically significant (p value<0.05) improvement from placebo. There was no statistically significant improvement of the drug from placebo on any day | |
| End point type | Secondary |
| End point timeframe: Baseline (Day 1), Day 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 and 15 | |
| Notes: [4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: There was no statistically significant improvement of the drug from placebo on any day | |

| End point values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine | |
|-----------------------------|--------------------------------|---------------------------------|---------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 213 | 215 | 212 | |
| Units: Days | 999 | 999 | 999 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Major Symptom Score (MSS) development over the course of the study, Full Analysis Set

| | |
|--|---|
| End point title | Major Symptom Score (MSS) development over the course of the study, Full Analysis Set |
| End point description: The MSS combines the 5 most relevant symptoms of rhinosinusitis based on expert clinician recommendations (rhinorrhea/ anterior discharge, postnasal drip, nasal congestion, headache, and facial pain/pressure). The patient rated the severity of each of the five symptoms of the MSS using a four-point rating scale of increasing severity (0 = none/not present, 1 = mild, 2 = moderate, 3 = severe). The MSS is then the sum of single ratings with a possible range from 0 to 15. Mean change from baseline in the daily Major Symptom Score (MSS) over the entire treatment period was calculated as the average total score from Day 2 to 15 compared to Baseline (Day 1). Negative change from baseline means improvement. | |
| End point type | Secondary |

End point timeframe:

Baseline (Day 1), Day 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 and 15

| End point values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine | Group D: Placebo |
|--------------------------------------|--------------------------------|---------------------------------|---------------------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 235 | 236 | 238 | 230 |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (Baseline) | 9.634 (± 1.1181) | 9.640 (± 1.0647) | 9.702 (± 1.0101) | 9.683 (± 1.0652) |
| Day 2 | 9.021 (± 2.0348) | 9.004 (± 1.9883) | 9.038 (± 2.1235) | 9.074 (± 1.9866) |
| Day 3 | 8.485 (± 2.3376) | 8.513 (± 2.2303) | 8.416 (± 2.4390) | 8.609 (± 2.1298) |
| Day 4 | 7.821 (± 2.4482) | 7.695 (± 2.5130) | 7.723 (± 2.7156) | 7.761 (± 2.5058) |
| Day 5 | 6.983 (± 2.7284) | 6.979 (± 2.5706) | 7.013 (± 2.7490) | 6.917 (± 2.6312) |
| Day 6 | 6.323 (± 2.7807) | 6.203 (± 2.8719) | 6.315 (± 2.7980) | 6.039 (± 2.7838) |
| Day 7 | 5.528 (± 2.9747) | 5.538 (± 2.7449) | 5.576 (± 2.8508) | 5.126 (± 2.7096) |
| Day 8 | 4.766 (± 2.8631) | 4.750 (± 2.6755) | 4.891 (± 2.7598) | 4.387 (± 2.6004) |
| Day 9 | 4.204 (± 2.8149) | 4.322 (± 2.7254) | 4.445 (± 2.7381) | 3.839 (± 2.5924) |
| Day 10 | 3.634 (± 2.6815) | 3.763 (± 2.6391) | 3.845 (± 2.6634) | 3.404 (± 2.6805) |
| Day 11 | 3.051 (± 2.5229) | 3.284 (± 2.6658) | 3.256 (± 2.5716) | 2.843 (± 2.6469) |
| Day 12 | 2.609 (± 2.5200) | 2.754 (± 2.5680) | 2.756 (± 2.3795) | 2.413 (± 2.5608) |
| Day 13 | 2.038 (± 2.4202) | 2.246 (± 2.5296) | 2.218 (± 2.4293) | 1.943 (± 2.4174) |
| Day 14 | 1.583 (± 2.3289) | 1.941 (± 2.5375) | 1.836 (± 2.3300) | 1.596 (± 2.3637) |
| Day 15 | 1.332 (± 2.1485) | 1.614 (± 2.4459) | 1.634 (± 2.3178) | 1.352 (± 2.1882) |

Statistical analyses

No statistical analyses for this end point

Secondary: Major Symptom Score (MSS) development over the course of the study, Per-protocol Set

| | |
|-----------------|--|
| End point title | Major Symptom Score (MSS) development over the course of the study, Per-protocol Set |
|-----------------|--|

End point description:

The MSS combines the 5 most relevant symptoms of rhinosinusitis based on expert clinician recommendations (rhinorrhea/ anterior discharge, postnasal drip, nasal congestion, headache, and facial pain/pressure). The patient rated the severity of each of the five symptoms of the MSS using a four-

point rating scale of increasing severity (0 = none/not present, 1 = mild, 2 = moderate, 3 = severe). The MSS is then the sum of single ratings with a possible range from 0 to 15.

Mean change from baseline in the daily Major Symptom Score (MSS) over the entire treatment period was calculated as the average total score from Day 2 to 15 compared to Baseline (Day 1). Negative change from baseline means improvement.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 1), Day 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 and 15 | |

| End point values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine | Group D: Placebo |
|--------------------------------------|--------------------------------|---------------------------------|---------------------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 213 | 215 | 212 | 207 |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (Baseline) | 9.657 (± 1.1201) | 9.628 (± 1.0595) | 9.698 (± 1.0319) | 9.676 (± 1.0823) |
| Day 2 | 9.080 (± 2.0160) | 8.935 (± 2.0268) | 9.127 (± 2.0089) | 9.068 (± 2.0278) |
| Day 3 | 8.545 (± 2.2890) | 8.395 (± 2.2583) | 8.528 (± 2.2591) | 8.594 (± 2.1921) |
| Day 4 | 7.803 (± 2.4779) | 7.577 (± 2.5472) | 7.816 (± 2.5849) | 7.739 (± 2.5750) |
| Day 5 | 6.962 (± 2.7401) | 6.874 (± 2.5865) | 7.061 (± 2.6522) | 6.821 (± 2.6717) |
| Day 6 | 6.315 (± 2.7914) | 6.093 (± 2.8809) | 6.349 (± 2.7000) | 5.937 (± 2.8354) |
| Day 7 | 5.479 (± 2.9550) | 5.400 (± 2.7151) | 5.604 (± 2.7800) | 4.981 (± 2.7163) |
| Day 8 | 4.685 (± 2.8250) | 4.605 (± 2.6399) | 4.892 (± 2.7421) | 4.237 (± 2.5914) |
| Day 9 | 4.117 (± 2.7558) | 4.181 (± 2.6773) | 4.382 (± 2.6734) | 3.652 (± 2.5495) |
| Day 10 | 3.521 (± 2.6127) | 3.628 (± 2.5174) | 3.741 (± 2.5507) | 3.222 (± 2.6197) |
| Day 11 | 2.934 (± 2.4039) | 3.144 (± 2.5214) | 3.146 (± 2.4538) | 2.705 (± 2.6042) |
| Day 12 | 2.493 (± 2.3485) | 2.572 (± 2.3785) | 2.608 (± 2.2228) | 2.300 (± 2.4902) |
| Day 13 | 1.897 (± 2.2146) | 2.065 (± 2.2949) | 2.085 (± 2.2013) | 1.816 (± 2.3077) |
| Day 14 | 1.432 (± 2.0812) | 1.749 (± 2.2779) | 1.708 (± 2.1128) | 1.444 (± 2.2198) |
| Day 15 | 1.221 (± 1.9530) | 1.409 (± 2.1312) | 1.524 (± 2.0846) | 1.193 (± 1.9636) |

Statistical analyses

No statistical analyses for this end point

Secondary: Sino-Nasal Outcome Test (SNOT-22) by visit, Full Analysis set

| | |
|--|---|
| End point title | Sino-Nasal Outcome Test (SNOT-22) by visit, Full Analysis set |
| End point description: | |
| SNOT-22 Questionnaire is a disease specific Health-Related Quality of Life (HRQoL) measure that comprises a list of 22 symptoms and social or emotional consequences of the nasal disorder. Every participant is asked to rate how severe each problem had been on a scale from 0 (no problem) to 5 (problem as bad as it can be). The total score is the sum of the scores for all 22 items, ranging from 0 to 110, with a lower score indicating better HRQoL. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 1), Day 7 and Day 14 | |

| End point values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine | Group D: Placebo |
|--------------------------------------|--------------------------------|---------------------------------|---------------------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 235 | 236 | 238 | 230 |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (Baseline) | 37.8 (± 16.89) | 36.3 (± 15.82) | 36.7 (± 16.21) | 36.3 (± 17.00) |
| Day 7 | 23.6 (± 15.01) | 21.2 (± 13.14) | 22.3 (± 13.95) | 21.1 (± 13.56) |
| Day 14 | 7.2 (± 10.80) | 6.9 (± 11.15) | 7.0 (± 10.07) | 6.5 (± 10.28) |

Statistical analyses

No statistical analyses for this end point

Secondary: Sino-Nasal Outcome Test (SNOT-22) by visit, Per Protocol Set

| | |
|--|--|
| End point title | Sino-Nasal Outcome Test (SNOT-22) by visit, Per Protocol Set |
| End point description: | |
| SNOT-22 Questionnaire is a disease specific Health-Related Quality of Life (HRQoL) measure that comprises a list of 22 symptoms and social or emotional consequences of the nasal disorder. Every participant is asked to rate how severe each problem had been on a scale from 0 (no problem) to 5 (problem as bad as it can be). The total score is the sum of the scores for all 22 items, ranging from 0 to 110, with a lower score indicating better HRQoL. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 1), Day 7 and Day 14 | |

| End point values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine | Group D: Placebo |
|--------------------------------------|--------------------------------|---------------------------------|---------------------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 213 | 215 | 212 | 207 |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (Baseline) | 37.7 (± 16.64) | 36.7 (± 15.89) | 36.4 (± 15.86) | 36.2 (± 16.88) |
| Day 7 | 23.3 (± 14.92) | 21.2 (± 13.32) | 22.2 (± 14.27) | 21.0 (± 13.78) |

| | | | | |
|--------|--------------------|--------------------|-------------------|--------------------|
| Day 14 | 6.9 (\pm 10.49) | 7.1 (\pm 11.43) | 6.8 (\pm 9.67) | 6.6 (\pm 10.50) |
|--------|--------------------|--------------------|-------------------|--------------------|

Statistical analyses

No statistical analyses for this end point

Secondary: Sino-Nasal Outcome Test (SNOT-22) by change to baseline, Full Analysis Set

| | |
|-----------------|--|
| End point title | Sino-Nasal Outcome Test (SNOT-22) by change to baseline, Full Analysis Set |
|-----------------|--|

End point description:

SNOT-22 Questionnaire is a disease specific Health-Related Quality of Life (HRQoL) measure that comprises a list of 22 symptoms and social or emotional consequences of the nasal disorder. Every participant is asked to rate how severe each problem had been on a scale from 0 (no problem) to 5 (problem as bad as it can be). The total score is the sum of the scores for all 22 items, ranging from 0 to 110, with a lower score indicating better HRQoL. A negative change from baseline in SNOT-22 is considered a favorable outcome.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Day 7 and Day 14

| End point values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine | Group D: Placebo |
|--------------------------------------|--------------------------------|---------------------------------|---------------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 235 | 236 | 238 | 230 |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 7 | -35.8 (\pm 33.25) | -38.2 (\pm 37.48) | -36.7 (\pm 34.61) | -39.6 (\pm 30.42) |
| Day 14 | -79.3 (\pm 31.27) | -78.9 (\pm 31.11) | -78.6 (\pm 30.53) | -81.5 (\pm 26.54) |

Statistical analyses

No statistical analyses for this end point

Secondary: Sino-Nasal Outcome Test (SNOT-22) by change to baseline, Per Protocol Set

| | |
|-----------------|---|
| End point title | Sino-Nasal Outcome Test (SNOT-22) by change to baseline, Per Protocol Set |
|-----------------|---|

End point description:

SNOT-22 Questionnaire is a disease specific Health-Related Quality of Life (HRQoL) measure that comprises a list of 22 symptoms and social or emotional consequences of the nasal disorder. Every participant is asked to rate how severe each problem had been on a scale from 0 (no problem) to 5 (problem as bad as it can be). The total score is the sum of the scores for all 22 items, ranging from 0

to 110, with a lower score indicating better HRQoL. A negative change from baseline in SNOT-22 is considered a favorable outcome.

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 1), Day 7 and Day 14 | |

| End point values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine | Group D: Placebo |
|--------------------------------------|--------------------------------|---------------------------------|---------------------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 213 | 215 | 212 | 207 |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 7 | -36.4 (± 32.64) | -39.5 (± 36.68) | -36.7 (± 33.44) | -39.6 (± 30.60) |
| Day 14 | -79.8 (± 30.90) | -78.6 (± 31.77) | -79.1 (± 30.16) | -81.0 (± 27.10) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of responders and non-responders to treatment, Full Analysis Set

| | |
|--|---|
| End point title | Number of responders and non-responders to treatment, Full Analysis Set |
| End point description: | |
| Number of responders and non-responders to treatment based on the assessment of overall response to treatment by the investigator were reported. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 4, 7, 10 and 15 | |

| End point values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine | Group D: Placebo |
|-----------------------------|--------------------------------|---------------------------------|---------------------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 235 | 236 | 238 | 230 |
| Units: Participants | | | | |
| Day 4 Responders | 148 | 152 | 151 | 150 |
| Day 7 Responders | 209 | 206 | 212 | 209 |
| Day 10 Responders | 225 | 225 | 230 | 219 |
| Day 15 Responders | 230 | 226 | 230 | 224 |
| Day 4 Non-responders | 85 | 83 | 86 | 79 |
| Day 7 Non-responders | 23 | 29 | 15 | 18 |
| Day 10 Non-responders | 6 | 7 | 5 | 6 |

| | | | | |
|-----------------------|---|---|---|---|
| Day 15 Non-responders | 4 | 6 | 8 | 4 |
|-----------------------|---|---|---|---|

Statistical analyses

No statistical analyses for this end point

Secondary: Number of responders and non-responders to treatment, Per-Protocol Set

| | |
|--|--|
| End point title | Number of responders and non-responders to treatment, Per-Protocol Set |
| End point description: Number of responders and non-responders to treatment based on the assessment of overall response to treatment by the investigator were reported. | |
| End point type | Secondary |
| End point timeframe: Day 4, 7, 10 and 15 | |

| End point values | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine | Group D: Placebo |
|-----------------------------|--------------------------------|---------------------------------|---------------------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 213 | 215 | 212 | 207 |
| Units: Participants | | | | |
| Day 4 Responders | 138 | 140 | 132 | 134 |
| Day 7 Responders | 192 | 190 | 191 | 192 |
| Day 10 Responders | 207 | 210 | 209 | 202 |
| Day 15 Responders | 211 | 210 | 206 | 205 |
| Day 4 Non-responders | 75 | 75 | 80 | 73 |
| Day 7 Non-responders | 21 | 25 | 21 | 15 |
| Day 10 Non-responders | 6 | 5 | 3 | 5 |
| Day 15 Non-responders | 2 | 5 | 6 | 2 |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose of study treatment up to maximum duration of 22 days.

Adverse event reporting additional description:

Any signs or symptoms were collected from first dose of study treatment up to maximum duration of 22 days.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 24.0 |

Reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | Group A: 600 mg acetylcysteine |
|-----------------------|--------------------------------|

Reporting group description:

one tablet test product plus three tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily)

| | |
|-----------------------|---------------------------------|
| Reporting group title | Group B: 1200 mg acetylcysteine |
|-----------------------|---------------------------------|

Reporting group description:

two tablets test product plus two tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily)

| | |
|-----------------------|---------------------------------|
| Reporting group title | Group C: 2400 mg acetylcysteine |
|-----------------------|---------------------------------|

Reporting group description:

four tablets test product per day (taken as two tablets dissolved in a glass of water, twice daily)

| | |
|-----------------------|------------------|
| Reporting group title | Group D: Placebo |
|-----------------------|------------------|

Reporting group description:

four tablets placebo per day (taken as two tablets dissolved in a glass of water, twice daily).

| Serious adverse events | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine |
|---|--------------------------------|---------------------------------|---------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 0 / 238 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Concussion | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 0 / 238 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hand fracture | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 0 / 238 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Tibia fracture | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 0 / 238 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 0 / 238 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|--|--|
| Serious adverse events | Group D: Placebo | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 233 (0.43%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Concussion | | | |
| subjects affected / exposed | 1 / 233 (0.43%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hand fracture | | | |
| subjects affected / exposed | 1 / 233 (0.43%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 233 (0.43%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 1 / 233 (0.43%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| Non-serious adverse events | Group A: 600 mg acetylcysteine | Group B: 1200 mg acetylcysteine | Group C: 2400 mg acetylcysteine |
|---|--------------------------------|---------------------------------|---------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 235 (3.83%) | 15 / 238 (6.30%) | 15 / 238 (6.30%) |
| Investigations | | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 0 / 238 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 1 / 238 (0.42%) |
| occurrences (all) | 0 | 0 | 1 |
| Human chorionic gonadotropin increased | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 1 / 238 (0.42%) |
| occurrences (all) | 0 | 0 | 1 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 238 (0.42%) | 0 / 238 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 1 / 238 (0.42%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 235 (0.85%) | 1 / 238 (0.42%) | 2 / 238 (0.84%) |
| occurrences (all) | 2 | 1 | 2 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 1 / 238 (0.42%) |
| occurrences (all) | 0 | 0 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 1 / 238 (0.42%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear and labyrinth disorders | | | |
| Ear congestion | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 2 / 238 (0.84%) | 0 / 238 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 1 / 238 (0.42%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 2 / 238 (0.84%) | 1 / 238 (0.42%) |
| occurrences (all) | 1 | 2 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 238 (0.00%) | 1 / 238 (0.42%) |
| occurrences (all) | 1 | 0 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 3 / 238 (1.26%) | 2 / 238 (0.84%) |
| occurrences (all) | 0 | 3 | 2 |
| Nausea | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 238 (0.00%) | 1 / 238 (0.42%) |
| occurrences (all) | 1 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 238 (0.42%) | 0 / 238 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 238 (0.42%) | 0 / 238 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasal crusting | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 0 / 238 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal obstruction | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 1 / 238 (0.42%) | 0 / 238 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 238 (0.42%) | 0 / 238 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 238 (0.00%) | 1 / 238 (0.42%) |
| occurrences (all) | 1 | 0 | 1 |
| Rhinorrhoea | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 235 (0.00%) 0 | 1 / 238 (0.42%) 1 | 0 / 238 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 0 / 238 (0.00%) | 0 / 238 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 1 / 238 (0.42%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 1 / 238 (0.42%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 238 (0.42%) | 0 / 238 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 1 / 235 (0.43%) | 1 / 238 (0.42%) | 1 / 238 (0.42%) |
| occurrences (all) | 1 | 1 | 1 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 238 (0.42%) | 0 / 238 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Otitis media bacterial | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 0 / 238 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulpitis dental | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 0 / 238 (0.00%) | 1 / 238 (0.42%) |
| occurrences (all) | 0 | 0 | 1 |
| Sinusitis bacterial | | | |
| subjects affected / exposed | 0 / 235 (0.00%) | 1 / 238 (0.42%) | 0 / 238 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|------------------|--|--|
| Non-serious adverse events | Group D: Placebo | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 233 (3.43%) | | |

| | | | |
|--|-----------------|--|--|
| Investigations | | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 233 (0.43%) | | |
| occurrences (all) | 1 | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 1 / 233 (0.43%) | | |
| occurrences (all) | 1 | | |
| Human chorionic gonadotropin increased | | | |
| subjects affected / exposed | 0 / 233 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 233 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 233 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 233 (0.43%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 233 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 233 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ear and labyrinth disorders | | | |
| Ear congestion | | | |
| subjects affected / exposed | 0 / 233 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 233 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--|----------------------|--|--|
| Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Dyspepsia subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Nausea subjects affected / exposed occurrences (all) | 1 / 233 (0.43%) 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Nasal crusting subjects affected / exposed occurrences (all) | 1 / 233 (0.43%) 1 | | |
| Nasal obstruction subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Productive cough subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Rhinitis allergic subjects affected / exposed occurrences (all) | 1 / 233 (0.43%) 1 | | |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|--|----------------------|--|--|
| Dermatitis allergic subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Erythema subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Rash subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Infections and infestations Acute sinusitis subjects affected / exposed occurrences (all) | 1 / 233 (0.43%) 1 | | |
| COVID-19 subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Otitis media bacterial subjects affected / exposed occurrences (all) | 1 / 233 (0.43%) 1 | | |
| Pulpitis dental subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |
| Sinusitis bacterial subjects affected / exposed occurrences (all) | 0 / 233 (0.00%) 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 23 August 2019 | This amendment was country specific and was valid for Germany only. The amendment was not used in the present trial as it was replaced by the GLOBAL Amendment 5.0 (Version 1.0, dated 14-Aug-2020). |
| 10 September 2019 | This amendment was country specific and was valid for Bulgaria and Moldova only. The amendment was not used in the present trial as it was replaced by the GLOBAL Amendment 5.0 (Version 1.0, dated 14-Aug-2020). |
| 15 October 2019 | This amendment was country specific and was valid for Russia only. The amendment was not used in the present trial as it was replaced by the GLOBAL Amendment 5.0 (Version 1.0, dated 14-Aug-2020). |
| 01 November 2019 | Amendment 4.0 (Version 1.0, dated 01-Nov-2019) to study protocol This amendment was country specific and was valid for Moldova only. The amendment was not used in the present trial as it was replaced by the GLOBAL Amendment 5.0 (Version 1.0, dated 14-Aug-2020). |
| 14 August 2020 | By this amendment the changes in sponsor's project management were introduced with effective date 19-Aug-2020. |

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.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use <https://www.novctrd.com/CtrdWeb/home.nov> for complete trial results

Notes: