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 (± 10.49)	7.1 (± 11.43)	6.8 (± 9.67)	6.6 (± 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 (± 33.25)	-38.2 (± 37.48)	-36.7 (± 34.61)	-39.6 (± 30.42)
Day 14	-79.3 (± 31.27)	-78.9 (± 31.11)	-78.6 (± 30.53)	-81.5 (± 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		

Frequency threshold for reporting non-serious adverse events: 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	0 / 235 (0.00%)	1 / 238 (0.42%)	0 / 238 (0.00%)
occurrences (all)	0	1	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: