Clinical trial results:
Prospective, controlled, randomized double-blind study to determine the sensory perception of two nasal sprays using the model of treatment of post-operative complaints after surgery on the nasal mucosa.

Summary

EudraCT number	2019-004936-52
Trial protocol	DE
Global end of trial date	04 December 2020

Results information

Result version number	v1 (current)
This version publication date	23 June 2022
First version publication date	23 June 2022

Trial information

Trial identification

Sponsor protocol code	CASK0119

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Cassella-med GmbH & Co KG
Sponsor organisation address	Gereonsmühlengasse 1, Cologne, Germany, 50670
Public contact	Clinical Operations, Cassella-med GmbH & Co. KG, +49 8001652200, dialog@cassella-med.eu
Scientific contact	Clinical Operations, Cassella-med GmbH & Co. KG, clinical.operations@klosterfrau.de

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	07 September 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the study is to assess the sensory quality of the nasic neo nasal spray compared to a comparative preparation with the same active ingredient composition.
It is assumed that the modified galenics due to the addition of hyaluronic acid improves the sensory quality of the nasal spray.

Protection of trial subjects:

Physical examinations were carried out at screening visit. Only patients presented normal physical examination were included into the study. During the course of study for all patients the use of non-steroidal analgesics was allowed.
Patients had the right to withdraw from the trial at any time and this irrespective of the reason.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 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	Germany: 51
Worldwide total number of subjects	51
EEA total number of subjects	51

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)	51
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

After the patients have undergone surgery on the nasal mucosa by medical members of the study group, they were informed about the study and were given the Patient Information Form. After having given written informed consent, the patients were examined for suitability according to the inclusion and exclusion criteria.

Pre-assignment

Screening details:

Subjects were eligible for inclusion, if the main criteria were met:

- post-operative nasal breathing disabilities after surgery on the nasal septum or the nasal conchae
- surgical intervention must have taken place at least one week prior to enrolment
- signed and dated Informed Consent

Period 1

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

Blinding implementation details:

This clinical trial was performed as a randomised, double-blind, controlled study in a crossover design. The treatment kits with the treatment sequence corresponding to the randomisation list were delivered with the sealed emergency envelopes. No person involved in the conduct or evaluation of the study did know the treatment sequence of the individual patients.

Arms

Are arms mutually exclusive?	No
Arm title	Period 1 - IMP

Arm description:

When randomized to treatment sequence 1, the IMP Nasic Neo was given to the patients at the first visit (V1) at the trial site.

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

Dosage and administration details:

At the first visit at the trial site, the patients were given nasal spray Nasic Neo when randomized to treatment sequence 1. The initial applicated dose was one spray shot per nostril. The patients applied the nasal spray independently at home (one spray shot per nostril, maximum three times a day).

Arm title	Period 2 - Comparator

Arm description:

When randomized to treatment sequence 1, the comparator NasenDuo was given after wash-out at visit 3 to the patients at the trial site.

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

Dosage and administration details:

After wash-out, the patients were given nasal spray NasenDuo at visit 3 when randomized to treatment sequence 1. The initial applicated dose was one spray shot per nostril. The patients applied the nasal spray independently at home (one spray shot per nostril, maximum three times a day).

Number of subjects in period 1	Period 1 - IMP	Period 2 - Comparator
Started	26	25
Completed	26	25

Period 2

Period 2 title	Treatment Sequence 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

This clinical trial was performed as a randomised, double-blind, controlled study in a crossover design. The treatment kits with the treatment sequence corresponding to the randomisation list were delivered with the sealed emergency envelopes. No person involved in the conduct or evaluation of the study did know the treatment sequence of the individual patients.

Arms

Are arms mutually exclusive?	No
Arm title	Period 1 - Comparator

Arm description:

When randomized to treatment sequence 2, the comparator NasenDuo was given at visit 1 to the patients at the trial site.

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

Dosage and administration details:

At the first visit at the trial site, the patients were given nasal spray NasenDuo when randomized to treatment sequence 2. The initial applicated dose was one spray shot per nostril. The patients applied the nasal spray independently at home (one spray shot per nostril, maximum three times a day).

Arm title	Period 2 - IMP

Arm description:

When randomized to treatment sequence 2, the IMP Nasic Neo was given after wash-out at visit 3 to the patients at the trial site.

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

Dosage and administration details:

After wash-out, the patients were given nasal spray Nasic Neo at visit 3 when randomized to treatment sequence 2. The initial applicated dose was one spray shot per nostril. The patient applied the nasal spray independently at home (one spray shot per nostril, maximum three times a day).

Number of subjects in period 2	Period 1 - Comparator	Period 2 - IMP
Started	25	26
Completed	23	26
Not completed	2	0
Consent withdrawn by subject	1	-
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups[1]

Reporting group title	Treatment Sequence 1

Reporting group description: -

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: For the comparison of the inter- and intra-group changes in the sensory evaluation, the baseline values at V1 and V3 were assessed. This applies to Treatment Sequence 1 and also to Treatment Sequence 2, resulting overall in 51 subjects who attended the baseline period.

Reporting group values	Treatment Sequence 1	Total	
Number of subjects	26	26	
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)	26	26	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	9	9	
Male	17	17	

Subject analysis sets

Subject analysis set title	Intergroup comparison - Treatment sequence 1
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Inter-group comparison for the sum score of the sensoric assessment, ΔV1-V2 vs. ΔV3-V4

Subject analysis set title	Intergroup comparison - Treatment sequence 2
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Inter-group comparison for the sum score of the sensoric assessment, ΔV1-V2 vs. ΔV3-V4

Subject analysis set title	Intragroup comparison - Treatment sequence 1
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intra-group comparison for further clinical effects- ΔV1-V2 vs. ΔV3-V4

Subject analysis set title	Intragroup comparison - Treatment sequence 2
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intra-group comparison for further clinical effects- ΔV1-V2 vs. ΔV3-V4

Reporting group values	Intergroup comparison - Treatment sequence 1	Intergroup comparison - Treatment sequence 2	Intragroup comparison - Treatment sequence 1
Number of subjects	26	23	26
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)	26	23	26
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	9	10	9
Male	17	13	17

Reporting group values	Intragroup comparison - Treatment sequence 2		
Number of subjects	23		
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)	23		
From 65-84 years	0		
85 years and over	0		
Gender categorical Units: Subjects			
Female	10		
Male	13		

End points

End points reporting groups

Reporting group title	Period 1 - IMP
Reporting group description:	
When randomized to treatment sequence 1, the IMP Nasic Neo was given to the patients at the first visit (V1) at the trial site.	
Reporting group title	Period 2 - Comparator
Reporting group description:	
When randomized to treatment sequence 1, the comparator NasenDuo was given after wash-out at visit 3 to the patients at the trial site.	
Reporting group title	Period 1 - Comparator
Reporting group description:	
When randomized to treatment sequence 2, the comparator NasenDuo was given at visit 1 to the patients at the trial site.	
Reporting group title	Period 2 - IMP
Reporting group description:	
When randomized to treatment sequence 2, the IMP Nasic Neo was given after wash-out at visit 3 to the patients at the trial site.	
Subject analysis set title	Intergroup comparison - Treatment sequence 1
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Inter-group comparison for the sum score of the sensoric assessment, ΔV1-V2 vs. ΔV3-V4	
Subject analysis set title	Intergroup comparison - Treatment sequence 2
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Inter-group comparison for the sum score of the sensoric assessment, ΔV1-V2 vs. ΔV3-V4	
Subject analysis set title	Intragroup comparison - Treatment sequence 1
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Intra-group comparison for further clinical effects- ΔV1-V2 vs. ΔV3-V4	
Subject analysis set title	Intragroup comparison - Treatment sequence 2
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Intra-group comparison for further clinical effects- ΔV1-V2 vs. ΔV3-V4	

Primary: Primary efficacy - sum scores of the assessments of the 14 items NSSS - inter group comparison

End point title	Primary efficacy - sum scores of the assessments of the 14 items NSSS - inter group comparison
End point description:	
The primary endpoint of the study was the difference in the total-score of the sensory-assessments from the Nasal-Spray-Sensoric-Scale (14 items) between IMP and the comparative preparation after first application. The differences between the 2 nasal sprays were analysed independently of each other in the cross-over design in the assessments at V1 und V3 at the respective first application of the nasal sprays (inter-group-differences).	
End point type	Primary
End point timeframe:	
Visit 1 to visit 4	

End point values	Intergroup comparison - Treatment sequence 1	Intergroup comparison - Treatment sequence 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	23		
Units: other				
arithmetic mean (standard deviation)				
V1: NSSS	1172.38 (± 147.215)	1123.78 (± 199.424)		
V2: NSSS	1102.27 (± 222.836)	1078.48 (± 214.222)		
V3: NSSS	1230.69 (± 149.01)	1217.57 (± 162.76)		
V4: NSSS	1146.77 (± 265.751)	1145.26 (± 198.816)		

Statistical analyses

Statistical analysis title	Descriptive analysis for primary endpoint

Statistical analysis description:

The analysis of the data of the primary end point was conducted using descriptive statistics.

Comparison groups	Intergroup comparison - Treatment sequence 1 v Intergroup comparison - Treatment sequence 2
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.487
Method	ANCOVA

Notes:

[1] - The inter-group-differences of the sum scores in both treatment sequences showed a numerical superiority for the IMP.

Secondary: Assessment of the sensory quality of nasal sprays, NSSS - intra group comparison

End point title	Assessment of the sensory quality of nasal sprays, NSSS - intra group comparison

End point description:

The comparison of intra-group changes in the sum score of the sensory evaluation from the Nasal Spray Sensory Scale over the course of treatment (ΔV1-V2 vs. ΔV3-V4).

End point type	Secondary

End point timeframe:

Visit 1 to visit 4

End point values	Intragroup comparison - Treatment sequence 1	Intragroup comparison - Treatment sequence 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	23		
Units: other				
arithmetic mean (standard deviation)				
Sensory quality - ΔV1-V2	-2.35 (± 14.762)	-5.96 (± 24.08)		
Sensory quality - ΔV3-V4	5.69 (± 19.857)	-2.61 (± 30.449)		

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of the sensory quality of nasal sprays, Rhinoscopy score - inter group comparison

End point title	Assessment of the sensory quality of nasal sprays, Rhinoscopy score - inter group comparison

End point description:

The comparison of the inter-group differences in the individual sensory queries of the Nasal Spray Sensory Scale at V1 and V3 at the respective first use of the nasal sprays.

End point type	Secondary

End point timeframe:

Visit 1 to Visit 4

End point values	Intergroup comparison - Treatment sequence 1	Intergroup comparison - Treatment sequence 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	23		
Units: other				
arithmetic mean (standard deviation)				
Rhinoscopy score - ΔV1-V2	0.69 (± 1.569)	1.22 (± 1.347)		
Rhinoscopy score - ΔV3-V4	1.19 (± 1.96)	0.91 (± 2.151)		

Statistical analyses

No statistical analyses for this end point

Secondary: Further clinical effects, nasal obstruction, VAS - intra group comparison

End point title	Further clinical effects, nasal obstruction, VAS - intra group comparison

End point description:

The clinical effects of using the two nasal sprays were assessed by the change in nasal obstruction on a visual analogue scale (VAS) between V1 and V2, V1 and V3 and between V3 and V4.

End point type	Secondary

End point timeframe:

Visit 1 to Visit 4

End point values	Intragroup comparison - Treatment sequence 1	Intragroup comparison - Treatment sequence 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	23		
Units: other				
arithmetic mean (standard deviation)				
VAS - ΔV1-V2	5.5385 (± 24.02038)	4.6957 (± 29.08988)		
VAS - ΔV3-V4	5.7692 (± 23.70031)	16.2609 (± 37.5139)		
VAS - ΔV1-V3	12.92 (± 28.53)	-12.913 (± 36.55)		

Statistical analyses

Statistical analysis title	Nasal obstruction on VAS, difference V1 - V3

Statistical analysis description:

Nasal obstruction significantly improved from first to second treatment period after treatment with the IMP demonstrating an advantage of the IMP over the comparative product.

Comparison groups	Intragroup comparison - Treatment sequence 2 v Intragroup comparison - Treatment sequence 1
Number of subjects included in analysis	49
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.008
Method	t-test, 2-sided

Secondary: Individual sensory score - Estimation of the nasal moisturization

End point title	Individual sensory score - Estimation of the nasal moisturization

End point description:

The 10th item of the NSSS "Estimation of the nasal moisturization" was analysed separately for the first and the second period for the treatment with the IMP and the comparative product, respectively.

End point type	Secondary

End point timeframe:

Visit 1 to visit 4

End point values	Intragroup comparison - Treatment sequence 1	Intragroup comparison - Treatment sequence 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	23		
Units: other				
arithmetic mean (standard deviation)				
ΔV1-V3	-4.12 (± 20.95)	-0.74 (± 25.80)		
ΔV1-V2	-4.50 (± 24.28)	0.78 (± 25.07)		
ΔV3-V4	-1.85 (± 21.91)	-8.96 (± 20.39)		

Statistical analyses

Statistical analysis title	Nasal moisturization, difference V3-V4

Statistical analysis description:

The improvement of nasal moisturization during period 2 (V3-V4) was significant after treatment with the IMP.

Comparison groups	Intragroup comparison - Treatment sequence 1 v Intragroup comparison - Treatment sequence 2
Number of subjects included in analysis	49
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.026
Method	Wilcoxon (Mann-Whitney)

Secondary: Final efficacy evaluation

End point title	Final efficacy evaluation

End point description:

Patients' assessment of overall efficacy of the two nasal sprays considering 4 evaluation points.

End point type	Secondary

End point timeframe:

Day 0 - 3 and day 7 - 10.

End point values	Period 1 - IMP	Period 1 - Comparator	Period 2 - Comparator	Period 2 - IMP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	25	25	26
Units: numbers				
very good	7	3	8	10
good	16	14	11	10
satisfactory	2	6	4	3
non satisfactory	1	1	1	3
no answer	0	1	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Overall tolerability

End point title	Overall tolerability

End point description:

Patients' assessment of overall tolerability of the two nasal sprays considering 4 evaluation points.

End point type	Secondary

End point timeframe:

Day 0 - 3 and day 7 - 10

End point values	Period 1 - IMP	Period 1 - Comparator	Period 2 - Comparator	Period 2 - IMP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	25	25	26
Units: numbers				
very good	13	9	12	14
good	12	10	9	7
satisfactory	1	4	2	4
non satisfactory	0	0	0	1
no answer	0	2	2	0

Statistical analyses

No statistical analyses for this end point

Secondary: Overall preference

End point title	Overall preference

End point description:

At V4 (day 10) or at the early termination follow up visit, patients were asked to indicate a preference of one of the two nasal sprays.

End point type	Secondary

End point timeframe:
Day 0-3 and day 7-10

End point values	Intragroup comparison - Treatment sequence 1	Intragroup comparison - Treatment sequence 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	23		
Units: numbers				
Nasal spray on day 0-3	11	6		
Nasal spray on day 7-10	11	17		
none of the nasal sprays	4	0		

Statistical analyses

Statistical analysis title	Overall preference

Statistical analysis description:

At V4 or at the early termination follow up visit, patients were asked to indicate a preference of one of the two nasal sprays. The results show a significant advantage of the IMP over the comparative product.

Comparison groups	Intragroup comparison - Treatment sequence 1 v Intragroup comparison - Treatment sequence 2
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.037
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Within time frame of drug administration (V1 through V4)

Adverse event reporting additional description:

Any adverse event experienced by a subject to whom one of the tested products had been administered, which was not necessarily causally related to that treatment was defined as adverse event

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	Full safety set

Reporting group description: -

Serious adverse events	Full safety set		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 51 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Full safety set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 51 (9.80%)		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	8		
Dizziness			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	8		
General disorders and administration site conditions			
Local reaction			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	1		

Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 51 (3.92%)		
occurrences (all)	8		
Rhinalgia			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	8		
Infections and infestations			
Herpes zoster			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	8		
Otitis media			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences (all)	8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/34689304