Clinical trial results:
Randomized, placebo-controlled, double-blind, cross-over trial with Bronchipret and Sinupret to evaluate acceleration of mucociliary clearance (MCC)

Summary

EudraCT number	2012-004864-24
Trial protocol	BE
Global end of trial date	27 December 2013

Results information

Result version number	v1 (current)
This version publication date	06 January 2023
First version publication date	06 January 2023

Trial information

Trial identification

Sponsor protocol code	COPD-1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bionorica SE
Sponsor organisation address	Kerschensteinerstraße 11-15, Neumarkt, Germany, 92318
Public contact	Head of cooperate communication, Bionorica SE, info@bionorica.de
Scientific contact	Head of research and development, Bionorica SE, research.development@bionorica.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	09 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 December 2013
Global end of trial reached?	Yes
Global end of trial date	27 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The overall aim of this trial was the proof of concept that the herbal drugs Bronchipret® and/or Sinupret® accelerate mucociliary clearance (MCC) of the respiratory tract.

Protection of trial subjects:

This study was conducted in compliance with the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use Good Clinical Practice, including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 June 2013
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	Belgium: 56
Worldwide total number of subjects	56
EEA total number of subjects	56

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)	56
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Of the 67 screened subjects, 56 were randomised to one of the two treatments (Bronchipret® or Sinupret®). Of the 56 subjects, 28 subjects were treated with Bronchipret® and Bronchipret® placebo and 28 subjects were treated with Sinupret® and Sinupret® placebo. None of the screening failures were treated with trial medication.

Pre-assignment

Screening details:

Up to 14 days before subject's randomisation to the treatment, a screening visit V 0 was performed to test subject's general eligibility for the trial. It was supposed that trial subjects have already developed a mild to moderate impairment of mucociliary clearance due to their smoking habits.

Period 1

Period 1 title	Period 1 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Arms

Are arms mutually exclusive?	No
Arm title	Bronchipret Treatment

Arm description:

At Visit 1 (Day 0), subjects were randomly assigned to the following blinded treatment groups:
Group A: Treatment period 1: 2 FCTs of Bronchipret® (verum) TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Bronchipret® placebo TID for 7 days (±1 day).
Group B: Treatment period 1: 2 FCTs of Bronchipret® placebo TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Bronchipret® (verum) TID for 7 days (±1 day).

Arm type	Experimental
Investigational medicinal product name	Bronchipret®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

2 film coated tablets (FCTs) three times daily (TID) for 7 days (±1 day)

Arm title	Sinupret Treatment

Arm description:

At Visit 1 (Day 0), subjects were randomly assigned to the following blinded treatment groups:
Group C: Treatment period 1: 2 CTs of Sinupret® (verum) TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 CTs of Sinupret® placebo TID for 7 days (±1 day).
Group D: Treatment period 1: 2 CTs of Sinupret® placebo TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Sinupret® (verum) TID for 7 days (±1 day).

Arm type	Experimental
Investigational medicinal product name	Sinupret® extract mite
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

2 coated tablets (CTs) TID for 7 days (±1 day)

Arm title	Bronchipret-Placebo Treatment

Arm description:

At Visit 1 (Day 0), subjects were randomly assigned to the following blinded treatment groups:
Group A: Treatment period 1: 2 FCTs of Bronchipret® (verum) TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Bronchipret® placebo TID for 7 days (±1 day).
Group B: Treatment period 1: 2 FCTs of Bronchipret® placebo TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Bronchipret® (verum) TID for 7 days (±1 day).

Arm type	Placebo
Investigational medicinal product name	Bronchipret® placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

2 film coated tablets (FCTs) three times daily (TID) for 7 days (±1 day)

Arm title	Sinupret-Placebo Treatment

Arm description:

At Visit 1 (Day 0), subjects were randomly assigned to the following blinded treatment groups:
Group C: Treatment period 1: 2 CTs of Sinupret® (verum) TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 CTs of Sinupret® placebo TID for 7 days (±1 day).
Group D: Treatment period 1: 2 CTs of Sinupret® placebo TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Sinupret® (verum) TID for 7 days (±1 day).

Arm type	Placebo
Investigational medicinal product name	Sinupret Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

2 coated tablets TID for 7 days (±1 day)

Number of subjects in period 1	Bronchipret Treatment	Sinupret Treatment	Bronchipret-Placebo Treatment
Started	28	28	28
End of treatment with Verum	28	28	28
End of wash-out period	28	28	28
End of treatment with Placebo	28	28	28
Completed	28	28	28

Number of subjects in period 1	Sinupret-Placebo Treatment
Started	28
End of treatment with Verum	28
End of wash-out period	28
End of treatment with Placebo	28
Completed	28

Baseline characteristics

Reporting groups	
Reporting group title	Bronchipret Treatment
Reporting group description:	
At Visit 1 (Day 0), subjects were randomly assigned to the following blinded treatment groups: Group A: Treatment period 1: 2 FCTs of Bronchipret® (verum) TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Bronchipret® placebo TID for 7 days (±1 day). Group B: Treatment period 1: 2 FCTs of Bronchipret® placebo TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Bronchipret® (verum) TID for 7 days (±1 day).	
Reporting group title	Sinupret Treatment
Reporting group description:	
At Visit 1 (Day 0), subjects were randomly assigned to the following blinded treatment groups: Group C: Treatment period 1: 2 CTs of Sinupret® (verum) TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 CTs of Sinupret® placebo TID for 7 days (±1 day). Group D: Treatment period 1: 2 CTs of Sinupret® placebo TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Sinupret® (verum) TID for 7 days (±1 day).	
Reporting group title	Bronchipret-Placebo Treatment
Reporting group description:	
At Visit 1 (Day 0), subjects were randomly assigned to the following blinded treatment groups: Group A: Treatment period 1: 2 FCTs of Bronchipret® (verum) TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Bronchipret® placebo TID for 7 days (±1 day). Group B: Treatment period 1: 2 FCTs of Bronchipret® placebo TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Bronchipret® (verum) TID for 7 days (±1 day).	
Reporting group title	Sinupret-Placebo Treatment
Reporting group description:	
At Visit 1 (Day 0), subjects were randomly assigned to the following blinded treatment groups: Group C: Treatment period 1: 2 CTs of Sinupret® (verum) TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 CTs of Sinupret® placebo TID for 7 days (±1 day). Group D: Treatment period 1: 2 CTs of Sinupret® placebo TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Sinupret® (verum) TID for 7 days (±1 day).	

Reporting group values	Bronchipret Treatment	Sinupret Treatment	Bronchipret-Placebo Treatment
Number of subjects	28	28	28
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)	28	28	28
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	32.6	30.9	32.6
standard deviation	± 5.2	± 3.8	± 5.2
Gender categorical Units: Subjects			
Female	15	12	15

Male	13	16	13

Reporting group values	Sinupret-Placebo Treatment	Total	
Number of subjects	28	56	
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)	0	0	
Adults (18-64 years)	28	56	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	30.9		
standard deviation	± 3.8	-	
Gender categorical Units: Subjects			
Female	12	27	
Male	16	29	

Subject analysis sets

Subject analysis set title	Bronchipret-FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS for the efficacy analysis included all randomised subjects with at least one documented application of the investigational drug and evaluable saccharin tests at the beginning and end of the active treatment period and the beginning and end of the corresponding placebo period.

Subject analysis set title	Bronchipret-PP
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population for the efficacy analysis included all FAS subjects who did not show protocol deviations which could have a relevant influence on the assessment of the primary endpoint.
To be accountable for the PP population a trial subject took 80 – 120% of IMP during each of the both treatment periods and the last three scheduled doses of IMP prior to the saccharin test at the end of treatment period 1 (V 2) and the end of treatment period 2 (V 4).

Subject analysis set title	Sinupret-FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS for the efficacy analysis included all randomised subjects with at least one documented application of the investigational drug and evaluable saccharin tests at the beginning and end of the active treatment period and the beginning and end of the corresponding placebo period.

Subject analysis set title	Sinupret-PP
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population for the efficacy analysis included all FAS subjects who did not show protocol

deviations which could have a relevant influence on the assessment of the primary endpoint.
To be accountable for the PP population a trial subject took 80 – 120% of IMP during each of the both treatment periods and the last three scheduled doses of IMP prior to the saccharin test at the end of treatment period 1 (V 2) and the end of treatment period 2 (V 4).

Reporting group values	Bronchipret-FAS	Bronchipret-PP	Sinupret-FAS
Number of subjects	28	25	28
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)	28	25	28
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	32.6	32.8	30.9
standard deviation	± 5.2	± 5.3	± 3.8
Gender categorical Units: Subjects			
Female	15	15	12
Male	13	10	16

Reporting group values	Sinupret-PP		
Number of subjects	21		
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)	21		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	31.1		
standard deviation	± 4.0		
Gender categorical Units: Subjects			
Female	9		
Male	12		

End points

End points reporting groups

Reporting group title	Bronchipret Treatment

Reporting group description:

At Visit 1 (Day 0), subjects were randomly assigned to the following blinded treatment groups:
Group A: Treatment period 1: 2 FCTs of Bronchipret® (verum) TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Bronchipret® placebo TID for 7 days (±1 day).
Group B: Treatment period 1: 2 FCTs of Bronchipret® placebo TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Bronchipret® (verum) TID for 7 days (±1 day).

Reporting group title	Sinupret Treatment

Reporting group description:

At Visit 1 (Day 0), subjects were randomly assigned to the following blinded treatment groups:
Group C: Treatment period 1: 2 CTs of Sinupret® (verum) TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 CTs of Sinupret® placebo TID for 7 days (±1 day).
Group D: Treatment period 1: 2 CTs of Sinupret® placebo TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Sinupret® (verum) TID for 7 days (±1 day).

Reporting group title	Bronchipret-Placebo Treatment

Reporting group description:

At Visit 1 (Day 0), subjects were randomly assigned to the following blinded treatment groups:
Group A: Treatment period 1: 2 FCTs of Bronchipret® (verum) TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Bronchipret® placebo TID for 7 days (±1 day).
Group B: Treatment period 1: 2 FCTs of Bronchipret® placebo TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Bronchipret® (verum) TID for 7 days (±1 day).

Reporting group title	Sinupret-Placebo Treatment

Reporting group description:

At Visit 1 (Day 0), subjects were randomly assigned to the following blinded treatment groups:
Group C: Treatment period 1: 2 CTs of Sinupret® (verum) TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 CTs of Sinupret® placebo TID for 7 days (±1 day).
Group D: Treatment period 1: 2 CTs of Sinupret® placebo TID for 7 days (±1 day), Wash-out for 7 days (+7 days), Treatment period 2: 2 FCTs of Sinupret® (verum) TID for 7 days (±1 day).

Subject analysis set title	Bronchipret-FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS for the efficacy analysis included all randomised subjects with at least one documented application of the investigational drug and evaluable saccharin tests at the beginning and end of the active treatment period and the beginning and end of the corresponding placebo period.

Subject analysis set title	Bronchipret-PP
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population for the efficacy analysis included all FAS subjects who did not show protocol deviations which could have a relevant influence on the assessment of the primary endpoint.
To be accountable for the PP population a trial subject took 80 – 120% of IMP during each of the both treatment periods and the last three scheduled doses of IMP prior to the saccharin test at the end of treatment period 1 (V 2) and the end of treatment period 2 (V 4).

Subject analysis set title	Sinupret-FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS for the efficacy analysis included all randomised subjects with at least one documented application of the investigational drug and evaluable saccharin tests at the beginning and end of the active treatment period and the beginning and end of the corresponding placebo period.

Subject analysis set title	Sinupret-PP
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population for the efficacy analysis included all FAS subjects who did not show protocol deviations which could have a relevant influence on the assessment of the primary endpoint.
To be accountable for the PP population a trial subject took 80 – 120% of IMP during each of the both treatment periods and the last three scheduled doses of IMP prior to the saccharin test at the end of

treatment period 1 (V 2) and the end of treatment period 2 (V 4).

Primary: Relative time to perception of sweetness after 7 days treatment with Bronchipret

End point title	Relative time to perception of sweetness after 7 days treatment with Bronchipret[1]

End point description:

The primary endpoint was defined as the time to perception of sweetness following the placement of a particle of sodium saccharin on the surface of the inferior nasal concha after 7 days of oral treatment with the investigational products or placebo - relative to the time to perception of sweetness at the beginning of treatment.

End point type	Primary

End point timeframe:

The relative time to perception of sweetness (tps) after 7 days of treatment with the investigational products (relative to the tps before the beginning of treatment) in each treatment period is defined as the primary endpoint.

Notes:

[1] - 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: The overall aim of this trial was to demonstrate the superiority of Bronchipret® and/or Sinupret® over placebo regarding acceleration of MCC . Therefore, 2 analyses were performed for the primary endpoint: one comparing the treatment with Bronchipret vs. Bronchipret placebo and another one comparing the treatment with Sinupret vs. Sinupret placebo regarding the acceleration of MCC.

End point values	Bronchipret Treatment	Bronchipret-Placebo Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: seconds				
arithmetic mean (standard deviation)	101.2 (± 59.2)	111.6 (± 59.1)		

Statistical analyses

Statistical analysis title	Treatment difference of Bronchipret® and placebo

Statistical analysis description:

Treatment difference of Bronchipret® and placebo on relative time to perception of sweetness after 7 days treatment tested by ANOVA

Comparison groups	Bronchipret Treatment v Bronchipret-Placebo Treatment
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.364
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.16

Primary: Relative time to perception of sweetness after 7 days treatment with Sinupret

End point title	Relative time to perception of sweetness after 7 days treatment with Sinupret[2]

End point description:

The primary endpoint was defined as the time to perception of sweetness following the placement of a particle of sodium saccharin on the surface of the inferior nasal concha after 7 days of oral treatment with the investigational products or placebo - relative to the time to perception of sweetness at the beginning of treatment.

End point type	Primary

End point timeframe:

The relative time to perception of sweetness (tps) after 7 days of treatment with the investigational products (relative to the tps before the beginning of treatment) in each treatment period is defined as the primary endpoint.

Notes:

[2] - 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: The overall aim of this trial was to demonstrate the superiority of Bronchipret® and/or Sinupret® over placebo regarding acceleration of MCC . Therefore, 2 analyses were performed for the primary endpoint: one comparing the treatment with Bronchipret vs. Bronchipret placebo and another one comparing the treatment with Sinupret vs. Sinupret placebo regarding the acceleration of MCC.

End point values	Sinupret Treatment	Sinupret-Placebo Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: seconds				
arithmetic mean (standard deviation)	128.6 (± 91.2)	107.8 (± 57.2)		

Statistical analyses

Statistical analysis title	Relative tps after 7 days treatment

Statistical analysis description:

Treatment difference of Sinupret® and placebo on relative time to perception of sweetness tested by ANOVA

Comparison groups	Sinupret Treatment v Sinupret-Placebo Treatment
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.66
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.51

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs during the treatment period are reported. All AEs occurring during wash-out periods were added to the preceding active treatment or placebo period, respectively.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Sinupret-Placebo Treatment
Reporting group description: -	
Reporting group title	Sinupret Treatment
Reporting group description: -	
Reporting group title	Bronchipret Treatment
Reporting group description: -	
Reporting group title	Bronchipret-Placebo Treatment
Reporting group description: -	

Serious adverse events	Sinupret-Placebo Treatment	Sinupret Treatment	Bronchipret Treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Bronchipret-Placebo Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (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	Sinupret-Placebo Treatment	Sinupret Treatment	Bronchipret Treatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 28 (53.57%)	13 / 28 (46.43%)	15 / 28 (53.57%)

Vascular disorders			
Haematoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Mole excision			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	1 / 28 (3.57%)	0 / 28 (0.00%)
occurrences (all)	1	1	0
Influenza like illness			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Breast inflammation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Dyspnoea exertional			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Increased upper airway secretion			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 28 (7.14%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	2	0	0
Nasal obstruction			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Oropharyngeal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	1 / 28 (3.57%)
occurrences (all)	0	1	1
Rhinorrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	2 / 28 (7.14%)	2 / 28 (7.14%)
occurrences (all)	0	2	2
Upper-airway cough syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	1 / 28 (3.57%)	2 / 28 (7.14%)
occurrences (all)	1	1	4
Injury, poisoning and procedural complications			
Muscle rupture			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Wound			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 28 (17.86%)	5 / 28 (17.86%)	5 / 28 (17.86%)
occurrences (all)	5	5	6
Migraine			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Tremor			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye pruritus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Eye swelling			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Constipation			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	3 / 28 (10.71%)	1 / 28 (3.57%)
occurrences (all)	1	3	1
Dry mouth			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Flatulence			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	2 / 28 (7.14%)	2 / 28 (7.14%)
occurrences (all)	1	2	2
Frequent bowel movements			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	1 / 28 (3.57%)	0 / 28 (0.00%)
occurrences (all)	1	1	0
Gingival inflammation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Reflux gastritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1

Toothache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Dry skin			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Pruritus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Rash			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Myalgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Infections and infestations			
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Lower respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 28 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Pulpitis dental			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	1 / 28 (3.57%)	0 / 28 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Bronchipret-Placebo Treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 28 (64.29%)		
Vascular disorders			
Haematoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			

Mole excision			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Influenza like illness			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Breast inflammation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Dyspnoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Dyspnoea exertional			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Increased upper airway secretion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Nasal obstruction			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Oropharyngeal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Rhinorrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Upper-airway cough syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Muscle rupture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Wound			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Migraine			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Tremor			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Eye disorders			
Eye pruritus			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Eye swelling			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Constipation			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Diarrhoea			
alternative assessment type: Non-systematic			

subjects affected / exposed	2 / 28 (7.14%)			
occurrences (all)	2			
Dry mouth				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Flatulence				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			
Frequent bowel movements				
alternative assessment type: Non-systematic				
subjects affected / exposed	2 / 28 (7.14%)			
occurrences (all)	2			
Gingival inflammation				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			
Haemorrhoids				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Nausea				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			
Reflux gastritis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Toothache				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences (all)	1			

Skin and subcutaneous tissue disorders			
Acne			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Dry skin			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pruritus			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Rash			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Myalgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Pain in extremity			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Infections and infestations			

Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Lower respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Oral herpes			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pulpitis dental			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 October 2013	The Amendment No. 1 was necessary to implement that the inclusion criterion number 4 is proven by assessing ability to taste sweetness of saccharin on the basis of saccharin test (perception of sweetness within 30 minutes after placement of saccharin behind nasal valve) at V 0. Therefore, placing saccharin particles on the tongue for the "assessment of the ability to taste sweetness of saccharin" as required by protocol at V 0 was not necessary and was deleted. Due to the fact that the taste of saccharin can persist a certain time, it is not adequate to apply saccharin on tongue shortly prior the saccharin test. Furthermore some editorial corrections for clarification were done. Additionally, the planned time lines of trial conduct were adapted. These changes had no substantial implications on the scientific value of the trial, the conduct of the trial or the safety of the trial subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported