Clinical trial results:
Randomized, placebo-controlled, parallel group, double-blind, multi-center Phase III study to assess the inhibition of plaque formation of 0.1% octenidine mouthwash vs placebo in subjects with a gingival index 1.5

Summary

EudraCT number	2017-001697-42
Trial protocol	DE
Global end of trial date	14 December 2018

Results information

Result version number	v1 (current)
This version publication date	05 April 2020
First version publication date	05 April 2020

Trial information

Trial identification

Sponsor protocol code	OML-III-A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03322124
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Schülke & Mayr GmbH
Sponsor organisation address	Robert-Koch-Straße 2, Norderstedt, Germany, 22851
Public contact	Clinical trials information, Schülke & Mayr GmbH, Schülke & Mayr GmbH, +49 40 52100-0, info@schuelke.com
Scientific contact	Clinical trials information, Schülke & Mayr GmbH, Schülke & Mayr GmbH, +49 40 52100-0, info@schuelke.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	14 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 December 2018
Global end of trial reached?	Yes
Global end of trial date	14 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstration of superiority of 0.1% octenidine mouthwash (OML, "Octenidin Mundspüllösung") to placebo in the inhibition of plaque formation

Protection of trial subjects:

The study was performed in accordance with the International Council on Harmonisation (ICH) Guideline for Good Clinical Practice (GCP, CPMP/ICH/135/95), the appropriate national regulations and the Declaration of Helsinki.
Before any study-related procedures were performed, the investigator obtained written informed consent from all subjects. The investigator ensured that the subject was fully informed (verbally and in writing) about the aims, procedures, potential risks, discomforts, and expected benefits of the clinical study. The subject had ample time to ask questions and to decide whether or not to participate.
Only subjects that met all study inclusion criteria and none of the exclusion criteria were entered in the study. Participation in the study was voluntary and all subjects had the right to withdraw from the clinical study at any time and for any reason without any disadvantages for their medical care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 January 2018
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: 101
Worldwide total number of subjects	101
EEA total number of subjects	101

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)	101
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 3 centers in Germany. The first subject signed the informed consent form on 16-Jan-2018 and the last subject completed the study on 14-Dec-2018.

Pre-assignment

Screening details:

A total of 108 subjects were screened, of whom 7 subjects were screening failures.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	OML arm

Arm description:

0.1% octenidine mouthwash (OML)

Arm type	Experimental
Investigational medicinal product name	0.1% octenidine mouthwash
Investigational medicinal product code	
Other name	OML
Pharmaceutical forms	Mouthwash
Routes of administration	Oromucosal use

Dosage and administration details:

Subjects performed 10 applications of OML (mouth rinse with 10 mL OML for 30 s) over 5 days (3 times on Day 1, twice daily on Days 2-4, once on Day 5).

Arm title	Placebo arm

Arm description: -

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

Dosage and administration details:

Subjects performed 10 applications (mouth rinse with 10 mL placebo for 30 s) over 5 days (3 times on Day 1, twice daily on Days 2-4, once on Day 5).

Number of subjects in period 1	OML arm	Placebo arm
Started	77	24
Completed	77	24

Baseline characteristics

Reporting groups	
Reporting group title	OML arm
Reporting group description: 0.1% octenidine mouthwash (OML)	
Reporting group title	Placebo arm
Reporting group description: -	

Reporting group values	OML arm	Placebo arm	Total
Number of subjects	77	24	101
Age categorical Units: Subjects			
Adults (18-64 years)	77	24	101
Age continuous Units: years			
median	25	24	
full range (min-max)	18 to 47	20 to 35	-
Gender categorical Units: Subjects			
Female	44	15	59
Male	33	9	42
Gingival index Units: Subjects			
<= 1.0	70	23	93
> 1.0	7	1	8
Nicotine use Units: Subjects			
No	50	20	70
Yes	27	4	31

End points

End points reporting groups

Reporting group title	OML arm
Reporting group description: 0.1% octenidine mouthwash (OML)	
Reporting group title	Placebo arm
Reporting group description: -	

Primary: Total mean plaque index after 5 days of treatment at Visit 2

End point title	Total mean plaque index after 5 days of treatment at Visit 2[1]

End point description:

The thickness and extension of plaque along the gingival margin were assessed using the plaque index (PI) according to Silness and Löe, 1964. Evaluation of the PI was limited to "Ramfjord teeth" (16, 21, 24, 36, 41, 44 or their replacement teeth 17, 11, 25, 37, 31, 45). For each of the 4 surfaces a grade from 0 to 3 was given. The total mean PI was the sum of the individual grades divided by the number of investigated sites.

End point type	Primary

End point timeframe:

Day 5

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: Results of the statistical analysis could not be entered in the system.
The superiority of OML over placebo in inhibiting plaque formation was demonstrated using the van Elteren test stratified by gingival status at Visit 1 and center (1-sided p-value <0.0001; point estimate -0.950 [median difference, OML minus placebo]).

End point values	OML arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	24		
Units: total mean plaque index				
median (full range (min-max))	0.380 (0.00 to 1.42)	1.330 (0.33 to 1.96)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From time of first study drug administration (Day 1) until end of treatment (completion of study, Day 5).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	OML arm

Reporting group description:

Subjects performed 10 mouth rinses with OML over 5 days.

Reporting group title	Placebo arm

Reporting group description:

Subjects performed 10 mouth rinses with placebo over 5 days.

Serious adverse events	OML arm	Placebo arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 77 (0.00%)	0 / 24 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	OML arm	Placebo arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 77 (44.16%)	6 / 24 (25.00%)	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	21 / 77 (27.27%)	2 / 24 (8.33%)	
occurrences (all)	21	2	
Headache			
subjects affected / exposed	3 / 77 (3.90%)	2 / 24 (8.33%)	
occurrences (all)	4	2	
Gastrointestinal disorders			

Tongue discolouration			
subjects affected / exposed	5 / 77 (6.49%)	0 / 24 (0.00%)	
occurrences (all)	5	0	
Oral discomfort			
subjects affected / exposed	0 / 77 (0.00%)	2 / 24 (8.33%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 July 2017	To comply with requests from the German competent authority, the protocol was amended (protocol Version 3.0) to include a more detailed description of the required contraception measures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 March 2018	The study was halted, since metallic (zinc) contaminants were found in a substance that was used for the solution of the study drug flavors. All study drug bottles at centers that were still recruiting subjects at this time were controlled for visible particles using the 4-eye principle, and if found, contaminated bottles were quarantined, and the center was supplied with new study drug. Study drug with no visible particles was considered safe. Patients who had already completed the study were informed about the study drug contamination.	09 May 2018

Notes:

Limitations and caveats

None reported