



Clinical trial results: Four Week Clinical Efficacy of an Ethyl Lauroyl Arginate HCl (LAE) Mouth Rinse: Effect on Gingivitis

Summary

EudraCT number	2013-003548-22
Trial protocol	GB
Global end of trial date	31 July 2014

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	03 August 2015

Trial information

Trial identification

Sponsor protocol code	LAEBBA0005
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Johnson & Johnson Consumer & Personal Products Worldwide, Division of Johnson & Johnson Consumer Companies, Inc.
Sponsor organisation address	199 Grandview Road, Skillman, NJ, United States, 08558-9418
Public contact	Lisa Fitzgerald, Johnson & Johnson Consumer & Personal Products Worldwide, +1 908 904-6235, Lfitzge6@its.jnj.com
Scientific contact	Michael C Lynch, Johnson & Johnson Consumer & Personal Products Worldwide, +1 908 904-3039, Mlynch23@its.jnj.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 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2014
Global end of trial reached?	Yes
Global end of trial date	31 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this randomized, examiner-blind, single-centre, multi-site controlled, parallel-design clinical trial is to determine the efficacy of a 0.15 percentage (%) Ethyl Lauroyl Arginate HCL (LAE)-containing mouth rinse on whole-mouth mean gingival bleeding index (BI) scores as an adjunct to brushing through four weeks of use.

Protection of trial subjects:

Ethical Conduct of the Study

The study was performed in accordance with the protocol, with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines, including ICH E6 and in accordance with ISO 14155:2011. In addition, all local regulatory requirements will be followed.

Subject Information and Consent

All parties will ensure protection of subject personal data and will not include subject names on any forms, reports, publications, or in any other disclosures. In case of data transfer, Sponsor will maintain high standards of confidentiality and protection of subject personal data. The informed consent form in this study must be agreed to by the Sponsor and the Institutional Review Board (IRB)/Independent Ethics Committee (IEC) and must be in compliance with ICH GCP, local regulatory requirements, and legal requirements including International Organization for Standardization (ISO) 14155:2011. The Site will advise the Sponsor and the IRB/IEC if any administrative changes need to be made to the informed consent form during the course of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 March 2014
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	United Kingdom: 240
Worldwide total number of subjects	240
EEA total number of subjects	240

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)	237
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 240 subjects were enrolled in to the study and randomized into groups. Of which, 226 subjects completed the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor ^[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	Negative Control

Arm description:

Participants received placebo (5% Hydroalcohol Solution), rinse with 20ml for 30 seconds twice a day.

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

Dosage and administration details:

Participants received placebo (5% Hydroalcohol Solution), rinse with 20ml for 30 seconds twice a day.

Arm title	0.2 Percent (%) Chlorhexidine (CHX)
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Arm description:

Participants received 0.2 % CHX containing mouthrinse, rinse mouth with water and then rinse with 10ml for 60 seconds twice a day.

Arm type	Active comparator
Investigational medicinal product name	Corsodyl®Mint Mouthwash
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal solution
Routes of administration	Oromucosal use

Dosage and administration details:

Participants received 0.2 % CHX containing mouthrinse, rinse mouth with water and then rinse with 10ml for 60 seconds twice a day.

Arm title	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)
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Arm description:

Participants received 0.15% LAE containing mouthrinse, rinse mouth with 20ml for 30 seconds twice a day.

Arm type	Experimental
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Investigational medicinal product name	LISTERINE® Advanced Defence Gum Treatment
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal solution
Routes of administration	Oromucosal use

Dosage and administration details:

Participants received 0.15% LAE containing mouthrinse, rinse mouth with 20ml for 30 seconds twice a day.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The examiner and recorder were blinded to the treatment administered to subjects.

Number of subjects in period 1	Negative Control	0.2 Percent (%) Chlorhexidine (CHX)	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)
Started	60	60	120
Completed	56	56	114
Not completed	4	4	6
Consent withdrawn by subject	-	1	3
Antibiotic Use During Study	1	-	-
Adverse event, non-fatal	1	3	1
Lost to follow-up	1	-	2
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	Negative Control
Reporting group description:	
Participants received placebo (5% Hydroalcohol Solution), rinse with 20ml for 30 seconds twice a day.	
Reporting group title	0.2 Percent (%) Chlorhexidine (CHX)
Reporting group description:	
Participants received 0.2 % CHX containing mouthrinse, rinse mouth with water and then rinse with 10ml for 60 seconds twice a day.	
Reporting group title	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)
Reporting group description:	
Participants received 0.15% LAE containing mouthrinse, rinse mouth with 20ml for 30 seconds twice a day.	

Reporting group values	Negative Control	0.2 Percent (%) Chlorhexidine (CHX)	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)
Number of subjects	60	60	120
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	58	60	119
From 65 to 84 years	2	0	1
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	39.6	38.5	38.6
standard deviation	± 11.6	± 10.83	± 10.37
Title for Gender Units: subjects			
Female	44	50	91
Male	16	10	29

Reporting group values	Total		
Number of subjects	240		
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	237		
From 65 to 84 years	3		
85 years and over	0		
Title for AgeContinuous Units: years			
arithmetic mean			
standard deviation	-		

Title for Gender			
Units: subjects			
Female	185		
Male	55		

End points

End points reporting groups

Reporting group title	Negative Control
Reporting group description: Participants received placebo (5% Hydroalcohol Solution), rinse with 20ml for 30 seconds twice a day.	
Reporting group title	0.2 Percent (%) Chlorhexidine (CHX)
Reporting group description: Participants received 0.2 % CHX containing mouthrinse, rinse mouth with water and then rinse with 10ml for 60 seconds twice a day.	
Reporting group title	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)
Reporting group description: Participants received 0.15% LAE containing mouthrinse, rinse mouth with 20ml for 30 seconds twice a day.	

Primary: Whole-Mouth Mean Bleeding Index (BI) at Week 4

End point title	Whole-Mouth Mean Bleeding Index (BI) at Week 4
End point description: Each of four gingival areas (distobuccal, mid-buccal, mid-lingual, and mesiolingual) around each tooth was assessed. After approximately 30 seconds, bleeding at each gingival unit was recorded on scale 0 to 2. Where, 0 =Absence of bleeding after 30 seconds, 1 = Bleeding after 30 seconds and 2 = Immediate bleeding.	
End point type	Primary
End point timeframe: At Week 4	

End point values	Negative Control	0.2 Percent (%) Chlorhexidine (CHX)	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	56	114	
Units: units on scale				
arithmetic mean (standard deviation)	0.161 (± 0.1464)	0.076 (± 0.0977)	0.127 (± 0.1851)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Negative Control v 0.2 Percent (%) Chlorhexidine (CHX)

Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1364
upper limit	-0.0359

Statistical analysis title	Statistical Analysis 2
Comparison groups	Negative Control v 0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.108
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0789
upper limit	0.0079

Statistical analysis title	Statistical Analysis 3
Comparison groups	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE) v 0.2 Percent (%) Chlorhexidine (CHX)
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.663
Method	ANCOVA
Confidence interval	
level	Other: 97.5 %
sides	1-sided
upper limit	0.0429
Variability estimate	Standard error of the mean
Dispersion value	0.018225

Secondary: Whole-Mouth Mean Modified Gingival Index (MGI)

End point title	Whole-Mouth Mean Modified Gingival Index (MGI)
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End point description:

The MGI on the buccal and lingual marginal gingivae and interdental papillae of all scorable teeth on scale of 0 to 4. Where, 0 = Normal (absence of inflammation), 1 = Mild inflammation (slight change in

color, little change in texture) of any portion of the entire gingival unit, 2 = Mild inflammation of the entire gingival unit, 3 = Moderate inflammation (moderate glazing, redness, edema, and/or hypertrophy) of the gingival unit, and 4 = Severe inflammation (marked redness and edema/hypertrophy, spontaneous bleeding, or ulceration) of the gingival unit. Here "N" and 'n' signifies those who were evaluable for this outcome measure and at given time point respectively.

End point type	Secondary
End point timeframe:	
At Week 1, 2 and 4	

End point values	Negative Control	0.2 Percent (%) Chlorhexidine (CHX)	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	58	58	117	
Units: units on scale				
arithmetic mean (standard deviation)				
Week 1 (n=56, 58, 117)	2.012 (± 0.115)	1.962 (± 0.1328)	2.014 (± 0.1177)	
Week 2 (n= 58, 55, 113)	1.796 (± 0.3663)	1.605 (± 0.4642)	1.751 (± 0.3573)	
Week 4 (n= 56, 56, 114)	1.344 (± 0.662)	1.106 (± 0.7245)	1.188 (± 0.7477)	

Statistical analyses

No statistical analyses for this end point

Secondary: Whole-Mouth Mean Bleeding Index (BI) at Weeks 1 and 2

End point title	Whole-Mouth Mean Bleeding Index (BI) at Weeks 1 and 2
End point description:	
Each of four gingival areas (distobuccal, mid-buccal, mid-lingual, and mesiolingual) around each tooth was assessed. After approximately 30 seconds, bleeding at each gingival unit was recorded on scale 0 to 2. Where, 0 =Absence of bleeding after 30 seconds, 1 = Bleeding after 30 seconds and 2 = Immediate bleeding. Here "N" and 'n' signifies those who were evaluable for this outcome measure and at given time point respectively.	
End point type	Secondary
End point timeframe:	
At Week 1 and 2	

End point values	Negative Control	0.2 Percent (%) Chlorhexidine (CHX)	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	58	58	117	
Units: units on scale				

arithmetic mean (standard deviation)				
Week 1 (n= 56, 58, 117)	0.21 (± 0.1534)	0.136 (± 0.0966)	0.201 (± 0.1616)	
Week 2 (n= 58, 55, 113)	0.197 (± 0.1542)	0.096 (± 0.1335)	0.171 (± 0.1951)	

Statistical analyses

No statistical analyses for this end point

Secondary: Whole-Mouth Mean Extrinsic Stain Index Composite Score

End point title	Whole-Mouth Mean Extrinsic Stain Index Composite Score
End point description: The mean stain score per subject is determined by multiplying the individual area and intensity scores from each region and summing them then dividing by the number of sites scored. Here "N" and 'n' signifies those who were evaluable for this outcome measure and at given time point respectively.	
End point type	Secondary
End point timeframe: At Week 2 and 4	

End point values	Negative Control	0.2 Percent (%) Chlorhexidine (CHX)	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	58	58	117	
Units: units on scale				
arithmetic mean (standard deviation)				
Week 2 (n= 58, 55, 113)	0.29 (± 0.442)	0.836 (± 0.9736)	0.568 (± 0.8089)	
Week 4 (n= 56, 56, 114)	0.454 (± 0.6245)	1.707 (± 1.2294)	1.036 (± 1.1107)	

Statistical analyses

No statistical analyses for this end point

Secondary: Whole-Mouth Mean Plaque Index (PI)

End point title	Whole-Mouth Mean Plaque Index (PI)
End point description: The PI on six surfaces (distobuccal, midbuccal and mesiobuccal, distolingual, midlingual and mesiolingual) of all scorable teeth, following disclosing on scale of 0 to 5. Where, 0 = No Plaque; 1 = Separate flecks or discontinuous band of plaque around the gingival (cervical) margin; 2 = Thin (up to 1mm), continuous band of plaque at the gingival margin; 3 = Band of plaque wider than 1mm but less than 1/3 of the surface; 4 = Plaque covering 1/3 or more, but less than 2/3 of the surface; 5 = Plaque covering 2/3 or more of the surface. Here "N" and 'n' signifies those who were evaluable for this outcome measure and at given time point respectively.	

End point type	Secondary
End point timeframe:	
At Week 1, 2 and 4	

End point values	Negative Control	0.2 Percent (%) Chlorhexidine (CHX)	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	58	58	117	
Units: units on scale				
arithmetic mean (standard deviation)				
Week 1 (n= 56, 58, 117)	2.237 (± 0.3796)	1.292 (± 0.519)	1.639 (± 0.5589)	
Week 2 (n= 57, 55, 113)	2.309 (± 0.3422)	1.209 (± 0.6316)	1.61 (± 0.5825)	
Week 4 (n= 56, 56, 114)	2.311 (± 0.4004)	1.25 (± 0.7809)	1.704 (± 0.5857)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to week 4

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	Negative Control
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Reporting group description:

Participants received placebo (5% Hydroalcohol Solution), rinse with 20ml for 30 seconds twice a day.

Reporting group title	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)
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Reporting group description:

Participants received 0.15% LAE containing mouthrinse, rinse mouth with 20ml for 30 seconds twice a day.

Reporting group title	0.2 Percent (%) Chlorhexidine (CHX)
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Reporting group description:

Participants received 0.2 % CHX containing mouthrinse, rinse mouth with water and then rinse with 10ml for 60 seconds twice a day.

Serious adverse events	Negative Control	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)	0.2 Percent (%) Chlorhexidine (CHX)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)	0 / 120 (0.00%)	0 / 60 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Negative Control	0.15 Percent (%) Ethyl Lauroyl Arginate HCL (LAE)	0.2 Percent (%) Chlorhexidine (CHX)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 60 (20.00%)	14 / 120 (11.67%)	15 / 60 (25.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 60 (6.67%)	6 / 120 (5.00%)	2 / 60 (3.33%)
occurrences (all)	4	6	2
Gastrointestinal disorders			

Tongue Discolouration subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	4 / 120 (3.33%) 4	10 / 60 (16.67%) 10
Infections and infestations			
Oral Herpes subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	3 / 120 (2.50%) 3	2 / 60 (3.33%) 2
Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	2 / 120 (1.67%) 2	3 / 60 (5.00%) 3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 November 2013	The overall reason for the amendment was to make necessary changes to eliminate apparent immediate hazards to the subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported