Clinical trial results:
A multi-center, randomized, placebo-controlled, double-blind, dose-finding clinical trial investigating the short-term relief of symptoms of acute pharyngitis such as throat soreness pain and difficulty to swallow by treatment with three different doses of MYRAMISTIN™ oromucosal spray

Summary

EudraCT number	2018-002543-28
Trial protocol	DE AT
Global end of trial date	31 December 2021

Results information

Result version number	v1 (current)
This version publication date	18 January 2023
First version publication date	18 January 2023

Trial information

Trial identification

Sponsor protocol code	MIRA1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04470089
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MEGAINPHARM GmbH
Sponsor organisation address	Wörthersee-Süduferstraße 163c5, Maria Wörth, Austria, 9082
Public contact	Evgeni Gorokhov, MEGAINPHARM GmbH, 0043 15134733, evgorokhov@megainpharm.com
Scientific contact	Dr. Andrew Leary, regenold GmbH , 0049 07632 8226-418, andrew.leary@regenold.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	31 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2021
Global end of trial reached?	Yes
Global end of trial date	31 December 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the short-term efficacy of different MyramistinTM doses (0.005%, 0.01% and 0.02%) compared to placebo in the symptomatic treatment of acute pharyngitis.

Protection of trial subjects:

This clinical trial was designed and was implemented and reported in accordance with the ICH Harmonized Tripartite Guidelines for Good Clinical Practice, with applicable local regulations (including applicable European Directives, AMG and GCP-V), and with the ethical principles laid down in the Declaration of Helsinki. Every patient was informed verbally and also in writing, with a patient information leaflet explaining the nature of the study, its objectives, the study medication and potential risks, the rights and obligations of the participant and the fact that he was free to withdraw his consent at any time without giving any reason. Details of indemnity and insurance were also stated. All questions about the trial were answered to the satisfaction of the patient. Women of child bearing potential had to be informed that taking the IMP may involve unknown risks to the fetus if pregnancy occurred during the clinical trial and agree that in order to participate in the clinical trial, they must adhere to the contraception requirement for the duration of the clinical trial. Prior to the participation in the trial, a written informed consent form had to be signed and personally dated by the subject and by the person who conducted the informed consent. The patient's information and informed consent form were available in the local language. The final trial protocol together with the patient information sheet, the informed consent form and the Investigator's drug brochure were submitted to the involved Ethics Committees and were constituted to fulfil regulatory laws. The study was approved by all Ethics Committees before clinical trial start.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 February 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: 169
Worldwide total number of subjects	169
EEA total number of subjects	169

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	160
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients were recruited in Germany in practices of general practitioners and specialists for ear nose and throat. Recruitment started in February 2020 and was interrupted from March 2020 until September 2020 due to COVID. After restart recruitment was very slow.

Pre-assignment

Screening details:

Screening and first study medication application was possible the same day. Only one screening failure was identified during the study, who did not fulfil inclusion criteria and was not randomised.

Period 1

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

Blinding implementation details:

A randomisation list was created by an independent company containing the random numbers, code and treatment descriptions.
It was sorted by random number. Based on this list MoNo chem-pharm Produkte GmbH filled in the different doses in a white opaque spray, which is delivered in a white, neutral outer carton. The packaging and labeling of the IMP was done in accordance with the applicable regulatory requirements of each participating country and under the responsibility of MoNo.

Arms

Are arms mutually exclusive?	Yes
Arm title	Myramistin 0.005%

Arm description:

0.005% Myramistin oromucosal spray containing 0.05 mg myramistin per 1 ml
Unit dose amounts to 0.42 ml per application (3 puffs of 0.14 ml, administered to the back of the throat) in all treatment arms. Myramistin/Placebo is administered 3 times per day with a minimum of 4 hours between two subsequent doses. The total amount applied per day is 1.26 ml.

Arm type	Experimental
Investigational medicinal product name	Myramistin 0.005%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

Myramistin™ spray was applied to the back of the throat 3 times a day for 3 days with a minimum of 4 hours between two subsequent doses. Each application consisted of 3 puffs and each puff delivered 0.14 ml (i.e., a total of 0.42 ml per application). The first application was done at the study centre, whereas the following applications were administered at home. In total, Myramistin™ was to be applied 9-10 times during the trial.

Arm title	Myramistin 0.01%

Arm description:

0.01% of Myramistin oromucosal spray containing 0.1 mg myramistin per 1 ml
Unit dose amounts to 0.42 ml per application (3 puffs of 0.14 ml, administered to the back of the throat) in all treatment arms. Myramisti/Placebo is administered 3 times per day with a minimum of 4 hours between two subsequent doses. The total amount applied per day is 1.26 ml.

Arm type	Experimental

Investigational medicinal product name	Myramistin 0.01%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

Myramistin™ spray was applied to the back of the throat 3 times a day for 3 days with a minimum of 4 hours between two subsequent doses. Each application consisted of 3 puffs and each puff delivered 0.14 ml (i.e., a total of 0.42 ml per application). The first application was done at the study centre, whereas the following applications were administered at home. In total, Myramistin™ was to be applied 9-10 times during the trial.

Arm title	Myramistin 0.02%

Arm description:

0.02% of Myramistin oromucosal spray containing 0.2 mg myramistin per 1 ml,
Unit dose amounts to 0.42 ml per application (3 puffs of 0.14 ml, administered to the back of the throat) in all treatment arms. Myramistin/Placebo is administered 3 times per day with a minimum of 4 hours between two subsequent doses. The total amount applied per day is 1.26 ml.

Arm type	Experimental
Investigational medicinal product name	Myramistin 0.02%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

Myramistin™ spray was applied to the back of the throat 3 times a day for 3 days with a minimum of 4 hours between two subsequent doses. Each application consisted of 3 puffs and each puff delivered 0.14 ml (i.e., a total of 0.42 ml per application). The first application was done at the study centre, whereas the following applications were administered at home. In total, Myramistin™ was to be applied 9-10 times during the trial.

Arm title	Placebo

Arm description:

Placebo: matched control spray not containing myramistin.
Unit dose amounts to 0.42 ml per application (3 puffs of 0.14 ml, administered to the back of the throat) in all treatment arms. Myramistin/Placebo is administered 3 times per day with a minimum of 4 hours between two subsequent doses. The total amount applied per day is 1.26 ml.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

Placebo spray was applied to the back of the throat 3 times a day for 3 days with a minimum of 4 hours between two subsequent doses. Each application consisted of 3 puffs and each puff delivered 0.14 ml (i.e., a total of 0.42 ml per application). The first application was done at the study centre, whereas the following applications were administered at home. In total, Myramistin™ was to be applied 9-10 times during the trial.

Number of subjects in period 1	Myramistin 0.005%	Myramistin 0.01%	Myramistin 0.02%
Started	40	46	40
Completed	40	46	40

Number of subjects in period 1	Placebo
Started	43
Completed	43

Baseline characteristics

Reporting groups	
Reporting group title	Myramistin 0.005%
Reporting group description:	
0.005% Myramistin oromucosal spray containing 0.05 mg myramistin per 1 ml Unit dose amounts to 0.42 ml per application (3 puffs of 0.14 ml, administered to the back of the throat) in all treatment arms. Myramistin/Placebo is administered 3 times per day with a minimum of 4 hours between two subsequent doses. The total amount applied per day is 1.26 ml.	
Reporting group title	Myramistin 0.01%
Reporting group description:	
0.01% of Myramistin oromucosal spray containing 0.1 mg myramistin per 1 ml Unit dose amounts to 0.42 ml per application (3 puffs of 0.14 ml, administered to the back of the throat) in all treatment arms. Myramisti/Placebo is administered 3 times per day with a minimum of 4 hours between two subsequent doses. The total amount applied per day is 1.26 ml.	
Reporting group title	Myramistin 0.02%
Reporting group description:	
0.02% of Myramistin oromucosal spray containing 0.2 mg myramistin per 1 ml, Unit dose amounts to 0.42 ml per application (3 puffs of 0.14 ml, administered to the back of the throat) in all treatment arms. Myramistin/Placebo is administered 3 times per day with a minimum of 4 hours between two subsequent doses. The total amount applied per day is 1.26 ml.	
Reporting group title	Placebo
Reporting group description:	
Placebo: matched control spray not containing myramistin. Unit dose amounts to 0.42 ml per application (3 puffs of 0.14 ml, administered to the back of the throat) in all treatment arms. Myramistin/Placebo is administered 3 times per day with a minimum of 4 hours between two subsequent doses. The total amount applied per day is 1.26 ml.	

Reporting group values	Myramistin 0.005%	Myramistin 0.01%	Myramistin 0.02%
Number of subjects	40	46	40
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)	35	45	40
From 65-84 years	5	1	0
85 years and over	0	0	0
Age continuous Units: years			
median	40.7	36.0	38.5
full range (min-max)	19 to 68	18 to 68	18 to 64
Gender categorical Units: Subjects			
Female	29	28	28
Male	11	18	12

Smoking History Units: Subjects			
Non smoker	30	38	30
Smoker	9	8	7
Ex smoker	1	0	3

Reporting group values	Placebo	Total	
Number of subjects	43	169	
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)	40	160	
From 65-84 years	3	9	
85 years and over	0	0	
Age continuous Units: years			
median	39.8		
full range (min-max)	18 to 69	-	
Gender categorical Units: Subjects			
Female	28	113	
Male	15	56	
Smoking History Units: Subjects			
Non smoker	34	132	
Smoker	9	33	
Ex smoker	0	4	

Subject analysis sets

Subject analysis set title	Safety Evaluable Set (SES)
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety and tolerability evaluations were done using the SES including all randomized patients with at least one dose of study medication and at least had one safety assessment performed.

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Primary and secondary efficacy endpoints were evaluated using the FAS, defined as all randomized patients who received at least one dose of study medication and had at least one post-treatment efficacy assessment.

Reporting group values	Safety Evaluable Set (SES)	Full Analysis Set (FAS)	
Number of subjects	169	169	

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)	160	160	
From 65-84 years	9	9	
85 years and over	0	0	
Age continuous Units: years			
median	38,7	38,7	
full range (min-max)	18 to 69	18 to 69	
Gender categorical Units: Subjects			
Female	113	113	
Male	56	56	
Smoking History Units: Subjects			
Non smoker	132	132	
Smoker	33	33	
Ex smoker	4	4	

End points

End points reporting groups

Reporting group title	Myramistin 0.005%

Reporting group description:

0.005% Myramistin oromucosal spray containing 0.05 mg myramistin per 1 ml
Unit dose amounts to 0.42 ml per application (3 puffs of 0.14 ml, administered to the back of the throat) in all treatment arms. Myramistin/Placebo is administered 3 times per day with a minimum of 4 hours between two subsequent doses. The total amount applied per day is 1.26 ml.

Reporting group title	Myramistin 0.01%

Reporting group description:

0.01% of Myramistin oromucosal spray containing 0.1 mg myramistin per 1 ml
Unit dose amounts to 0.42 ml per application (3 puffs of 0.14 ml, administered to the back of the throat) in all treatment arms. Myramisti/Placebo is administered 3 times per day with a minimum of 4 hours between two subsequent doses. The total amount applied per day is 1.26 ml.

Reporting group title	Myramistin 0.02%

Reporting group description:

0.02% of Myramistin oromucosal spray containing 0.2 mg myramistin per 1 ml,
Unit dose amounts to 0.42 ml per application (3 puffs of 0.14 ml, administered to the back of the throat) in all treatment arms. Myramistin/Placebo is administered 3 times per day with a minimum of 4 hours between two subsequent doses. The total amount applied per day is 1.26 ml.

Reporting group title	Placebo

Reporting group description:

Placebo: matched control spray not containing myramistin.
Unit dose amounts to 0.42 ml per application (3 puffs of 0.14 ml, administered to the back of the throat) in all treatment arms. Myramistin/Placebo is administered 3 times per day with a minimum of 4 hours between two subsequent doses. The total amount applied per day is 1.26 ml.

Subject analysis set title	Safety Evaluable Set (SES)
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety and tolerability evaluations were done using the SES including all randomized patients with at least one dose of study medication and at least had one safety assessment performed.

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

Primary and secondary efficacy endpoints were evaluated using the FAS, defined as all randomized patients who received at least one dose of study medication and had at least one post-treatment efficacy assessment.

Primary: Summarized pain intensity differences (SPID-2Pain)

End point title	Summarized pain intensity differences (SPID-2Pain)

End point description:

The primary endpoint was SPID-2Pain, defined as pain intensity differences (PID) summarized over the time course of 2 hours after first application on Day 1 (Baseline). The sum was calculated over the time-weighted differences from each measured time point to Baseline using the 100 mm VAS Sore Throat Pain Intensity Scale (STPIS). The primary endpoint should show superiority of each of the individual active Myramistin doses (0.005%, 0.01% and 0.02%) versus Placebo.

End point type	Primary

End point timeframe:

From baseline summarized over 2 hours (SPID-2Pain) after first IMP application.

End point values	Myramistin 0.005%	Myramistin 0.01%	Myramistin 0.02%	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	46	40	43
Units: Pain intensity on 100 mm VAS score				
number (confidence interval 60%)	-1390.0 (-1521.68 to -1258.28)	-925.5 (-1047.96 to -803.13)	-1256.0 (-1387.90 to -1124.14)	-1492.8 (-1619.69 to -1365.92)

Statistical analyses

Statistical analysis title	Mixed-Model Repeated Measurement (MMRM)
Comparison groups	Myramistin 0.005% v Myramistin 0.01% v Myramistin 0.02% v Placebo
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.2
Method	Mixed models analysis

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Visit 1 after signing informed consent onwards to Visit 4.

Adverse event reporting additional description:

After the first IMP application patients were handed out a diary, which they had to complete twice daily. All adverse events were collected there and also through questioning the patient at visit 2. Lab values and vital signs were measured at each visit. Adverse events were assessed by the respective investigators.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Myramistin 0.005%

Reporting group description:

Seventeen adverse events were reported in this group, but only one patient, in this group described feeling of drunkenness assessed as related to the IMP. This adverse event resolved within one day. All other events were assessed as not related. Two adverse events were graded as moderate all other events as mild.

Reporting group title	Myramistin 0.01%

Reporting group description:

Seven adverse events were reported in this group. Only one of the adverse events in this group was assessed as related to the IMP. The patient reported about paresthesia in the tongue. All adverse events were graded as mild.

Reporting group title	Myramistin 0.02%

Reporting group description:

None of the eight reported adverse events in this group was assessed to be related to the IMP. All adverse events were graded as mild.

Reporting group title	Placebo

Reporting group description:

In total 10 adverse events were reported in this group. All adverse events were graded as mild. One patient reported about odynophagia, which was assessed as related to the IMP.

Serious adverse events	Myramistin 0.005%	Myramistin 0.01%	Myramistin 0.02%
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	0 / 46 (0.00%)	0 / 40 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 43 (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	Myramistin 0.005%	Myramistin 0.01%	Myramistin 0.02%
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 40 (17.50%)	4 / 46 (8.70%)	3 / 40 (7.50%)
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 40 (2.50%)	0 / 46 (0.00%)	0 / 40 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 40 (2.50%)	2 / 46 (4.35%)	2 / 40 (5.00%)
occurrences (all)	2	2	3
General disorders and administration site conditions			
Feeling drunk			
subjects affected / exposed	1 / 40 (2.50%)	0 / 46 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 40 (2.50%)	1 / 46 (2.17%)	0 / 40 (0.00%)
occurrences (all)	2	1	0
Gastrointestinal disorders			
Odynophagia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 46 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 40 (2.50%)	0 / 46 (0.00%)	1 / 40 (2.50%)
occurrences (all)	1	0	1
Paresthesia oral			
subjects affected / exposed	0 / 40 (0.00%)	1 / 46 (2.17%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			

subjects affected / exposed	0 / 40 (0.00%)	1 / 46 (2.17%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	2 / 40 (5.00%)	0 / 46 (0.00%)	0 / 40 (0.00%)
occurrences (all)	2	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 40 (0.00%)	0 / 46 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 46 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	2 / 40 (5.00%)	0 / 46 (0.00%)	0 / 40 (0.00%)
occurrences (all)	2	0	0
Cough			
subjects affected / exposed	0 / 40 (0.00%)	2 / 46 (4.35%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
Nasal congestion			
subjects affected / exposed	0 / 40 (0.00%)	0 / 46 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 40 (2.50%)	0 / 46 (0.00%)	0 / 40 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Pain in jaw			
subjects affected / exposed	1 / 40 (2.50%)	0 / 46 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 46 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Oral herpes			
subjects affected / exposed	0 / 40 (0.00%)	0 / 46 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
Bronchitis			

subjects affected / exposed	1 / 40 (2.50%)	0 / 46 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Pharyngitis	Additional description: Worsening of pharyngitis		
subjects affected / exposed	1 / 40 (2.50%)	0 / 46 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 43 (13.95%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	3		
General disorders and administration site conditions			
Feeling drunk			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Odynophagia			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Paresthesia oral			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Dyspepsia			

subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Epigastric discomfort subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0 1 / 43 (2.33%) 1 0 / 43 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	 0 / 43 (0.00%) 0 0 / 43 (0.00%) 0 1 / 43 (2.33%) 2 1 / 43 (2.33%) 1 0 / 43 (0.00%) 0		
Musculoskeletal and connective tissue disorders Pain in jaw subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all)	 0 / 43 (0.00%) 0 1 / 43 (2.33%) 1		
Infections and infestations Oral herpes subjects affected / exposed occurrences (all) Bronchitis	 0 / 43 (0.00%) 0		

subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Pharyngitis	Additional description: Worsening of pharyngitis		
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 October 2020	A substantial amendment was submitted to EC for restart after COVID in September 2020 but due to EC request a negative COVID test had to be added to the inclusion criteria. Furthermore, the study end was prolonged until end of second quarter of 2021.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 March 2020	Due to the high risks identified that patients, study personal and other people might get infected due to study visits, and the fact that there are alternative treatments, including available over the counter, the risk to patients at the current time was assessed to be higher than the benefit of clinical trial participation. In addition, there were several governmental rules in place requiring people to not leave the home in order to reduce "social contacts". This general societal aspect were also taken into consideration.	07 December 2020

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The results of the primary endpoint analysis indicate that Myramistin does not differentiate from placebo at any dose level. The same outcome was found for all secondary endpoints and all sensitivity analyses, and at all timepoints assessed.

Notes: