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**Clinical Study Report**

Investigational Product	ZYN®
Study code	SM 17-02
Report Version and date	Final; 21 March 2019

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**Open observational study of oral health associated with use of a non-tobacco-based nicotine pouch (ZYN®) among current daily snus users**

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**Study duration (FPI-LPO)** 06 November 2017 – 05 June 2018

**Sponsor signatory**

[REDACTED]  
Swedish Match  
Box 17037  
SE-104 62 Stockholm, Sweden  
Maria Skolgata 83  
SE-118 85 Stockholm, Sweden

**Principal Investigator**

[REDACTED]  
Department of Cariologi,  
Institute of Odontology, Sahlgrenska Academy  
University of Gothenburg  
SE-405 30 Gothenburg, Sweden

**Clinical study conduct and management:**

CTC Clinical Trial Consultants AB  
Dag Hammarskjöldsväg 10B  
SE-752 37 Uppsala, Sweden

**This clinical study was conducted, and essential study documentation archived, in compliance with company SOPs and standards, which incorporate the requirements of the EU Clinical Studies Directive 2001/20/EC and ICH Guideline for Good Clinical Practice.**

## 2 STUDY SYNOPSIS

<b>Study Title</b>	
Open observational study of oral health associated with use of a non-tobacco-based nicotine pouch (ZYN <sup>®</sup> ) among current daily snus users	
<b>Study code</b>	
SM 17-02	
<b>Study period</b>	
Date of first subject screened: 06 November 2017 Date of last subject completed: 05 June 2018	
<b>Principle Investigator</b>	
<div style="background-color: black; width: 200px; height: 1.2em; margin-bottom: 5px;"></div> Institute of Odontology, Gothenburg, Sweden	
<b>Study centre</b>	
CTC Clinical Trial Consultants AB Uppsala University Hospital, Entrance 85 SE-751 85 Uppsala, Sweden	
<b>Publication (reference)</b>	
Not applicable.	
<b>Study design</b>	
Part 1: Open, randomized, 4-way crossover, single administration trial Part 2: Open, observational, follow-up study for 6 weeks	
<b>Objectives</b>	
<u>Primary objective</u>	
The primary objective of the present study was to evaluate the amount of dental plaque acidogenicity from the non-tobacco-based nicotine pouch.	
Part 1:	
<ul style="list-style-type: none"> <li>Assessment of dental plaque acidogenicity after short-term exposure (60 min) to study products (a flavored and an unflavored brand of the nicotine pouch), 10% sucrose (positive control) and 10% xylitol (negative control)</li> </ul>	
Part 2:	
<ul style="list-style-type: none"> <li>Assessment of dental plaque acidogenicity during a total of 6 weeks of ad libitum use of the nicotine pouch</li> </ul>	

**Objectives (cont)****Secondary objectives**

The secondary objective of the present study was to evaluate the clinical tolerability and safety of ZYN<sup>®</sup> with respect to effects on the oral mucosa.

Part 1:

- Adverse events (AEs)

Part 2:

- AEs
- Changes in the oral microflora
- Oral mucosal lesions

**Number of subjects**

The planned number of subjects were 20 participants (with available data on all 4 test articles) in Part 1 and 60 participants in Part 2.

In total, 83 subjects (23 in Part 1 and 60 in Part 2) were screened and 79 subjects were enrolled into the study. Of the 20 subjects enrolled in Part 1, 18 subjects completed the study and 2 subjects were withdrawn. All subjects who were randomized to treatment sequence A (n=5) and B (n=5) completed the study. Of the 5 subjects randomized to treatment sequence C (n=5) and D (n=5), 4 completed the study and 1 subject was withdrawn in each treatment group. For treatment sequences, see the section Methodology below. Of the 59 subjects enrolled in Part 2, 57 subjects completed the study and 2 subjects were withdrawn.

**Diagnosis and main eligibility criteria**

Healthy subjects aged  $\geq 19$  years who had used tobacco-based snus for  $\geq 1$  year with a weekly consumption of 3 or more snus cans (brands with nicotine content  $\leq 1\%$ ) or 2 or more cans (brands with nicotine content  $> 1\%$ ) and normal stimulated salivary secretion rate ( $\geq 0.7$  ml/min) were considered eligible to participate in the study.

Pregnant women, subjects who had a history of hypertension or any cardiovascular disease, subjects with allergy toward composite materials, and those with a history of use of antibiotics during or within the last 4 weeks prior to the study were excluded.

**Methodology**

For both Part 1 and Part 2, potential subjects were initially screened for study eligibility and informed consent procedures. Subjects in Part 1 were eligible to later on also participate in Part 2 after a new Screening visit. Before study entry, subjects signed an informed consent form and subsequently underwent a routine dental and oral examination, assessment of saliva buffer capacity, number of mutans streptococci and lactobacilli.

The subjects in both parts of the study refrained from approximal tooth cleaning during 72 h prior to visit and toothbrushing during the last 48 h prior to visit. They did not eat or drink anything during the last 2 h prior to visit.

Part 1: Subjects visited the clinic on a total of 4 occasions for testing of the 4 test articles (in randomized order). Each visit was estimated to take 75 min.

Part 2: Subjects participated in a 6-week observational study during which they were encouraged to substitute as much as possible of their snus with the ZYN<sup>®</sup> test articles. Subjects could choose ad libitum from ZYN<sup>®</sup> Smooth 3 mg or 6 mg nicotine, ZYN<sup>®</sup> Peppermint 3 mg or 6 mg nicotine, or ZYN<sup>®</sup> Cinnamon 3 mg or 6 mg nicotine pouches. Use of ZYN<sup>®</sup> products, snus, or any other nicotine delivery product was monitored, based on self-reports.

**Methodology (cont)**

Clinical visits were scheduled at screening, after 2 weeks, after 4 weeks and after 6 weeks. At each visit data were collected on product use since last visit, AEs, plaque acidogenicity, oral microflora, plaque amount, and oral lesions. Clinical photos were taken to facilitate comparisons. “Snus lesions” at the site where participants typically place their snus/ZYN<sup>®</sup> pouch were assessed using a 4-degree scale as proposed by Axéll et al (1976). At each visit the subject reported any local and general adverse symptoms.

**Investigational Products (IP), dosage and mode of administration, batch number**

Test products:

Part 1: ZYN<sup>®</sup> Smooth 3 mg (batch number 91153)  
 ZYN<sup>®</sup> Peppermint 3 mg (batch number 91087)  
 10% sucrose  
 10% xylitol

Part 2: Ad libitum use of a ZYN<sup>®</sup> nicotine pouch, participants could choose from:  
 ZYN<sup>®</sup> Smooth 3 mg (batch number 91153)  
 ZYN<sup>®</sup> Smooth 6 mg (batch number 91250)  
 ZYN<sup>®</sup> Cinnamon 3 mg (batch number 91160)  
 ZYN<sup>®</sup> Cinnamon 6 mg (batch number 91166)  
 ZYN<sup>®</sup> Peppermint 3 mg (batch number 91087)  
 ZYN<sup>®</sup> Peppermint 6 mg (batch number 91241)

**Non-Investigational Products, dosage and mode of administration, batch number**

Not applicable.

**Duration of treatment**

Part 1: Single administration (60 min)

Part 2: 6 weeks

**Duration of subject's involvement in the study**

Part 1: Approximately 35 days (single visits)

Part 2: Approximately 6 weeks

**Efficacy assessments**

Part 1: Dental plaque acidogenicity

Part 2:

- AEs assessed at 2, 4 and 6 weeks
- Biofilm acidogenicity at 2, 4 and 6 weeks compared to baseline
- Changes compared to screening in the oral microflora at 2, 4 and 6 weeks
- Plaque amount at 2, 4 and 6 weeks compared to screening
- Appearance and number of oral mucosal lesions (including presence and grade of “snus lesions” at the site where the pouches typically are placed by the consumer), comparisons were made with screening findings

**Safety assessments**

Adverse events and serious adverse events (SAEs) were recorded from start of IP administration until the last Follow-up visit. Medical events occurring between screening and first treatment with IP were reported separately as baseline events. Adverse events were coded using the Medical Dictionary of Regulatory Activities (MedDRA).

## Statistical methods

Part 1: Based on previous experience with the described methodology, a total of 20 subjects were enough to reliably detect a clinically significant increased plaque acidogenicity with the pouched products versus the negative control.

Part 2: A 6-week observation period was reasonable to assess putative changes in the oral mucosa resulting from use of the nicotine pouches given that “snus lesions” among habitual snus users regress within a few weeks after cessation of exposure (Wallström et al, [1999] [3]). A 6-week observation period was also supported by the fact that the other measures of oral health to be assessed are known to potentially change within a few weeks. With an estimated dropout rate of 25% a total of 45 fully evaluable subjects were expected with a total inclusion of 60 subjects.

Summary statistics was used to present all continuous variables and frequency tables for categorical variables.

### *Dental plaque acidogenicity (Part 1 and Part 2) - Minimum value*

Part 1: The minimum value after baseline was selected and presented using summary statistics by product. Any differences were assessed by using the Wilcoxon signed rank sum test. One analysis compared the differences between the site which the product was closest to and the site on the opposite side in the upper jaw.

Part 2: The minimum value after baseline at each visit was selected and presented using summary statistics. The absolute and percent change from baseline were calculated and described using summary statistics and analyzed using the Wilcoxon signed rank sum test.

### *Dental plaque acidogenicity (Part 1 and Part 2) - Maximum/minimum change*

Part 1: The maximum and minimum change were defined as the lowest and highest change by using the actual baseline value and the lowest and highest values obtained during measurement. The maximum and minimum changes are presented using summary statistics by product. Any differences were assessed by using the Wilcoxon signed rank test.

Part 2: The maximum and minimum change were defined as the lowest and highest change by using the actual values after baseline for each visit. The maximum and minimum changes are described using summary statistics and analyzed using the Wilcoxon signed rank sum test.

### *Dental plaque acidogenicity (Part 1 and Part 2) - AUC dental plaque acidogenicity*

Part 1 and Part 2 definition: Area under the curve (AUC) for dental plaque acidogenicity was estimated by calculating the area under the reference limit to the observed dental plaque acidogenicity. Two different reference limits were used: 6.2 pH and 5.5 pH. Any area which was above the reference limit was subtracted from the total area between the reference limit and observed dental plaque acidogenicity.

Part 1: The AUC was described using summary statistics for each product and analyzed between products using the Wilcoxon signed rank sum test.

Part 2: The AUC, the absolute and percent change from baseline were described using summary statistics for each visit and analyzed using the Wilcoxon signed rank sum test.

### *Biofilm acidogenicity (Part 2)*

The total index for each tooth and total index are presented using summary statistics for actual values, absolute change and percent change from baseline to each subsequent visit. Changes over time were analyzed using Wilcoxon signed rank sum test.

### *Changes in oral microflora (Part 2)*

Actual and log microflora are presented using summary statistics for actual values, absolute change and percent change from baseline to each subsequent visit. Changes over time were analyzed using Wilcoxon signed rank sum test.

*Oral mucosal lesions (Part 2)*

The oral mucosal lesions are presented using frequency tables at each visit (n, %). Absolute changes in oral mucosal lesions were calculated between visits and baseline. The absolute change was analyzed using the Mc Nemar's test. The correlation at each visit using the change in oral mucosal and the percent usage of IPs vs. ordinary Swedish snus was calculated at each visit.

All AE data were fully listed by Investigator terms and MedDRA Preferred Term (PT). Adverse event data were summarized by System Organ Class (SOC) and PT.

**EFFICACY RESULTS**

After single dose administration of IP in Part 1, the minimum change from baseline in dental plaque acidogenicity was significantly smaller for ZYN<sup>®</sup> Smooth compared to xylitol and maximum change from baseline was significantly larger for ZYN<sup>®</sup> Smooth and ZYN<sup>®</sup> Peppermint compared to xylitol. The minimum value in dental plaque acidogenicity was significantly higher, the minimum change from baseline was significantly smaller, the maximum change was significantly larger and AUC for dental plaque acidogenicity (pH 5.5 and pH 6.2) was significantly larger for the ZYN<sup>®</sup> products and xylitol compared to sucrose. There were no statistical differences between the ZYN<sup>®</sup> products.

After ad libitum administration of nicotine-containing pouches in Part 2, the minimum value in dental plaque acidogenicity was significantly higher and the absolute minimum change from baseline was significantly smaller during the study compared to baseline for all subjects. The absolute change in AUC (and AUC where values over baseline were set to zero) for dental plaque acidogenicity (pH 6.2 and pH 5.5) during the study was significantly smaller compared to baseline for all subjects which implicates that the pH\*time was larger during study.

For the majority of assessments of plaque amount there were no statistically significant changes for the subjects during Part 2.

The number of S Mutans at Visit 4 and Visit 5 was significantly higher compared to baseline. There were no statistically significant changes from baseline for Lactobacilli during Part 2.

The number of subjects with lesions and the degree of lesions changed during Part 2. The number of subjects with no lesions increased from 9% at screening to 30% at Visit 5. The degree of lesions in the mucosa at placement of the pouch was significantly lower at Visits 3, 4 and 5 compared to baseline and the number of subjects with lesions decreased from 90% to 70%. There was a statistically significant correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used for all visits except for the female subjects at Visit 4. There was no indication of changes in the incidence of gingival retraction during the study, it varied between 54%-57% during the study.

**SAFETY RESULTS**

Administration of single doses in Part 1 and ad libitum administration in Part 2 of nicotine-containing pouches was safe and well tolerated by the healthy subjects. There were no AEs assessed by the investigator as related to IP in Part 1 and 5 in Part 2. There were no SAEs or discontinuations due to AEs during the study.

## **CONCLUSION**

The study showed that non-tobacco-based nicotine pouches (ZYN<sup>®</sup> products) do not adversely affect dental plaque acidogenicity after single dose administration in healthy snus users.

After ad libitum administration of nicotine-containing pouches for 6 weeks, no adverse effect of dental plaque acidogenicity was observed.

The study showed that increased usage of non-tobacco-based nicotine pouch (ZYN<sup>®</sup> products) in favour over snus improved oral mucosal lesions in healthy snus users after administration ad libitum for 6 weeks.

Administration of single doses in Part 1 and ad libitum administration in Part 2 of the ZYN<sup>®</sup> products were safe and well tolerated by the healthy subjects. The number of subjects reporting AEs and the number of AEs were low.

### 3 TABLE OF CONTENTS

2	STUDY SYNOPSIS .....	2
3	TABLE OF CONTENTS .....	8
4	LIST OF ABBREVIATIONS AND DEFINITION OF TERMS.....	13
5	ETHICAL AND REGULATORY REQUIREMENTS.....	14
5.1	Ethical conduct of the study.....	14
5.2	Ethics and regulatory review .....	14
5.3	Subject information and consent.....	14
5.4	Subject data protection.....	14
6	INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE .....	15
7	INTRODUCTION.....	16
7.1	Project background .....	16
7.2	Investigational product.....	17
7.3	Risk/benefit assessment .....	17
8	STUDY OBJECTIVES AND ENDPOINTS.....	18
8.1	Primary objective.....	18
8.1.1	Primary endpoint.....	18
8.2	Secondary objective .....	18
8.2.1	Secondary endpoints .....	18
9	INVESTIGATIONAL PLAN .....	19
9.1	Overall study design and schedule of events .....	19
9.2	Rationale for study design and dose groups .....	20
9.3	Study population .....	20
9.3.1	Recruitment.....	20
9.3.2	Number of subjects .....	20
9.3.3	Inclusion criteria .....	21
9.3.4	Exclusion criteria .....	21
9.3.5	Restrictions during the study .....	21
9.3.6	Criteria for subjects' withdrawal.....	21
9.3.6.1	General withdrawal criteria .....	21
9.3.6.2	Procedures for discontinuation replacement.....	22
9.3.6.3	Subject replacement.....	22
9.3.6.4	Randomization.....	22
9.3.6.5	Blinding .....	22
9.4	Treatments.....	22
9.4.1	Identity of investigational products.....	22
9.4.2	Treatment administration .....	22
9.4.3	Treatment compliance.....	23
9.5	Study assessments .....	23
9.5.1	Demographics and other baseline characteristics .....	23
9.5.1.1	Informed consent .....	23
9.5.1.2	Demographic information.....	23
9.5.1.3	Medical/surgical history .....	23
9.5.1.4	Pregnancy urine test.....	23



9.5.1.5	Prior and concomitant medication .....	24
9.5.1.6	Baseline symptoms .....	24
9.5.2	Assessments related to primary and secondary endpoints .....	24
9.5.2.1	Examination of the oral cavity .....	24
9.5.2.2	Dental plaque acidogenicity .....	24
9.5.2.3	Plaque amount .....	25
9.5.2.4	Oral microflora .....	25
9.5.2.5	Saliva sampling.....	25
9.5.3	Adverse events .....	25
9.5.1	Appropriateness of measurements .....	25
<b>9.6</b>	<b>Data quality assurance .....</b>	<b>26</b>
<b>9.7</b>	<b>Statistical methods planned in the protocol and determination of sample size</b>	<b>26</b>
9.7.1	General.....	26
9.7.2	Determination of sample size.....	26
9.7.3	Definition of analysis data sets .....	27
9.7.3.1	Full analysis set.....	27
9.7.3.2	Per protocol analysis set .....	27
9.7.4	Description of study population.....	27
9.7.4.1	Demographics and baseline characteristics .....	27
9.7.4.2	Medical/surgical history and concomitant medication .....	27
9.7.4.3	Treatment compliance .....	27
9.7.5	Analysis of primary endpoints .....	27
9.7.5.1	Dental plaque acidogenicity (Part 1 and Part 2) .....	27
9.7.6	Analysis of secondary endpoints.....	29
9.7.6.1	Adverse events (Part 1 and Part 2) .....	29
9.7.6.2	Plaque amount (Part 2) .....	29
9.7.6.3	Oral microflora (Part 2) .....	29
9.7.6.4	Oral mucosal lesions (Part 2).....	29
9.7.7	Statistical/analytical issues.....	29
9.7.7.1	Adjustments for covariates .....	29
9.7.7.2	Handling of dropouts or missing data.....	29
9.7.7.3	Significance level.....	29
9.7.7.4	Multiple comparisons/multiplicity.....	30
9.7.7.5	Examination of subgroups .....	30
<b>9.8</b>	<b>Changes in the conduct of the study or planned analyses.....</b>	<b>30</b>
<b>10</b>	<b>STUDY SUBJECTS.....</b>	<b>30</b>
<b>10.1</b>	<b>Disposition of subjects .....</b>	<b>30</b>
10.1.1	Number of subjects .....	30
10.1.2	Study discontinuations .....	31
<b>10.2</b>	<b>Protocol deviations.....</b>	<b>32</b>
<b>10.3</b>	<b>Data sets analyzed .....</b>	<b>32</b>

10.4	Demographics and other baseline characteristics.....	32
10.5	Measurements of treatment compliance.....	34
11	EVALUATION OF RESULTS.....	34
11.1	Extent of exposure.....	34
11.2	Evaluation of primary endpoint.....	35
11.2.1	Dental plaque acidogenicity.....	35
11.2.1.1	Dental plaque acidogenicity after short-term exposure (Part 1).....	35
11.2.1.2	Dental plaque acidogenicity after 6 weeks of use (Part 2).....	36
11.3	Evaluation of secondary endpoints.....	37
11.3.1	Plaque amount (Part 2).....	37
11.3.2	Oral microflora (Part 2).....	37
11.3.3	Oral mucosal lesions (Part 2).....	37
11.3.4	Adverse events.....	38
11.4	Statistical/analytical issues.....	38
11.5	Summary of efficacy results.....	38
12	ADVERSE EVENTS.....	39
12.1	Brief summary of adverse events.....	39
12.2	Display of adverse events.....	40
12.3	Analysis of adverse events.....	40
12.4	Listing of adverse events by subject.....	40
12.5	Deaths, other serious adverse events and other significant adverse events.....	40
12.6	Summary of safety results.....	41
13	DISCUSSION AND OVERALL CONCLUSIONS.....	41
13.1	DISCUSSION.....	41
13.2	OVERALL CONCLUSIONS.....	42
14	TABLES, FIGURES AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT.....	43
14.1	Study subjects.....	43
14.2	Demographic data and other baseline characteristics.....	48
14.3	Primary and secondary endpoints.....	48
14.3.1	Primary endpoint.....	50
14.3.1.1	Dental plaque acedogenicity.....	90
14.3.1	Secondary endpoints.....	123
14.4	Adverse events.....	185
14.4.1	Displays of adverse events.....	185
14.4.2	Listings of deaths, other serious adverse events and significant adverse events.....	186
14.4.3	Narratives of deaths, other serious adverse events and significant adverse events.....	187
14.4.4	Abnormal laboratory value listing (each subject).....	187
15	REFERENCE LIST.....	188
16	APPENDICES.....	188
16.1	Study information.....	188
16.2	Subject data listings.....	188
16.3	Case report forms.....	189

**List of Tables**

Table 9.1-1	Overall schedule of events (Part 1).....	19
Table 9.1-2	Overall schedule of events (Part 2).....	20
Table 9.4-1	Definition of treatment sequences (Part 1) .....	23
Table 10.4-1	Summary of demographic data and other baseline characteristics (Part 1). 32	
Table 10.4-2	Summary of demographic data and other baseline characteristics (Part 2). 33	
Table 12.1-1	Overview of adverse events (FAS) (Part 1).....	39
Table 12.1-2	Overview of adverse events (FAS) (Part 2).....	39
Table 14.1-1	Subject disposition (Part 1).....	43
Table 14.1-2	Subject disposition (Part 2).....	43
Table 14.1-3	Pregnancy test results (FAS) (Part 1) .....	44
Table 14.1-4	Pregnancy test results (FAS) (Part 2) .....	44
Table 14.1-5	Medical history events by SOC and PT (FAS) (Part 1) .....	44
Table 14.1-6	Medical history events by SOC and PT (FAS) (Part 2) .....	45
Table 14.1-7	Physical examination tongue and mucosa (FAS) (Part 1).....	46
Table 14.1-8	Physical examination tongue and mucosa (FAS) (Part 2).....	46
Table 14.1-9	Physical examination tooth status (FAS) (Part 1) .....	47
Table 14.1-10	Physical examination tooth status (FAS) (Part 2) .....	47
Table 14.1-11	Ratio ZYN <sup>®</sup> products/total nicotine products used (FAS) (Part 2).....	48
Table 14.1-12	IP usage per study day (FAS) (Part 2).....	48
Table 14.3-1	Exposure to study product (Part 1) .....	48
Table 14.3-2	Exposure to study product (FAS) (Part 2).....	49
Table 14.3-3	Dental plaque acidogenicity between group comparison (PPS) (Part 1).....	50
Table 14.3-4	Dental plaque acidogenicity measurements by timepoint (PPS) (Part 1)....	51
Table 14.3-5	Dental plaque acidogenicity measurements by timepoint (PPS) (Part 2)....	61
Table 14.3-6	Minimum and maximum dental plaque acidogenicity measurements (PPS) (Part 1) .....	90
Table 14.3-7	Minimum and maximum dental plaque acidogenicity measurements (PPS) (Part 2) .....	91
Table 14.3-8	AUC dental plaque acidogenicity (PPS) (Part 1) .....	104
Table 14.3-9	AUC dental plaque acidogenicity (values over baseline set to zero) (PPS) (Part 1) .....	105
Table 14.3-10	AUC dental plaque acidogenicity (PPS) (Part 2) .....	106
Table 14.3-11	Plaque amount (Silness-Löe index) (PPS) (Part 2) .....	123
Table 14.3-12	Oral microflora (PPS) (Part 2).....	169
Table 14.3-13	Gingival retraction and lesions in the mucosa at the placement of the pouch (PPS) (Part 2).....	172
Table 14.3-14	Degree of lesions in the mucosa at the placement of the pouch (PPS) (Part 2) .....	174
Table 14.3-15	Correlation between change in oral mucosal lesions and percent of ZYN <sup>®</sup> products used (PPS) (Part 2).....	176
Table 14.4-1	Adverse events by SOC and PT (FAS) (Part 1) .....	185
Table 14.4-2	Adverse events by SOC and PT (FAS) (Part 2) .....	185
Table 14.4-3	Adverse events: severity and relation, with subject identifications (FAS) (Part 1) .....	186
Table 14.4-4	Adverse events: severity and relation, with subject identifications (FAS) (Part 2) .....	186

**List of Figures**

Figure 10.1-1	Disposition of subjects (Part 1) .....	31
Figure 10.1-2	Disposition of subjects (Part 2) .....	31
Figure 11.2-1	Dental plaque acidogenicity (pH) vs time, mean (PPS) .....	36
Figure 11.2-2	Dental plaque acidogenicity (pH) vs time, mean (PPS) .....	37
Figure 14.3-1	Correlation between change in oral mucosal lesions and percent of ZYN <sup>®</sup> products used (Part 2), All subjects, Visit 3 .....	176
Figure 14.3-2	Correlation between change in oral mucosal lesions and percent of ZYN <sup>®</sup> products used (Part 2), All subjects, Visit 4 .....	177
Figure 14.3-3	Correlation between change in oral mucosal lesions and percent of ZYN <sup>®</sup> products used (Part 2), All subjects, Visit 5 .....	178
Figure 14.3-4	Correlation between change in oral mucosal lesions and percent of ZYN <sup>®</sup> products used (Part 2), Female subjects, Visit 3.....	179
Figure 14.3-5	Correlation between change in oral mucosal lesions and percent of ZYN <sup>®</sup> products used (Part 2), Female subjects, Visit 4.....	180
Figure 14.3-6	Correlation between change in oral mucosal lesions and percent of ZYN <sup>®</sup> products used (Part 2), Female subjects, Visit 5.....	181
Figure 14.3-7	Correlation between change in oral mucosal lesions and percent of ZYN <sup>®</sup> products used (Part 2), Male subjects, Visit 3 .....	182
Figure 14.3-8	Correlation between change in oral mucosal lesions and percent of ZYN <sup>®</sup> products used (Part 2), Male subjects, Visit 4 .....	183
Figure 14.3-9	Correlation between change in oral mucosal lesions and percent of ZYN <sup>®</sup> products used (Part 2), Male subjects, Visit 5 .....	184

#### 4 LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation or term	Explanation
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
AUC	Area Under the Curve
CRF	Case Report Form
CSP	Clinical Study Protocol
CSR	Clinical Study Report
CTC	CTC Clinical Trial Consultants AB
CV	Coefficient of Variation
DMFT	Decayed Missing and Filled Teeth index
FAS	Full Analysis Set
FPI	First Patient In
GCP	Good Clinical Practice
h	Hour
ICF	Informed Consent Form
ICH	International Council for Harmonization
IEC	Independent Ethics Committee
IP	Investigational Product
LPO	Last Patient Out
MedDRA	Medical Dictionary for Regulatory Activities
min	Minute
N/n	Number
nmiss	Number of missing values
PPS	Per Protocol Set
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDV	Source Data Verification
SIL	Snus Induced Lesion
SOC	System Organ Class
SOP	Standard Operating Procedures
WHO	World Health Organization

## **5 ETHICAL AND REGULATORY REQUIREMENTS**

### **5.1 Ethical conduct of the study**

The study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Council for Harmonization (ICH)/Good Clinical Practice (GCP), European Union Clinical Trials Directive, and applicable local regulatory requirements.

### **5.2 Ethics and regulatory review**

The study did not start until approval of the clinical study protocol (CSP), the Subject Information and the Informed Consent Forms (ICFs) had been obtained from the Independent Ethics Committee (IEC) in Uppsala, Sweden. It was the responsibility of the Investigator to forward a copy of the written approval and, where possible, a list of the members, their titles or occupations, and their institutional affiliations, to CTC Clinical Trial Consultants AB (CTC)/the Sponsor. The approval included a study identification and the date of review.

### **5.3 Subject information and consent**

It was the responsibility of the Investigator or designee to give each subject prior to inclusion in the study, full and adequate verbal and written information regarding the objectives and procedures of the study and the possible risks involved. The subjects were informed about their right to withdraw from the study at any time. Written subject information was given to each subject before enrolment. The written subject information was not to be changed without prior discussion with CTC/the Sponsor. All subjects were required to provide written informed consent prior to initiation of any study procedures. Furthermore, it was the responsibility of the Investigator or designee to obtain signed ICF from all subjects prior to inclusion in the study.

The signed ICFs were filed by the Investigator or designee for review by the Monitor. The Investigator confirmed receipt of the ICF from each subject by signing the appropriate page of the Case Report Form (CRF).

The written Subject Information and ICF are included in Appendix 16.1.3.

### **5.4 Subject data protection**

The Investigator kept a subject identification list not available to the Sponsor, including sufficient information to link records, i.e. CRFs and medical records. The subjects were informed that the data were stored and analyzed by computer, that Swedish and local regulations for the handling of computerized data was followed and described in the written subject information and that identification of individual subject data was only possible for the Investigator. Furthermore, the subjects were informed about the possibility of inspection of relevant parts of the records by representatives of CTC and/or Authorities.

## 6 INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

**Principal Investigator:**

[REDACTED]  
Department of Cariologi,  
Institute of Odontology, Sahlgrenska Academy  
University of Gothenburg  
SE-405 30 Gothenburg, Sweden

**Sponsor  
representative:**

[REDACTED]  
Swedish Match  
Box 17037  
SE-104 62 Stockholm, Sweden  
Maria Skolgata 83  
SE-118 85 Stockholm, Sweden

**Monitor:**

[REDACTED]  
Sub-contracted by CTC AB from Scandinavian CRO, Uppsala, Sweden

**Project manager:**

[REDACTED]  
CTC Clinical Trial Consultants AB  
Dag Hammarskjöldsväg 10B  
SE-752 37 Uppsala, Sweden

**Research nurse:**

[REDACTED]  
Department of Cariologi,  
Institute of Odontology, Sahlgrenska Academy  
University of Gothenburg  
SE-405 30 Gothenburg, Sweden

**Data manager:**

[REDACTED]  
CTC Clinical Trial Consultants AB  
Dag Hammarskjöldsväg 10B  
SE-752 37 Uppsala, Sweden

**Statistician:**

[REDACTED]  
CTC Clinical Trial Consultants AB  
Dag Hammarskjöldsväg 10B  
SE-752 37 Uppsala, Sweden

**Senior scientific  
advisor  
pharmacokineticist**

[REDACTED]  
CTC Clinical Trial Consultants AB  
Dag Hammarskjöldsväg 10B  
SE-752 37 Uppsala, Sweden

**Medical writer:**

[REDACTED]  
CTC Clinical Trial Consultants AB  
Dag Hammarskjöldsväg 10B  
SE-752 37 Uppsala, Sweden

Signatures required are included in Appendix 16.1.5.

## 7 INTRODUCTION

### 7.1 Project background

Clinical experience does not indicate that habitual use of regular, tobacco-based snus affects biofilm acidogenicity. Contributing factors may be that snus includes food approved pH regulating substances (such as sodium carbonate) which maintains a relatively high pH in the snus pinch/pouch (ca. pH 8-8.5), nicotine itself does not seem to affect biofilm acidogenicity, and that the tobacco does not function as a substrate for the oral microflora. These circumstances may help to explain why caries does not seem to be more prevalent among snus users than among non-tobacco users. The non-tobacco-based nicotine pouch (ZYN<sup>®</sup>) is an alternative form of orally delivered nicotine. The physical properties of ZYN<sup>®</sup> in terms of pH is the same as with regular, tobacco-based snus and the product is used the same way, that is, it is placed in the upper sulcus for 30-60 min. However, the matrix for the nicotine in ZYN<sup>®</sup> is different from that in regular snus: microcrystals of maltitol and cellulose instead of ground tobacco leaves. In foodstuff, maltitol and cellulose have not been associated with changes in biofilm acidogenicity. However, the prolonged exposure (ca. 30-60 min) associated with use in a product like ZYN<sup>®</sup> constitutes a somewhat different type of exposure. Therefore, although there are no priori reasons to believe that use of ZYN<sup>®</sup> will adversely affect biofilm acidogenicity, it is reasonable to rigorously assess this possibility in the context of a controlled clinical trial. Particularly since ZYN<sup>®</sup> is marketed as a consumer product and therefore is used ad libitum by consumers.

Smokers frequently exhibit oral mucosal lesions which can be located anywhere in the oral mucosa, such as leukoedema, smoker's palate, smokers's melanosis, lingua villosa/nigra, leukoplakia and erythroplakia (1). It is generally assumed that the main reason for these lesions is the smoker's exposure to the combustion products in tobacco smoke, most of which are found in the tar particles in the smoke. Regular snus users may develop mucosal lesions, "snus induced lesions" (SILs) in the upper sulcus at the site where they typically place the snus pinch/pouch, however, to a significantly lesser extent than among smokers (2). The biology of these lesions is clearly different from most of the mucosal lesions associated with smoking: they are strictly localized to the site of exposure in the upper sulcus, they are reversible within weeks after cessation of exposure or if the snus user changes the location of the snus pouch, and they do not appear to be pre-malignant. The exact mechanism behind these lesions remains unclear. It has been suggested that the high pH of snus could result in a localized, chemical irritation of the mucosa. However, the observation that snus lesions are much less prevalent among users of pouched snus compared to loose snus suggests that physical irritation from the tobacco particles in snus may also play a role. The nicotine in snus may be another significant factor. For instance, mucosal lesions have been observed with lozenges of pharmaceutical nicotine replacement therapy. A recent study assessed the oral safety of a sublingual tablet containing 2 mg nicotine with regard to lesions at the site of application (3). In a prospective follow-up of smokers using the sublingual nicotine tablet over a period of 3-6 months, 8/30 subjects displayed lesions in the floor of the mouth during the 6-month medication period, all of which appeared in the first 1-6 weeks. By the 6-month-visit all such lesions had resolved (3).

The physical properties of ZYN<sup>®</sup> in terms of pH is the same as with regular, tobacco-based snus (pH ca. 8-8.5) and it is used the same way as snus, that is, it is placed in the upper sulcus for 30-60 min. Because of these circumstances it is unclear to what extent use of ZYN<sup>®</sup> may



cause similar mucosal lesions as regular, tobacco-based snus. The comparable pH and the nicotine delivery may indicate a similar potential, but the absence of tobacco particles may result in less physical irritation.

The main aim of the present study was to assess the safety and tolerability of the non-tobacco-based nicotine pouch (ZYN<sup>®</sup>), particularly with regard to its potential to adversely affect biofilm acidogenicity. A secondary aim was to investigate to which extent ZYN<sup>®</sup> has the potential to produce mucosal lesions at the site of application in the oral cavity similar to those occasionally observed among regular snus users and whether pre-existing snus lesions among the included subjects may improve or resolve during a 6-week observation period during which the participants substitute their regular snus with ZYN<sup>®</sup> products.

Adverse events (AEs) were recorded at all visits, with particular focus on local irritation at the site of the oral mucosa where the pouch is placed, or in the throat, and hiccups and heartburn (which are common side effects with all types of nicotine exposure).

## 7.2 Investigational product

The non-tobacco-based nicotine pouch (ZYN<sup>®</sup>) was delivered in identical glass vials for Part 1 and in its original container for Part 2.

Part 1: ZYN<sup>®</sup> Smooth 3 mg  
 ZYN<sup>®</sup> Peppermint 3 mg  
 10% sucrose solution  
 10% xylitol solution

Part 2: Ad libitum use of a ZYN<sup>®</sup> nicotine pouch, participants could choose from 3 or 6 mg pouches of ZYN<sup>®</sup> Smooth, ZYN<sup>®</sup> Peppermint and ZYN<sup>®</sup> Cinnamon.

For further details regarding the investigational products (IPs) used in this study, refer to Section 9.4.

## 7.3 Risk/benefit assessment

It may be considered problematic to expose research subjects to a novel nicotine delivery product the properties of which are not yet fully known. The assessments of plaque acidogenicity require participants to refrain from brushing their teeth for 48 h prior to the examination, and the procedure involved exposure to a positive control substance (sucrose) that lower their plaque pH. This could theoretically have adverse effects on the participants' dental health, but previous studies had shown no such clinical adverse effects after refraining from toothbrushing for such a short period of time.

All mentioned potentially adverse effects of study participation were likely to be minor and clinically insignificant. As to the nicotine exposure, all research subjects were required to be daily snus users since at least 1 year (with an average or above snus consumption) so the participants were well acquainted with and used to the effects of nicotine. Aside from the nicotine, all ingredients used in the test products were food-approved (similar to ingredients in snus).

Pregnant women or individuals with a history of hypertension or any other cardiovascular disease who could have been particularly vulnerable to nicotine exposure were excluded from participation. Individuals with a lower than average saliva production were also excluded as adverse effects related to xerostomia could adversely influence outcomes and thus bias the

results (it was expected that few if any of the included participants had problems related to xerostomia as they were all regular snus users since more than 1 year).

The procedures used to assess oral health, including measurements of plaque acidogenicity, were standard procedures used at odontological research facilities and were not associated with any major discomfort or significant AEs. The procedures were unlikely to adversely affect the participants' oral health in the long-term because of their limited duration. In fact, theoretically, participation in the study could help to improve participants' long-term oral health through an increased awareness of the significance of dental hygiene. The study did not involve invasive procedures.

The theoretical adverse effects of the study procedures, which were likely to be minor and/or insignificant, were from a research ethics perspective counterbalanced by the potential positive health effects of the novel nicotine pouch as a low-toxic alternative to cigarettes or conventional snus among current tobacco users.

## **8 STUDY OBJECTIVES AND ENDPOINTS**

### **8.1 Primary objective**

The primary objective of the present study was to evaluate the amount of dental plaque acidogenicity from the non-tobacco-based nicotine pouch.

Part 1: Assessment of dental plaque acidogenicity after short-term exposure (60 min) to study products (a flavored and an unflavored brand of the nicotine pouch), 10% sucrose (positive control), and 10% xylitol (negative control)

Part 2: Assessment of dental plaque acidogenicity during a total of 6 weeks of ad libitum use of the nicotine pouch

#### **8.1.1 Primary endpoint**

Part 1: Assessment of dental plaque acidogenicity after short-term exposure (60 min) of nicotine pouch

Part 2: Assessment of dental plaque acidogenicity after 6 weeks of use of nicotine pouch

### **8.2 Secondary objective**

The secondary objective of the present study was to evaluate the clinical tolerability and safety of ZYN<sup>®</sup> with respect to effects on the oral mucosa.

#### **8.2.1 Secondary endpoints**

The secondary endpoints were:

- AEs (Part 1 and Part 2)
- Changes in the oral microflora (Part 2)
- Oral mucosal lesions (Part 2)

## 9 INVESTIGATIONAL PLAN

### 9.1 Overall study design and schedule of events

Part 1 of the study was an open, randomized, 4-way crossover, single administration. Subjects were randomized to 1 of 4 treatment sequences using a flavored and an unflavored brand of the nicotine pouch, 10% sucrose (positive control) and 10% xylitol (negative control) with 1-week washout. The nicotine pouch was kept in the vestibule during 60 min and the negative and positive control was rinsed in the mouth for 1 min. Dental plaque acidogenicity measurements were performed at 0 min and at 2, 5, 10, 20, 30, 40, 50 and 60 min after administration. Each visit lasted for about 75 min. The number of healthy subjects needed to be evaluated (completing the 4-way crossover part) was estimated to be 20.

Schedule of events are presented in Table 9.1-1 (Part 1) and Table 9.1-2 (Part 2).

*Table 9.1-1 Overall schedule of events (Part 1)*

Event	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Follow-up
	Screening Day -10 – -3	Day 0	Day 7(+2)	Day 14(+2)	Day 21(+2)	Day 28(+/-2)
Informed consent	✓					
Eligibility check	✓					
Health check (physical exam)	✓					
Medical history	✓					
Urine pregnancy test	✓					
Concomitant medication <sup>1</sup>	✓	✓	✓	✓	✓	✓
Dosage of IP <sup>1</sup>		✓	✓	✓	✓	
AE interview <sup>1</sup>	✓	✓	✓	✓	✓	✓
Dental plaque acidogenicity <sup>1</sup>		✓	✓	✓	✓	

<sup>1</sup> For details of Visits 2-5, see Detailed schedule of events in Section 12.1 in the Clinical Study Protocol (CSP) (Appendix 16.1.1).

Part 2 of the study was an open, observational, safety and tolerability study during 6 weeks. The subjects used the non-tobacco-based nicotine pouch (ZYN<sup>®</sup>) ad libitum. The subjects were allowed to switch between the study products but were recommended to replace as many as possible of their regular snus products with ZYN<sup>®</sup> products. At each visit the subject reported any local and general adverse symptoms. All subjects were seen on an individual basis and each visit lasted for about 90 min.

*Table 9.1-2 Overall schedule of events (Part 2)*

Event	Visit 1 Screening Day -2	Visit 2 Day 0	Visit 3 Day 14 (+/-2)	Visit 4 Day 28 (+/-3)	Visit 5 Day 42 (+/-4)	Follow-up Day 49 (+/-2)
Informed consent	✓					
Eligibility check	✓					
Health check (physical exam)	✓					
Medical history	✓					
Urine pregnancy test	✓					
Concomitant medication	✓	✓	✓	✓	✓	✓
AE interview	✓	✓	✓	✓	✓	✓
Photo	✓		✓	✓	✓	
Inspection of oral cavity (mucosal lesions)	✓		✓	✓	✓	
Dental plaque acidogenicity	✓		✓	✓	✓	
Oral microflora	✓		✓	✓	✓	
Plaque amount	✓		✓	✓	✓	
Diary for compliance			✓	✓	✓	
Supply of IP	✓	✓	✓	✓		

## 9.2 Rationale for study design and dose groups

The rationale for the choice of the study design was from a recent study that assessed the oral safety of a sublingual tablet containing 2 mg nicotine with regard to lesions at the site of application (3) and from a prospective follow-up of smokers using the sublingual nicotine tablet over a period of 3-6 months, 8/30 subjects displayed lesions in the floor of the mouth during the 6-month medication period, all of which appeared in the first 1-6 weeks. By the 6-month-visit all such lesions had resolved (3).

## 9.3 Study population

### 9.3.1 Recruitment

Healthy adult males and females were recruited using an advertisement in the local newspaper. Following a telephone interview to evaluate eligibility, potential participants were invited to a Screening visit. The potential participants then submitted a Health Declaration that was checked by the responsible Investigator.

### 9.3.2 Number of subjects

Part 1: 20 participants (with available data on all 4 test articles)

Part 2: 60 participants

### 9.3.3 Inclusion criteria

For inclusion in the study, subjects had to fulfill the following criteria:

1. Snus user, with a minimum weekly consumption of 3 or more snus cans (brands with nicotine content <1%) or 2 or more cans (brands with nicotine content >1%) since  $\geq 1$  year
2. Consent to participate voluntarily and sign ICF prior to any study procedure
3. Healthy male/female, age  $\geq 19$ . Female subjects had to have a negative pregnancy test.
4. Willing and able to comply with study procedures
5. Normal stimulated salivary secretion rate ( $\geq 0.7$  ml/min)

### 9.3.4 Exclusion criteria

Subjects were not allowed to enter the study if any of the following exclusion criteria were fulfilled:

1. A history or presence of diagnosed hypertension or any cardiovascular disease
2. Surgery within 6 months of the Screening visit that, in the opinion of the investigator, could negatively impact on the subject's participation in the clinical study
3. Any surgical or medical condition, which, in the judgment of the clinical investigator, might interfere with the absorption, distribution, metabolism or excretion of nicotine
4. Subjects who were pregnant
5. Allergy towards composite materials
6. Antibiotic use during or within the last 4 weeks prior to the study period

### 9.3.5 Restrictions during the study

The subjects in both parts of the study refrained from approximal tooth cleaning during the 72 h prior to visit and toothbrushing during the last 48 h prior to visit. They did not eat or drink anything during the last 2 h prior to visit.

Other therapy considered necessary for the subject's welfare could be given at the discretion of the Investigator. All such therapy had to be recorded in the CRF.

Study subjects were not allowed to participate in any other clinical study during the study period.

### 9.3.6 Criteria for subjects' withdrawal

#### 9.3.6.1 General withdrawal criteria

A subject could be withdrawn from the study treatment if, in the opinion of the Investigator, it was medically necessary, or if it was the wish of the subject. The reason for withdrawal was clearly described and the subject was, whenever possible, irrespective of the reason for withdrawal, medically examined as soon as possible. Relevant samples were obtained and all relevant assessments were completed, preferably according to the schedule for the final assessment. The CRFs were completed as far as possible.

### **9.3.6.2      *Procedures for discontinuation replacement***

A subject who prematurely discontinued participation in the study was to be asked about the reason(s) for discontinuation and the presence of any AEs. If possible, they were to be seen by the Investigator and assessed according to the procedures scheduled for the Follow-up visit. Any ongoing AEs were to be followed as described in Section 12.6.6 in the CSP (Appendix 16.1.1).

### **9.3.6.3      *Subject replacement***

Subjects who were prematurely withdrawn from the study for any reason except the occurrence of treatment emergent AEs assessed as possibly or probably related to study treatment were not to be replaced during the course of the study.

### **9.3.6.4      *Randomization***

The subjects in Part 1 were assigned to the treatments using a computer-generated randomization list.

### **9.3.6.5      *Blinding***

Part 1 of the study was an open, randomized study. Subjects were administered each dose by the personnel according to the randomization list.

## **9.4            Treatments**

### **9.4.1            Identity of investigational products**

Part 1: ZYN<sup>®</sup> Smooth 3 mg (batch number 91153)  
 ZYN<sup>®</sup> Peppermint 3 mg (batch number 91087)  
 10% sucrose solution  
 10% xylitol solution

Part 2: Ad libitum use of a ZYN<sup>®</sup> nicotine pouch, participants could choose from:  
 ZYN<sup>®</sup> Smooth 3 mg (batch number 91153)  
 ZYN<sup>®</sup> Smooth 6 mg (batch number 91250)  
 ZYN<sup>®</sup> Cinnamon 3 mg (batch number 91160)  
 ZYN<sup>®</sup> Cinnamon 6 mg (batch number 91166)  
 ZYN<sup>®</sup> Peppermint 3 mg (batch number 91087)  
 ZYN<sup>®</sup> Peppermint 6 mg (batch number 91241)

### **9.4.2            Treatment administration**

Part 1: A single dose was given on each study day. See Table 9.4-1 for the treatment sequences to which the subjects were randomized.

**Table 9.4-1**     *Definition of treatment sequences (Part 1)*

Description of Element	Description of Planned Arm			
	Treatment Sequence	Treatment Sequence	Treatment Sequence	Treatment Sequence
	A	B	C	D
ZYN® Smooth 3 mg	1	2	3	4
ZYN® Peppermint 3 mg	2	3	4	1
10% sucrose (pos control)	3	4	1	2
10% xylitol (neg control)	4	1	2	3

SM17\_02\_A\_14\_01\_02\_01 treatment definitions, SAS program: treatment\_definitions.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:46:22

Part 2: The subjects were recommended to replace as many as possible of their regular snus products (ideally all) with ZYN® products during the 6-week period and to use as much ZYN® as they need.

The duration of the treatment period was 6 weeks. It was entirely at the discretion of the subject when he/she used the pouch during the day and how many pouches per day that were used.

### 9.4.3     **Treatment compliance**

All IPs in Part 1 were administered at the research clinic under supervision of the clinical staff to ensure compliance. The subjects in Part 2 received enough IPs for 14 days. The amount of IPs was recorded in a paper diary.

## 9.5     **Study assessments**

### 9.5.1     **Demographics and other baseline characteristics**

#### 9.5.1.1     *Informed consent*

Signed informed consent was obtained before any screening procedures were initiated. The informed consent procedure is further described in Section 5.3.

#### 9.5.1.2     *Demographic information*

The following demographic data were recorded: gender, age and ethnic origin (race).

#### 9.5.1.3     *Medical/surgical history*

Medical/surgical history was obtained by interview in order to verify that the eligibility criteria were met.

#### 9.5.1.4     *Pregnancy urine test*

Pregnancy urine test was performed at the Screening visit (females only) using dip sticks.

#### **9.5.1.5     *Prior and concomitant medication***

Prior medication was obtained by interview and documented in the CRF in order to verify that eligibility criteria were met.

Medications were classified as prior medications if the stop date was before or on the day of the first dose administration and as concomitant if ongoing at, and stopped after, the first dose administration, or started after the first dose administration.

Any use of concomitant medication from 2 weeks prior to screening until the last Follow-up visit was documented in the CRF. Relevant information (i.e. name of medication, dose, unit, indication, reason for administration, dose form, frequency, route, start and stop dates) were recorded. All changes in medication were noted in the CRF.

#### **9.5.1.6     *Baseline symptoms***

A baseline symptom was an event that occurred after a subject had signed the ICF up until the first administration of IP (i.e. during the screening period).

### **9.5.2        *Assessments related to primary and secondary endpoints***

#### **9.5.2.1     *Examination of the oral cavity***

Clinical examination of the oral cavity was performed at screening and at Visits 3, 4 and 5.

The oral mucosa was inspected and any pathological changes were recorded and classified. Lesions in the mucosa at the placement of the pouch, particularly SILs, were registered according to 4 grade clinical scale suggested by Axéll et al (1). In addition, gingival retractions were recorded.

Clinical examination of the oral cavity was performed according to Axéll et al (1976) (1):

- Degree 1. A superficial lesion with a color similar to the surrounding mucosa and with slight wrinkling. No obvious mucosal thickening.
- Degree 2. A superficial, whitish or yellowish lesion with wrinkling. No obvious thickening.
- Degree 3. A whitish-yellowish to brown, wrinkled lesion with intervening furrows of normal mucosal colors, obvious thickening.
- Degree 4. A marked yellowish to brown and heavily wrinkled lesion with intervening deep reddened furrows and/or heavy thickening.

By the 6-week visit (study termination) it was summarized to which extent such lesions had changed (according to the above scale or have resolved completely). Oral leukoplakias and erythroplakias were followed up according to standard clinical routines. The oral cavity was documented by photography.

Local symptoms reported by the subject were recorded at each visit, elicited using open-ended general questions. Other AEs reported spontaneously were also recorded and duration thereof.

#### **9.5.2.2     *Dental plaque acidogenicity***

Plaque acidogenicity was measured using the microtouch method. An iridium microelectrode (Beetrode MEPH-1, WPI Instruments, New Haven, Conn., USA) was inserted into the plaque on 2 buccal surfaces in the upper jaw and 2 approximal surfaces in the upper and lower jaw.



The electrode was connected to an Orion SA720 pH/ISE Meter (Orion Research, Boston, Mass., USA) to which also a reference electrode was connected. The reference electrode was placed into a solution of 3 M KCl to which also a finger of the volunteer was placed in order to create a salt bridge. Prior to and during each test session, the electrode was calibrated against a standard buffer at pH 7.00. After baseline registration (0 min), the subjects rinsed with the sucrose or xylitol solution for 1 min or used the study products for 60 min. pH was measured at 8 different time points up to 60 min.

#### **9.5.2.3     *Plaque amount***

The plaque amount was assessed with a plaque score calculated by the index described by Silness and Loe (1964) (4). The amount of plaque was measured on all surfaces. For each tooth, 6 sites (mesio-buccal, buccal, disto- buccal, disto-lingual, lingual and mesio-lingual) were scored 0-3.

#### **9.5.2.4     *Oral microflora***

Pooled plaque samples were collected by a sterile toothpick according to Kristoffersson and Bratthall (1982) (5) from the buccal areas of respective quadrants.

#### **9.5.2.5     *Saliva sampling***

The salivary factors pH and flow rate (unstimulated and stimulated) were measured. Saliva was collected into a beaker and the secretion rate calculated in ml/min. The buffer capacity was determined using a chairside kit (CRT Buffer<sup>®</sup>, Vivadent, Germany).

### **9.5.3     *Adverse events***

Collection of baseline events started after the subject signed the ICF and continued until the first administration of IP. Collection of AEs started with administration of the IP and continued until the last follow-up assessment. Any AE with start date on the day of first IP administration were recorded with start time. At the Follow-up visit, information on new AEs or serious adverse events (SAEs), if any, and stop dates for AEs recorded and on-going during the dosing period were recorded.

All AEs were followed until they were resolved, or the subject's participation in the study ended. In addition, all SAEs and those non-serious events assessed by the investigator as possibly related to the investigational medication/product were followed even after the subject's participation in the study was over. Such events were followed until they were resolved or until the Investigator assessed them as "chronic" or "stable".

The Investigator reported SAEs to the Sponsor immediately (within 24 h) after becoming aware of them.

For detailed definition and reporting procedures, see Section 12.6 in the CSP (Appendix 16.1.1 to this report).

#### **9.5.1     *Appropriateness of measurements***

Measurements used in the study are standard assessments in oral health research. Standardized methods for measurements of safety and tolerability were used.

## 9.6 Data quality assurance

The study was performed in compliance with GCP, applicable regulations and CTC Standard Operating Procedures (SOPs).

Before inclusion of the first subject into the study, a study initiation visit was performed by a sponsor representative at the research clinic in order to inform and train relevant study staff. The Investigator was thereafter responsible for providing appropriate study related training to new staff and to forward any new information of relevance to the performance of this study to the staff involved.

An CRF was completed for each subject included. A sample of the CRF is included as Appendix 16.1.2.

The study site was periodically visited by a Monitor from CTC. The Monitor had direct access to clinical records and original data for source data verification (SDV). For screening failures/non-included subjects, 100% SDV was performed for the Informed Consent procedure, demography (age and gender) and reason for non-inclusion. For all included subjects, protocol adherence and 100% SDV were performed for the Informed Consent procedure and all variables except prior and concomitant medications for which 100% SDV were performed on 5 subjects, randomly chosen.

All CRFs were reviewed for completion of recorded data, including missing data and inconsistencies in entered data.

## 9.7 Statistical methods planned in the protocol and determination of sample size

The statistical analyses performed in this study were initially specified in the CSP (see Appendix 16.1.1). Further details of the planned statistical analysis are provided in the Statistical Analysis Plan (SAP) (see Appendix 16.1.9), which was finalized prior to the clean file meeting and database lock. Any changes in the SAP compared to the CSP are described in Section 9.8.

### 9.7.1 General

Continuous data are presented using summary statistics. Data are presented in terms of number (n), arithmetic mean, median, standard deviation (SD), minimum and maximum value.

Categorical data are presented as counts and percentages. When applicable, summary data are presented by treatment and by assessment time. Individual subject data are listed by subject number, treatment and, where applicable, by assessment time.

Descriptive statistics are used for the reporting of the results.

### 9.7.2 Determination of sample size

Part 1: Based on previous experience with the described methodology, a total of 20 subjects was considered to be enough to reliably detect a clinically significant increased plaque acidogenicity with the pouched products versus the negative control.

Part 2: A 6-week observation period was considered reasonable to assess putative changes in the oral mucosa resulting from use of the nicotine pouches given that “snus lesions” among habitual snus users regress within a few weeks after cessation of exposure (Wallström et al, [1999] [3]). A 6-week observation period was also supported by the fact that the other

measures of oral health to be assessed (biofilm acidogenicity, oral microflora, plaque amount) are known to potentially change within a few weeks. With an estimated dropout rate of 25% a total of 45 fully evaluable subjects were expected with a total inclusion of 60 subjects. Descriptive statistics were used for reporting the results of monitoring of the oral mucosa and for subjective adverse symptoms.

### 9.7.3 **Definition of analysis data sets**

#### 9.7.3.1 ***Full analysis set***

Part 1: The full analysis set (FAS) consisted of all subjects who had been randomized and received at least 1 dose of the product. This population was used as safety analysis set.

Part 2: The FAS consisted of all enrolled subjects. This population was used as safety analysis set.

#### 9.7.3.2 ***Per protocol analysis set***

Part 1: The per protocol set (PPS) consists of all subjects who had been randomized and completed the study period without any major protocol deviations. All protocol violations were judged as major or minor at the clean file meeting.

Part 2: The PPS consists of all subjects who had been enrolled and completed the study period without any major protocol deviations. All protocol violations were judged as major or minor at the clean file meeting.

### 9.7.4 **Description of study population**

#### 9.7.4.1 ***Demographics and baseline characteristics***

The following baseline characteristics are summarized by treatment sequence (Part 1) or by gender (Part 2): age, gender, ethnicity (race), preferred snus placement, saliva buffer capacity, stimulated saliva secretion rate and unstimulated saliva secretion rate.

#### 9.7.4.2 ***Medical/surgical history and concomitant medication***

Medical/surgical history and prior/concomitant medications are listed. Medical/surgical history was coded using the Medical Dictionary for Regulatory Activities (MedDRA). Prior and concomitant medications were coded according to World Health Organization (WHO) Anatomic Therapeutic Chemical (ATC) classification system.

#### 9.7.4.3 ***Treatment compliance***

The number of subjects treated in each treatment period and their product are tabulated. In Part 2 it is also tabulated to which extent participants replaced their habitual snus with study products.

### 9.7.5 **Analysis of primary endpoints**

#### 9.7.5.1 ***Dental plaque acidogenicity (Part 1 and Part 2)***

The dental plaque acidogenicity is described using the following approaches (each site and the mean between sites were used):

### **Minimum value**

#### **Part 1:**

The minimum value after baseline was selected and presented using summary statistics by product. Any differences were assessed by using the Wilcoxon signed rank sum test. One analysis compared the differences between the site which the product was closest to and the site on the opposite side in the upper jaw.

#### **Part 2:**

The minimum value after baseline at each visit was selected and presented using summary statistics. The absolute and percent change from baseline were calculated and described using summary statistics and analyzed using the Wilcoxon signed rank sum test.

### **Maximum/minimum change**

#### **Part 1:**

The maximum and minimum change were defined as the lowest and highest change by using the actual baseline value and the lowest and highest values obtained during measurement. The maximum and minimum changes are presented using summary statistics by product. Any differences were assessed by using the Wilcoxon signed rank sum test.

#### **Part 2:**

The maximum and minimum change were defined as the lowest and highest change by using the actual values after baseline for each visit. The maximum and minimum changes are described using summary statistics and analyzed using the Wilcoxon signed rank sum test.

### **AUC dental plaque acidogenicity**

#### **Part 1 and part 2 definition:**

Area under the curve (AUC) for dental plaque acidogenicity was estimated by calculating the area under the reference limit to the observed dental plaque acidogenicity. The different reference limits used were:

- 6.2 pH
- 5.5 pH

Any area which was above the reference limit was subtracted from the total area between the reference limit and observed dental plaque acidogenicity.

#### **Part 1:**

The AUC was described using summary statistics for each product and analyzed between products using the Wilcoxon signed rank sum test.

#### **Part 2:**

The AUC, the absolute and percent change from baseline were described using summary statistics for each visit and analyzed using the Wilcoxon signed rank sum test.

## 9.7.6 Analysis of secondary endpoints

### 9.7.6.1 Adverse events (Part 1 and Part 2)

Adverse events and baseline events were coded using MedDRA. The following summaries of AEs and SAEs are given by treatment and in total:

- Total number of AEs
- Total number of related AEs
- Total number (%) of subjects with at least 1 AE
- Total number (%) of subjects with at least 1 related AE
- AEs by MedDRA System Organ Class (SOC) and preferred term (PT)
- AEs by relation of study product and MedDRA SOC and PT

### 9.7.6.2 Plaque amount (Part 2)

The total index for each tooth and total index are presented using summary statistics for actual values, absolute change and percent change from baseline to each subsequent visit. Changes over time were analyzed using Wilcoxon signed rank sum test.

### 9.7.6.3 Oral microflora (Part 2)

Actual (measured) and log microflora are presented using summary statistics for actual values, absolute change and percent change from baseline to each subsequent visit. Changes over time were analyzed using Wilcoxon signed rank sum test.

### 9.7.6.4 Oral mucosal lesions (Part 2)

The oral mucosal lesions are presented using frequency tables at each visit (with n and %). Absolute changes in oral mucosal lesions were calculated between visits and baseline. The absolute change was analyzed using the Mc-Nemar's test.

The correlation at each visit using the change in oral mucosal and the percent usage of IPs vs. ordinary Swedish snus was calculated at each visit (the percentage usage was calculated as the number of test products divided by the total number of pouches used).

## 9.7.7 Statistical/analytical issues

### 9.7.7.1 Adjustments for covariates

No adjustments for covariates were performed.

### 9.7.7.2 Handling of dropouts or missing data

Outliers were included in summary tables and listings and were not handled separately in any analyses. No imputation of data was performed.

### 9.7.7.3 Significance level

All tests were performed using a 5% significance level.

#### **9.7.7.4      *Multiple comparisons/multiplicity***

No adjustments for multiplicity were performed.

#### **9.7.7.5      *Examination of subgroups***

Gender was used as a subgroup in Part 2.

### **9.8            Changes in the conduct of the study or planned analyses**

Pairwise comparison between the test products was not planned for in the CSP but was described in the SAP. Baseline and screening are viewed as the same visit in Part 2 of the study.

## **10            STUDY SUBJECTS**

### **10.1          Disposition of subjects**

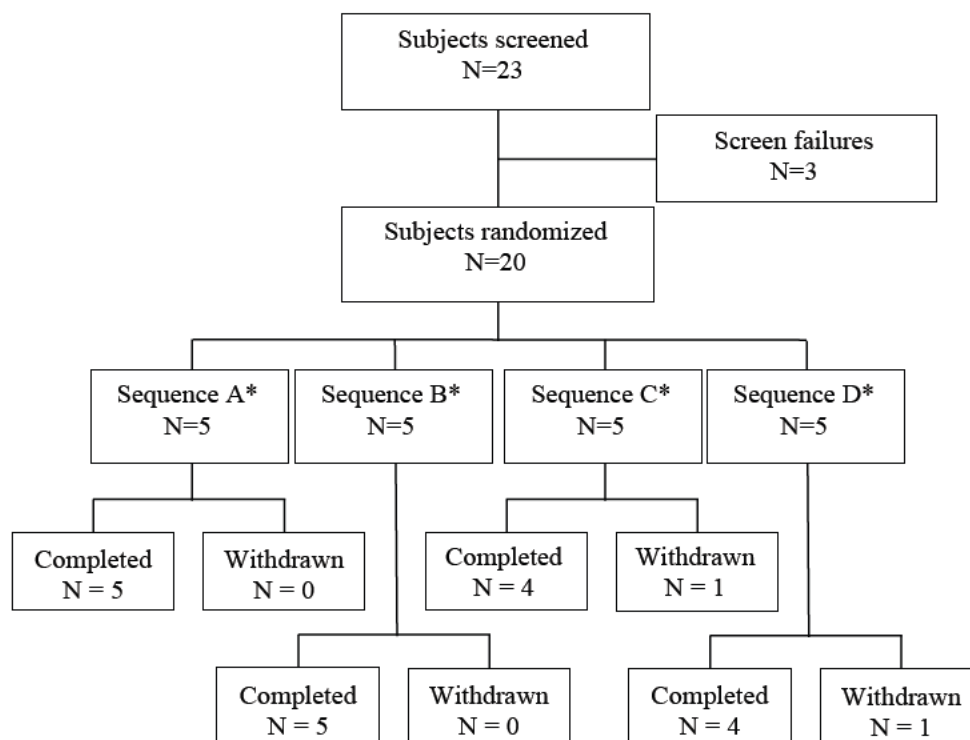
#### **10.1.1       Number of subjects**

In total, 83 subjects (23 subjects in Part 1 and 60 subjects in Part 2) were screened and 79 subjects who fulfilled all inclusion criteria and none of the exclusion criteria were enrolled into the study. The reason for non-inclusion in Part 1 (3 subjects) and Part 2 (1 subject) was screen failure. The first subject was screened on 06 November 2017, the first dose was administered on 14 November 2017 and the last subject completed the study on 05 June 2018 (the duration of Part 1 was 06 November 2017 – 06 February 2018; the duration of Part 2 was 05 February 2018 – 05 June 2018).

Of the 20 subjects enrolled in Part 1, 18 subjects completed the study and 2 subjects were withdrawn. Of the 59 subjects enrolled in Part 2, 57 subjects completed the study and 2 subjects were withdrawn. The disposition of subjects is shown in Figure 10.1-1 (Part 1) and Figure 10.1-2 (Part 2). The treatment sequences are found in Section 9.4.2. Summaries of study disposition are shown in Table 14.1-1 (Part 1) and Table 14.1-2 (Part 2).

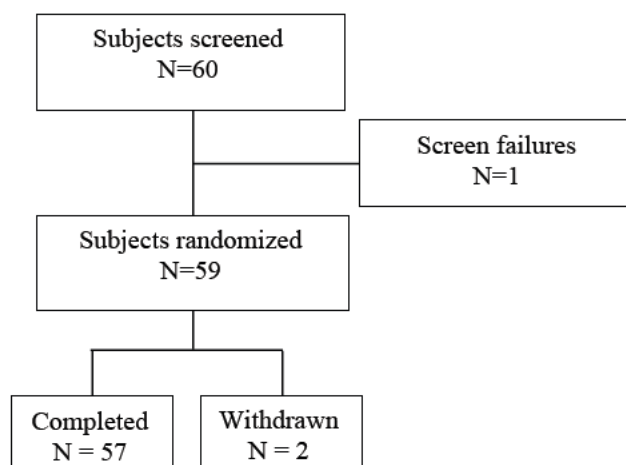
Individual subject data are presented in Appendix 16.2.9.

Figure 10.1-1 Disposition of subjects (Part 1)



\* For treatment sequences, see Section 9.4.2.

Figure 10.1-2 Disposition of subjects (Part 2)



### 10.1.2 Study discontinuations

In total 4 subjects were discontinued from the study. In Part 1, Subject 117 was withdrawn due to severe non-compliance and Subject 120 withdrew his consent, both subjects ended the study after Visit 2 (after the first administration of sucrose solution and ZYN® Peppermint, respectively). In Part 2, Subjects 206 (after Visit 3) and 249 (after screening but prior to the first administration) withdrew their consent. The subjects returned for an end-of-study visit. Individual subject data are provided in Appendix 16.2.1.

## 10.2 Protocol deviations

There were no major deviations in the study. The minor protocol deviations that occurred were not considered to affect the evaluation of the study results. Protocol deviations are listed in Appendix 16.2.2.

## 10.3 Data sets analyzed

In Part 1, 20 subjects were included in FAS and 18 subjects were included in PPS (Table 14.1-1). Subjects 117 and 120 were excluded from the PPS due to discontinuation from the study.

In Part 2, 59 subjects were included in FAS and 56 subjects were included in PPS (Table 14.1-2). Subjects 206 and 249 were excluded from the PPS due to withdrawal of consent and Subject 218 was excluded from PPS due to wrongly included (subject on hypertension medication).

Subject populations, subjects excluded from PPS and exceptions from inclusion/exclusion are listed in Appendix 16.2.3.

## 10.4 Demographics and other baseline characteristics

A total of 20 subjects (non-hispanic), 6 females and 14 males, were included in Part 1. The subjects had a mean±SD age of 35±11 years and a normal stimulated salivary secretion rate (mean±SD was 2.3±1.5 mL/min) at screening. Demographic data for all subjects are summarized by treatment sequence in Table 10.4-1 below. All female subjects had a negative pregnancy test at screening, see Table 14.1-3. For definitions of the treatment sequences, refer to Table 9.4-1 in Section 9.4.2. Fifteen (15) of the 20 subjects had a medical history, but of no clinical significance, at the Screening visit, see Table 14.1-5.

A total of 59 subjects (non-hispanic), 20 females and 39 males, were included in Part 2. The subjects had a mean±SD age of 31±10 years and a normal stimulated salivary secretion rate (mean±SD was 2.3±1.0 mL/min) at screening. Demographic data are summarized by female, male and all subjects in Table 10.4-2 below. All female subjects had a negative pregnancy test at screening, see Table 14.1-4. Nineteen (19) of the 59 subjects had a medical history, but of no clinical significance, at the Screening visit, see Table 14.1-6.

Individual subject demographic data, pregnancy test results, medical/surgical history and prior medications for all subjects randomized are presented in Appendix 16.2.4. Concomitant medications are presented in Appendix 16.2.5. Individual saliva status at screening is presented in Appendix 16.2.6.

Table 10.4-1 Summary of demographic data and other baseline characteristics (Part 1)

		Treatment Sequence A (N=5)	Treatment Sequence B (N=5)	Treatment Sequence C (N=5)	Treatment Sequence D (N=5)	Total (N=20)
Age (years)	n/nmiss	5/0	5/0	5/0	5/0	20/0
	Mean (SD)	33.2 (7.7)	47 (13.4)	27 (2.4)	31 (7.9)	34.6 (11.1)
	Median (Min, Max)	34 (24, 42)	43 (34, 64)	26 (24, 30)	30 (23, 44)	30.5 (23, 64)
Gender	Female	2 (40%)	1 (20%)	3 (60%)		6 (30%)
	Male	3 (60%)	4 (80%)	2 (40%)	5 (100%)	14 (70%)



		Treatment Sequence A (N=5)	Treatment Sequence B (N=5)	Treatment Sequence C (N=5)	Treatment Sequence D (N=5)	Total (N=20)
Ethnicity	Not Hispanic	5 (100%)	5 (100%)	5 (100%)	5 (100%)	20 (100%)
Preferred snus placement	Upper Jaw Sublabial Both Sides	3 (60%)	3 (60%)	4 (80%)	2 (40%)	12 (60%)
	Upper Jaw Sublabial Left Side		1 (20%)		1 (20%)	2 (10%)
	Upper Jaw Sublabial Right Side	2 (40%)	1 (20%)	1 (20%)	2 (40%)	6 (30%)
Saliva Buffer Capacity (pH)	n/nmiss	5/0	5/0	5/0	5/0	20/0
	Mean (SD)	6.1 (1.6)	6.4 (0.7)	5.9 (1.9)	6.7 (1.3)	6.27 (1.38)
	Median (Min, Max)	6.4 (4.2, 7.7)	6.7 (5.3, 7.2)	5.5 (3.6, 7.8)	6.9 (4.6, 8)	6.55 (3.6, 8)
Stimulated Saliva Secretion Rate (mL/min)	n/nmiss	5/0	5/0	5/0	5/0	20/0
	Mean (SD)	2 (0.4)	3.2 (2.7)	1.6 (0.7)	2.4 (1.2)	2.28 (1.53)
	Median (Min, Max)	2 (1.6, 2.4)	2.2 (1.4, 8)	1.3 (1.1, 2.7)	2.1 (1.5, 4.4)	1.95 (1.1, 8)
Unstimulated Saliva Secretion Rate (mL/min)	n/nmiss	5/0	5/0	5/0	5/0	20/0
	Mean (SD)	0.3 (0.1)	0.3 (0.2)	0.4 (0.4)	0.3 (0.2)	0.315 (0.223)
	Median (Min, Max)	0.3 (0.2, 0.4)	0.2 (0.2, 0.6)	0.2 (0.1, 1)	0.1 (0.1, 0.5)	0.2 (0.1, 1)

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summary\_demographics.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-  
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Table 10.4-2 Summary of demographic data and other baseline characteristics (Part 2)

		Female (N=20)	Male (N=39)	Total (N=59)
Age (years)	n/nmiss	20/0	39/0	59/0
	Mean (SD)	26.7 (5.6)	33.8 (11.1)	31.4 (10.1)
	Median (Min, Max)	25.5 (21, 46)	30 (21, 64)	27 (21, 64)
Gender	Female	20 (100%)		20 (34%)
	Male		39 (100%)	39 (66%)
Ethnicity	Not Hispanic	20 (100%)	39 (100%)	59 (100%)
Preferred snus placement	Lower Jaw Sublabial Left Side	1 (5%)		1 (2%)
	Other, Upper Jaw Sublabial Right Side And Middle		1 (3%)	1 (2%)
	Upper Jaw Sublabial Both Sides	12 (60%)	23 (59%)	35 (59%)
	Upper Jaw Sublabial Left Side	3 (15%)	5 (13%)	8 (14%)
	Upper Jaw Sublabial Right Side	4 (20%)	10 (26%)	14 (24%)
Saliva Buffer Capacity (pH)	n/nmiss	20/0	39/0	59/0
	Mean (SD)	5.4 (1.4)	6.6 (0.9)	6.18 (1.25)
	Median (Min, Max)	5.2 (3.6, 8)	6.7 (3.9, 7.9)	6.4 (3.6, 8)
Stimulated Saliva Secretion Rate (mL/min)	n/nmiss	20/0	39/0	59/0
	Mean (SD)	2.2 (1.1)	2.4 (1)	2.32 (1.04)
	Median (Min, Max)	2.1 (0.7, 4.6)	2.1 (1, 5)	2.1 (0.7, 5)
Unstimulated Saliva Secretion Rate (mL/min)	n/nmiss	20/0	39/0	59/0
	Mean (SD)	0.4 (0.3)	0.6 (0.4)	0.51 (0.365)
	Median (Min, Max)	0.3 (0.1, 1)	0.5 (0.1, 1.7)	0.4 (0.1, 1.7)

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summary\_demographics.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-  
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The physical examination of the tongue and oral mucosa at screening for subjects in Part 1 and Part 2 are presented in Table 14.1-7 and Table 14.1-8, respectively. Tooth status (DMFT) at screening of the subjects in Part 1 and Part 2 are summarized in Table 14.1-9 and Table 14.1-10, respectively. Individual subject data are presented in Appendix 16.2.6.

## **10.5 Measurements of treatment compliance**

All IPs in Part 1 were administered at the research clinic under supervision by study staff to ensure compliance. In Part 2, the subjects recorded the use of IPs in a paper diary. The ratio ZYN products of the total nicotine products used is presented in Table 14.1-11. The number of nicotine products used per study day is presented in Table 14.1-12.

# **11 EVALUATION OF RESULTS**

## **11.1 Extent of exposure**

In Part 1, pouches containing nicotine were administered as single doses:

- 18 subjects received 2 single doses containing 3 mg nicotine
- 1 subject received 1 single dose containing 3 mg nicotine

In Part 2, pouches containing nicotine were administered ad libitum during 6 weeks:

- 54 subjects used snus between Visits 2 and 3
- 48 subjects used snus between Visits 3 and 4
- 48 subjects used snus between Visits 4 and 5
- 28 subjects used ZYN<sup>®</sup> products containing 3 mg between Visits 2 and 3 (11, 19 and 14 subjects used ZYN<sup>®</sup> Cinnamon, ZYN<sup>®</sup> Peppermint and ZYN<sup>®</sup> Smooth, respectively)
- 25 subjects used ZYN<sup>®</sup> products containing 3 mg between Visits 3 and 4 (7, 12 and 13 subjects used ZYN<sup>®</sup> Cinnamon, ZYN<sup>®</sup> Peppermint and ZYN<sup>®</sup> Smooth, respectively)
- 23 subjects used ZYN<sup>®</sup> products containing 3 mg between Visits 4 and 5 (8, 11 and 10 subjects used ZYN<sup>®</sup> Cinnamon, ZYN<sup>®</sup> Peppermint and ZYN<sup>®</sup> Smooth, respectively)
- 40 subjects used ZYN<sup>®</sup> products containing 6 mg between Visits 2 and 3 (9, 28 and 16 subjects used ZYN<sup>®</sup> Cinnamon, ZYN<sup>®</sup> Peppermint and ZYN<sup>®</sup> Smooth, respectively)
- 40 subjects used ZYN<sup>®</sup> products containing 6 mg between Visits 3 and 4 (7, 29 and 16 subjects used ZYN<sup>®</sup> Cinnamon, ZYN<sup>®</sup> Peppermint and ZYN<sup>®</sup> Smooth, respectively)
- 39 subjects used ZYN<sup>®</sup> products containing 6 mg between Visits 4 and 5 (3, 29 and 14 subjects used ZYN<sup>®</sup> Cinnamon, ZYN<sup>®</sup> Peppermint and ZYN<sup>®</sup> Smooth, respectively)

Summaries of exposure in Part 1 and Part 2 are found in Table 14.3-1 and Table 14.3-2, respectively. Individual exposure data are presented in Appendix 16.2.5.

## **11.2 Evaluation of primary endpoint**

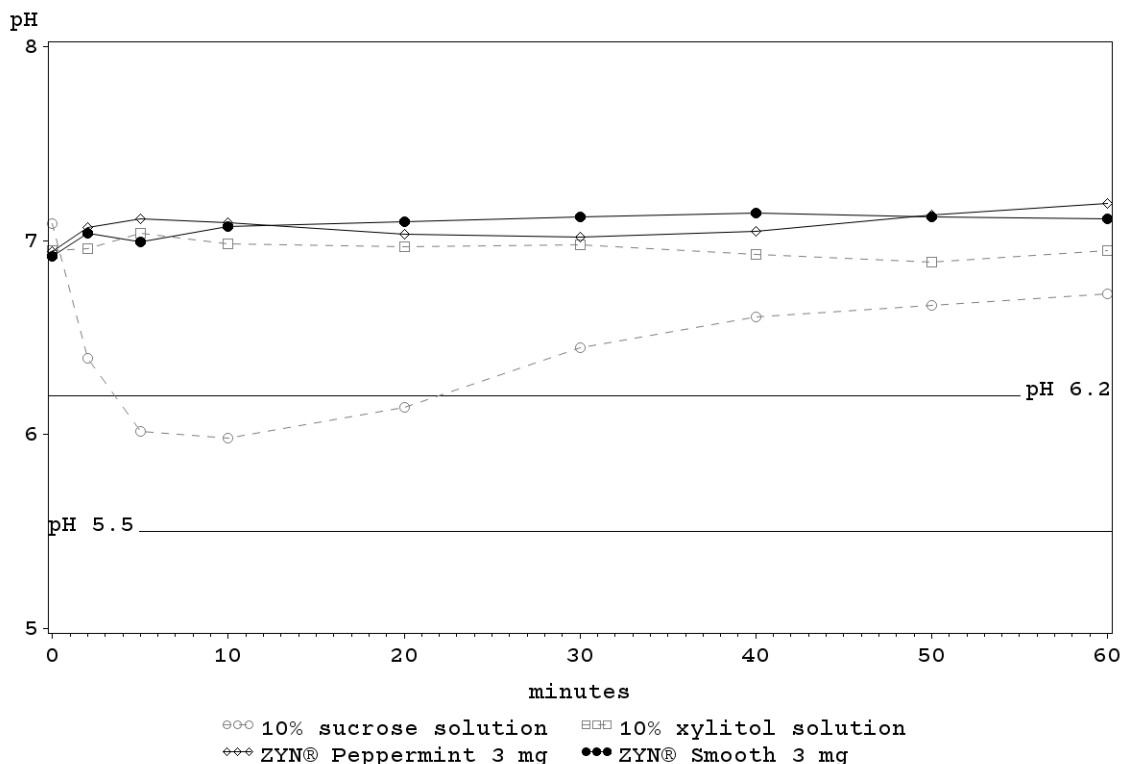
### **11.2.1 Dental plaque acidogenicity**

#### ***11.2.1.1 Dental plaque acidogenicity after short-term exposure (Part 1)***

There were statistically significant differences in minimum and maximum changes from baseline in dental plaque acidogenicity for the mean of sites 1 and 2 (and at site 2) between ZYN<sup>®</sup> Smooth and xylitol (negative control) and in maximum change from baseline in dental plaque acidogenicity for the mean of sites 1 and 2 (and at site 1 and site 2) between ZYN<sup>®</sup> Peppermint and xylitol. The minimum change from baseline was smaller and the maximum change was larger for the ZYN<sup>®</sup> products compared to xylitol. Additionally, there were statistically significant differences in minimum value, minimum and maximum changes from baseline in dental plaque acidogenicity, and AUC for dental plaque acidogenicity (pH 5.5 and pH 6.2) between the ZYN<sup>®</sup> products and sucrose (positive control), respectively and between xylitol and sucrose. The minimum value was higher, the minimum change from baseline was smaller, the maximum change from baseline was larger and AUC was larger for the ZYN<sup>®</sup> products and xylitol compared to sucrose. There were no statistical differences between the ZYN<sup>®</sup> products. Dental plaque acidogenicity between group comparison are presented in Table 14.3-3.

Summary statistics of dental plaque acidogenicity measurements by timepoint are presented in Table 14.3-4 and mean values are graphically presented in Figure 11.2-1. Summary statistics of minimum values, minimum and maximum changes from baseline are summarized in Table 14.3-6. Summary statistics of AUC for dental plaque acidogenicity are found in Table 14.3-8 and Table 14.3-9 (values over baseline set to zero). The values for AUC (where values over baseline were set to zero) were zero, except for treatment with sucrose, since there was no observed pH <6.2. Individual subject data are presented in Appendix 16.2.6.

Figure 11.2-1 Dental plaque acidogenicity (pH) vs time, mean (PPS)



SM17\_02\_A dental plaque acidogenicity (pH) figures, mean. SAS program: ph\_graphs\_mean.sas.  
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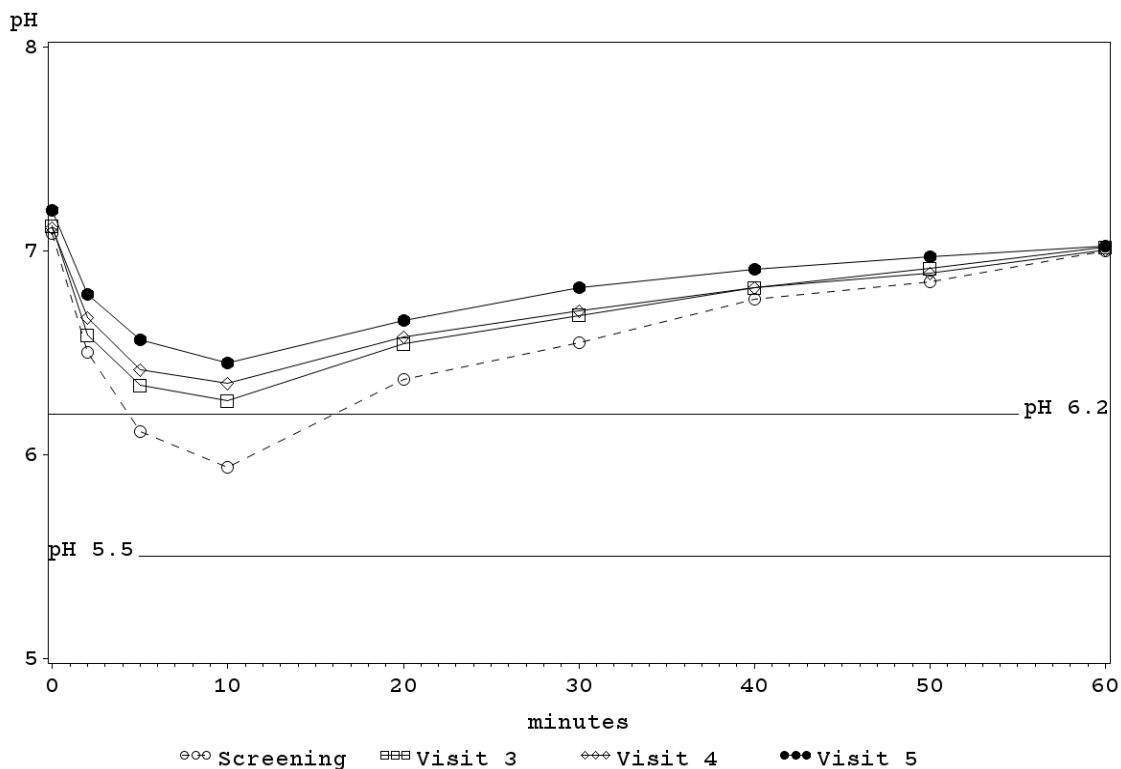
### 11.2.1.2 Dental plaque acidogenicity after 6 weeks of use (Part 2)

There were statistically significant differences in minimum value and in minimum absolute change from baseline in dental plaque acidogenicity for the mean of sites 1 and 2 (and at site 1 and site 2) at Visits 3, 4 and 5 compared to baseline for all subjects. The minimum value was higher and the minimum change from baseline was smaller during the study compared to baseline.

There were statistically significant differences in the absolute change in AUC (and AUC where values over baseline were set to zero) for dental plaque acidogenicity (pH 6.2 and pH 5.5) for the mean of sites 1 and 2 (and at site 1 and site 2) for Visits 3, 4 and/or 5 compared to baseline for all subjects. The AUC was lower during the study compared to baseline which implicates that the pH\*time was higher during the study.

Summary statistics of dental plaque acidogenicity measurements by timepoint are presented in Table 14.3-5 and mean values are graphically presented in Figure 11.2-2. Summary statistics of minimum values, minimum and maximum changes from baseline are summarized in Table 14.3-7. Summary statistics of AUC for dental plaque acidogenicity are found in Table 14.3-10. Individual subject data for site 1, site 2 and the mean of sites 1 and 2 are presented in Appendix 16.2.6.

Figure 11.2-2 Dental plaque acidogenicity (pH) vs time, mean (PPS)



SM17\_02\_B dental plaque acidogenicity (pH) figures, mean. SAS program: ph\_graphs\_mean.sas.  
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### 11.3 Evaluation of secondary endpoints

#### 11.3.1 Plaque amount (Part 2)

There were only a few occasional statistically significant changes from baseline in plaque amount at Visits 3, 4 and 5 for the females, males and all subjects, see Table 14.3-11. For example, the total index (for the males and all subjects) was lower during the study compared to baseline and the total index for the site mesio-buccal at Visit 3 and Visit 5 was higher compared to baseline. Individual subject data for each tooth and the mean are presented in Appendix 16.2.6.

#### 11.3.2 Oral microflora (Part 2)

There were statistically significant changes from baseline for S Mutans (both actual and log values) at Visits 4 and 5 for the female subgroup and in total, see Table 14.3-12. The number at Visit 4 and Visit 5 was higher compared to baseline. There were no statistically significant changes from baseline for Lactobacilli during the study. Individual subject data are presented in Appendix 16.2.6.

#### 11.3.3 Oral mucosal lesions (Part 2)

There was no indication of changes in the incidence of gingival retraction during the study, it varied between 54%-57% during the study. A summary of gingival retraction and lesions in the mucosa is presented in Table 14.3-13.

The number of subjects with lesions and the degree of lesions changed during the study. The number of subjects with no lesions increased from 9% at screening to 30% at Visit 5 and the

number of subjects with lesions of degree 3 and 4 decreased (the number of subjects with lesions of degree 1 and 2 increased). The number of subjects with lesions in the mucosa at placement of the pouch decreased from 90% to 70%.

There was a statistically significant change in the degree of lesions at the placement of the pouch between Visits 3, 4 and 5 compared to baseline for the subgroups and in total, see Table 14.3-14. The degree of lesions was lower at Visits 3, 4 and 5 compared to baseline. There was a statistically significant correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used for all visits except the female subjects at Visit 4, see Table 14.1-11, Table 14.1-12, Table 14.3-15 and Figure 14.3-1 to Figure 14.3-9.

Individual subject data are presented in Appendix 16.2.6.

#### 11.3.4 Adverse events

Refer to Section 12.

### 11.4 Statistical/analytical issues

Not applicable.

### 11.5 Summary of efficacy results

After single dose administration of IP in Part 1, the minimum change from baseline in dental plaque acidogenicity was significantly smaller for ZYN<sup>®</sup> Smooth compared to xylitol and maximum change from baseline was significantly larger for ZYN<sup>®</sup> Smooth and ZYN<sup>®</sup> Peppermint compared to xylitol. The minimum value in dental plaque acidogenicity was significantly higher, the minimum change from baseline was significantly smaller, the maximum change was significantly larger and AUC for dental plaque acidogenicity (pH 5.5 and pH 6.2) was significantly larger for the ZYN<sup>®</sup> products and xylitol compared to sucrose. There were no statistical differences between the ZYN<sup>®</sup> products.

After ad libitum administration of nicotine-containing pouches in Part 2, the minimum value in dental plaque acidogenicity was significantly higher and the absolute minimum change from baseline were significantly smaller during the study compared to baseline for all subjects. The absolute change in AUC (and AUC where values over baseline were set to zero) for dental plaque acidogenicity (pH 6.2 and pH 5.5) during the study was significantly smaller compared to baseline for all subjects which implicates that the pH\*time was larger during study.

For the majority of assessments of plaque amount there were no statistically significant changes for the subjects during Part 2.

The number of S Mutans at Visit 4 and Visit 5 was significantly higher compared to baseline. There were no statistically significant changes from baseline for Lactobacilli during Part 2.

The number of subjects with lesions and the degree of lesions changed during Part 2. The number of subjects with no lesions increased from 9% at screening to 30% at Visit 5. The degree of lesions in the mucosa at placement of the pouch was significantly lower at Visits 3, 4 and 5 compared to baseline and the number of subjects with lesions decreased from 90% to 70%. There was a statistically significant correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used for all visits except for the female subjects at Visit 4.

There was no indication of changes in the incidence of gingival retraction during the study, it varied between 54%-57% during the study.

## 12 ADVERSE EVENTS

### 12.1 Brief summary of adverse events

A total of 2 AEs was reported by 1 subject during Part 1. There were no SAEs or withdrawals due to AEs. The AEs were of mild intensity and assessed by the investigator as unrelated to treatment with IP.

A total of 10 AEs was reported by 9 subjects during Part 2. There were no SAEs or withdrawals due to AEs. The majority of AEs were of mild intensity and the rest were of moderate intensity. Half of the AEs were assessed by the investigator as unrelated to treatment with IP.

Overviews of AEs are presented in Table 12.1-1 (Part 1) and Table 12.1-2 (Part 2).

*Table 12.1-1 Overview of adverse events (FAS) (Part 1)*

	10% sucrose (pos control) N=19		10% xylitol (neg control) N=18		ZYN® Peppermint 3 mg N=19		ZYN® Smooth 3 mg N=18		WASH-OUT N=20		Total N=20	
	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m
<b>Any AE</b>	0	0	0	0	0	0	0	0	1(5%)	2	1(5%)	2
<b>Any SAE</b>	0	0	0	0	0	0	0	0	0	0	0	0
<b>Any AE leading to withdrawal</b>	0	0	0	0	0	0	0	0	0	0	0	0
<b>Any AE leading to death</b>	0	0	0	0	0	0	0	0	0	0	0	0
<b>Causality</b>												
Not Related	0	0	0	0	0	0	0	0	1(5%)	2	1(5%)	2
<b>Severity</b>												
Mild	0	0	0	0	0	0	0	0	1(5%)	2	1(5%)	2

n, number of subjects; m, number of events

Percentages are based on the number of subjects in the treatment period included in the full analysis set.

Wash-out defined as the period between treatments starting 24 hours after dosing.

Adverse events that occurred during follow-up are omitted from summary.

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*Table 12.1-2 Overview of adverse events (FAS) (Part 2)*

	Female N=20		Male N=39		Total N=59	
	n(%)	m	n(%)	m	n(%)	m
<b>Any AE</b>	4(20%)	5	5(13%)	5	9(15%)	10
<b>Any SAE</b>	0	0	0	0	0	0
<b>Any AE leading to withdrawal</b>	0	0	0	0	0	0
<b>Any AE leading to death</b>	0	0	0	0	0	0
<b>Causality</b>						
Not Related	2(10%)	2	3(8%)	3	5(8%)	5
Possible	1(5%)	2	1(3%)	1	2(3%)	3
Probable	1(5%)	1	1(3%)	1	2(3%)	2

	Female N=20		Male N=39		Total N=59	
	n(%)	m	n(%)	m	n(%)	m
<b>Severity</b>						
Mild	3(15%)	4	3(8%)	3	6(10%)	7
Moderate	1(5%)	1	2(5%)	2	3(5%)	3

n, number of subjects; m, number of events

Percentages are based on the number of subjects in the treatment period included in the full analysis set.

Adverse events that occurred during follow-up are omitted from summary.

SM17\_02\_B\_14\_03\_01\_01.rtf Overview of adverse events, FAS, SAS program: ae\_summary\_tables.sas.

Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:53:18

## 12.2 Display of adverse events

The 2 AEs reported in Part 1 were within the Infections and infestations SOC; 1 subject reported mild nasopharyngitis (2 events) during the wash-out period (the period between treatment starting 24 h after administration), the event was assessed by the investigator as not related to IP by the investigator.

The AEs reported in Part 2 (10 events) were within the Gastrointestinal disorders SOC (2 subjects reported nausea and dry mouth, gingival blister, lip pain were reported by 1 subject each), Infections and infestations SOC (diarrhea infectious, gastroenteritis viral, influenza and nasopharyngitis were reported by 1 subject each) and Nervous system disorder (dizziness was reported by 1 subject). The events assessed by the investigator as related to IP were nausea (2 events of mild intensity), dry mouth (mild), gingival blisters (moderate) and dizziness (mild).

The number and percentage of subjects on Part 1 who had at least 1 AE and the number of events are presented by SOC and PT in Table 14.4-1 and Table 14.4-3 (including severity and by relation to study product). The corresponding for Part 2 are presented in Table 14.4-2 and Table 14.4-4, respectively.

## 12.3 Analysis of adverse events

Overall, the number of subjects reporting AEs and the number of AEs were low. All AEs were of mild or moderate intensity. There were no AEs assessed by the investigator as related to IP in Part 1. Five (5) AEs were assessed as related to IP in Part 2 (nausea [2 events], dry mouth, gingival blisters and dizziness). One female subject reported nausea and dizziness. All other AEs reported during the study was assessed as not related to IP by the investigator. All AEs, except 2 events assessed by the investigator as unrelated to IP (cold in Part 1 and lip pain in Part 2), were resolved at study end.

## 12.4 Listing of adverse events by subject

Adverse events are listed by subject in Appendix 16.2.7.

## 12.5 Deaths, other serious adverse events and other significant adverse events

There were no deaths, other SAEs or other significant AEs during the study.



## 12.6 Summary of safety results

Administration of single doses in Part 1 and ad libitum administration in Part 2 of nicotine-containing pouches was safe and well tolerated by the healthy subjects. There were no AEs assessed by the investigator as related to IP in Part 1 and 5 in Part 2. There were no SAEs or discontinuations due to AEs during the study.

## 13 DISCUSSION AND OVERALL CONCLUSIONS

### 13.1 DISCUSSION

The main aim of the present study was to assess the safety and tolerability of the non-tobacco-based nicotine pouch (ZYN<sup>®</sup>), particularly with regard to its potential to adversely affect biofilm acidogenicity. A secondary aim was to investigate to which extent ZYN<sup>®</sup> has the potential to produce mucosal lesions at the site of application in the oral cavity similar to those occasionally observed among regular snus users and whether pre-existing snus lesions among the included subjects may improve or resolve during a 6-week observation period during which the participants substitute their regular snus with ZYN<sup>®</sup> products.

Part 1 of the study was an open, randomized, 4-way crossover, single administration. Subjects were randomized to 1 of 4 treatment sequences using a flavored and an unflavored brand of the nicotine pouch, 10% sucrose (positive control) and 10% xylitol (negative control) with 1-week washout. Part 2 of the study was an open, observational, safety and tolerability study during 6 weeks. The subjects used the non-tobacco-based nicotine pouch (ZYN<sup>®</sup>) ad libitum.

In Part 1, the results of AUC for dental plaque acidogenicity did not show any statistically significant differences between the ZYN<sup>®</sup> products and xylitol (negative control). In fact, the minimum and maximum changes from baseline were significantly more favourable values after administration of ZYN<sup>®</sup> products compared to xylitol.

After single dose administration there was no observed pH <6.2 for the ZYN<sup>®</sup> products and therefore there are no data for AUC (where values over baseline were set to zero) pH 5.5 or pH 6.2.

The results after ad libitum administration of nicotine-containing pouches in Part 2 showed a higher AUC (and AUC where values over baseline were set to zero) for dental plaque acidogenicity (pH 6.2 and pH 5.5) for all subjects during the study however, there were differences between the female and male subgroups.

The results showed an improvement in oral mucosal lesions during the study. The degree of lesions in the mucosa at placement of the pouch was significantly lower and a statistically significant correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used was shown. In addition, the number of subjects with no lesions increased and the number of subjects with lesions decreased during the study. There was no statistically significant change in the number Lactobacilli, however the number of S Mutans was significantly higher after 4 and 6 weeks compared to baseline. The differences were seen for the female subgroup and for all subjects but not for the male subjects. However, it is worth noting, that at baseline the observed number of S Mutans were considerably lower for the female subgroup compared to the male subgroup. It cannot be excluded that other factors, such as variations in dietary and oral hygiene habits, may have contributed to the changes in oral microorganisms observed throughout the study.

Adverse events were recorded at all visits with particular focus on common side effects with all types of nicotine exposure (local irritation at the site of the oral mucosa where the pouch is placed, or in the throat, and hiccups and heartburn), however the number of AEs reported was low and the only related events of this type reported were gingival blister and dry mouth.

## **13.2 OVERALL CONCLUSIONS**

The study showed that non-tobacco-based nicotine pouches (ZYN<sup>®</sup> products) do not adversely affect dental plaque acidogenicity after single dose administration in healthy snus users.

After ad libitum administration of nicotine-containing pouches for 6 weeks, no adverse effect of dental plaque acidogenicity was observed.

The study showed that increased usage of non-tobacco-based nicotine pouch (ZYN<sup>®</sup> products) in favour over snus improved oral mucosal lesions in healthy snus users after administration ad libitum for 6 weeks.

Administration of single doses in Part 1 and ad libitum administration in Part 2 of the ZYN<sup>®</sup> products were safe and well tolerated by the healthy subjects. The number of subjects reporting AEs and the number of AEs were low.

## 14 TABLES, FIGURES AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT

### 14.1 Study subjects

*Table 14.1-1 Subject disposition (Part 1)*

	SCREEN FAILURE	Treatment Sequence A	Treatment Sequence B	Treatment Sequence C	Treatment Sequence D	Total
Screened subjects	3	5	5	5	5	23
Subjects that entered the study	0	5	5	5	5	20
Withdrawn subjects	0	0	0	1	1	2
Completed subjects	0	5	5	4	4	18
Included in FAS	0	5	5	5	5	20
Included in PPS	0	5	5	4	4	18
Subjects at Screening	3	5	5	5	5	23
Subjects at Visit 2	0	5	5	5	5	20
Subjects at Visit 3	0	5	5	4	4	18
Subjects at Visit 4	0	5	5	4	4	18
Subjects at Visit 5	0	5	5	4	4	18
Subjects at Follow-up	0	5	5	4	4	18
Subjects at End Of Study	0	5	5	5	5	20

SM17\_02\_A\_14\_01\_01\_02.rtf Disposition, SAS program: disposition.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:44:24

*Table 14.1-2 Subject disposition (Part 2)*

	Female	Male	Total
Screened subjects	21	39	60
Subjects that entered the study	20	39	59
Withdrawn subjects	0	2	2
Completed subjects	20	37	57
Included in FAS	20	39	59
Included in PPS*	20	36	56
Subjects at Screening	21	39	60
Subjects at Visit 2	20	38	58
Subjects at Visit 3	20	38	58
Subjects at Visit 4	20	37	57
Subjects at Visit 5	20	37	57
Subjects at Follow-up	20	37	57
Subjects at End of Study	20	39	59

\*: Subject 218 completed the study but was excluded from PPS due to wrongly included (subject on hypertension medication).

SM17\_02\_B\_14\_01\_01\_02.rtf Disposition, SAS program: disposition.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:58:03

Table 14.1-3 Pregnancy test results (FAS) (Part 1)

Assessment	Visit Name	Result	Treatment Sequence A	Treatment Sequence B	Treatment Sequence C
Pregnancy test	Screening	Negative	2(100%)/2	1(100%)/1	3(100%)/3

Data based on Full Analysis Set population. Results are presented as n(%) / N, where N is the total number of observations at that specific timepoint.  
SM17\_02\_A Pregnancy test results, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:43:54

Table 14.1-4 Pregnancy test results (FAS) (Part 2)

Assessment	Visit Name	Result	Female	Total
Pregnancy test	Screening	Negative	20(100%)/20	20(100%)/20

Data based on Full Analysis Set population. Results are presented as n(%) / N, where N is the total number of observations at that specific timepoint.  
SM17\_02\_B Pregnancy test results, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:54:59

Table 14.1-5 Medical history events by SOC and PT (FAS) (Part 1)

System organ class Preferred term	Treatment Sequence A N=5		Treatment Sequence B N=5		Treatment Sequence C N=5		Treatment Sequence D N=5		Total N=20	
	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m
<b>Total</b>	<b>4(80%)</b>	<b>6</b>	<b>4(80%)</b>	<b>7</b>	<b>4(80%)</b>	<b>8</b>	<b>3(60%)</b>	<b>3</b>	<b>15(75%)</b>	<b>24</b>
<b>Psychiatric disorders</b>	<b>2(40%)</b>	<b>4</b>	<b>2(40%)</b>	<b>2</b>	<b>2(40%)</b>	<b>3</b>	<b>0</b>	<b>0</b>	<b>6(30%)</b>	<b>9</b>
Anxiety	0	0	0	0	1(20%)	1	0	0	1(5%)	1
Bipolar disorder	1(20%)	1	0	0	0	0	0	0	1(5%)	1
Depression	1(20%)	1	2(40%)	2	2(40%)	2	0	0	5(25%)	5
Insomnia	2(40%)	2	0	0	0	0	0	0	2(10%)	2
<b>Immune system disorders</b>	<b>0</b>	<b>0</b>	<b>1(20%)</b>	<b>1</b>	<b>2(40%)</b>	<b>3</b>	<b>1(20%)</b>	<b>1</b>	<b>4(20%)</b>	<b>5</b>
Allergy to animal	0	0	0	0	0	0	1(20%)	1	1(5%)	1
Food allergy	0	0	0	0	1(20%)	1	0	0	1(5%)	1
Seasonal allergy	0	0	1(20%)	1	2(40%)	2	0	0	3(15%)	3
<b>Surgical and medical procedures</b>	<b>2(40%)</b>	<b>2</b>	<b>1(20%)</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>3(15%)</b>	<b>3</b>
Appendicectomy	1(20%)	1	0	0	0	0	0	0	1(5%)	1
Thyroidectomy	1(20%)	1	0	0	0	0	0	0	1(5%)	1
Wisdom teeth removal	0	0	1(20%)	1	0	0	0	0	1(5%)	1
<b>Metabolism and nutrition disorders</b>	<b>0</b>	<b>0</b>	<b>2(40%)</b>	<b>3</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>2(10%)</b>	<b>3</b>
Diabetes mellitus	0	0	1(20%)	1	0	0	0	0	1(5%)	1
Gout	0	0	1(20%)	1	0	0	0	0	1(5%)	1
Lactose intolerance	0	0	1(20%)	1	0	0	0	0	1(5%)	1
<b>Gastrointestinal disorders</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>1(20%)</b>	<b>1</b>	<b>1(5%)</b>	<b>1</b>
Aphthous ulcer	0	0	0	0	0	0	1(20%)	1	1(5%)	1
<b>Infections and infestations</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>1(20%)</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>1(5%)</b>	<b>1</b>
Rhinitis	0	0	0	0	1(20%)	1	0	0	1(5%)	1
<b>Investigations</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>1(20%)</b>	<b>1</b>	<b>1(5%)</b>	<b>1</b>
Thyroid hormones decreased	0	0	0	0	0	0	1(20%)	1	1(5%)	1

System organ class Preferred term	Treatment Sequence A N=5		Treatment Sequence B N=5		Treatment Sequence C N=5		Treatment Sequence D N=5		Total N=20	
	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m
<b>Respiratory, thoracic and mediastinal disorders</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>1(20%)</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>1(5%)</b>	<b>1</b>
Pneumothorax	0	0	0	0	1(20%)	1	0	0	1(5%)	1

n, number of subjects; m, number of events

Percentages are based on the number of subjects in the full analysis set

SM17\_02\_A\_14\_01\_04.rtf Medical history events by system organ class and preferred term, SAS program: MH\_summary\_by\_soc\_and\_pt.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:45:39

*Table 14.1-6 Medical history events by SOC and PT (FAS) (Part 2)*

System organ class Preferred term	Female N=20		Male N=39		Total N=59	
	n(%)	m	n(%)	m	n(%)	m
<b>Total</b>	<b>10(50%)</b>	<b>12</b>	<b>9(23%)</b>	<b>11</b>	<b>19(32%)</b>	<b>23</b>
<b>Psychiatric disorders</b>	<b>6(30%)</b>	<b>8</b>	<b>3(8%)</b>	<b>3</b>	<b>9(15%)</b>	<b>11</b>
Anxiety	1(5%)	1	0	0	1(2%)	1
Depression	4(20%)	4	2(5%)	2	6(10%)	6
Insomnia	3(15%)	3	1(3%)	1	4(7%)	4
<b>Immune system disorders</b>	<b>0</b>	<b>0</b>	<b>4(10%)</b>	<b>4</b>	<b>4(7%)</b>	<b>4</b>
Hypersensitivity	0	0	2(5%)	2	2(3%)	2
Seasonal allergy	0	0	2(5%)	2	2(3%)	2
<b>Metabolism and nutrition disorders</b>	<b>2(10%)</b>	<b>2</b>	<b>1(3%)</b>	<b>1</b>	<b>3(5%)</b>	<b>3</b>
Type 1 diabetes mellitus	2(10%)	2	1(3%)	1	3(5%)	3
<b>General disorders and administration site conditions</b>	<b>0</b>	<b>0</b>	<b>1(3%)</b>	<b>1</b>	<b>1(2%)</b>	<b>1</b>
Chronic fatigue syndrome	0	0	1(3%)	1	1(2%)	1
<b>Nervous system disorders</b>	<b>1(5%)</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>1(2%)</b>	<b>1</b>
Narcolepsy	1(5%)	1	0	0	1(2%)	1
<b>Reproductive system and breast disorders</b>	<b>1(5%)</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>1(2%)</b>	<b>1</b>
Premenstrual syndrome	1(5%)	1	0	0	1(2%)	1
<b>Respiratory, thoracic and mediastinal disorders</b>	<b>0</b>	<b>0</b>	<b>1(3%)</b>	<b>1</b>	<b>1(2%)</b>	<b>1</b>
Asthma	0	0	1(3%)	1	1(2%)	1
<b>Vascular disorders</b>	<b>0</b>	<b>0</b>	<b>1(3%)</b>	<b>1</b>	<b>1(2%)</b>	<b>1</b>
Hypertension	0	0	1(3%)	1	1(2%)	1

n, number of subjects; m, number of events

Percentages are based on the number of subjects in the full analysis set

SM17\_02\_B\_14\_01\_04.rtf Medical history events by system organ class and preferred term, SAS program: MH\_summary\_by\_soc\_and\_pt.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:57:15

Table 14.1-7 Physical examination tongue and mucosa (FAS) (Part 1)

Assessment	Visit Name	Result	Treatment Sequence A	Treatment Sequence B	Treatment Sequence C	Treatment Sequence D
Oral Mucosa	Screening	ABNORMAL NCS	4(80%)/5	4(80%)/5	4(80%)/5	5(100%)/5
		NORMAL	1(20%)/5	1(20%)/5	1(20%)/5	0
Tongue	Screening	ABNORMAL NCS	0	2(40%)/5	0	0
		NORMAL	5(100%)/5	3(60%)/5	5(100%)/5	5(100%)/5

Data based on Full Analysis Set population. Results are presented as n(%) / N, where N is the total number of observations at that specific timepoint.

SM17\_02\_A Physical examination tongue and mucosa, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:43:54

Table 14.1-8 Physical examination tongue and mucosa (FAS) (Part 2)

Assessment	Visit Name	Result	Female	Male	Total
Oral Mucosa	Screening	ABNORMAL CS, SEVERE GINGIVAL OVERGROWTH + BLEEDING BUCCALLY UPPER JAW. EXTREMELY BAD ORAL HYGIENE.	0	1(2.6%)/39	1(1.7%)/59
		ABNORMAL NCS	2(10%)/20	5(13%)/39	7(12%)/59
		NORMAL	18(90%)/20	33(85%)/39	51(86%)/59
Tongue	Screening	ABNORMAL NCS	0	3(7.7%)/39	3(5.1%)/59
		NORMAL	20(100%)/20	36(92%)/39	56(95%)/59

Data based on Full Analysis Set population. Results are presented as n(%) / N, where N is the total number of observations at that specific timepoint.

SM17\_02\_B Physical examination tongue and mucosa, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:54:59

Table 14.1-9 Physical examination tooth status (FAS) (Part 1)

Assessment	Result Category	Visit Name	Treatment Sequence A	Treatment Sequence B	Treatment Sequence C	Treatment Sequence D
Tooth Status (DMFT)	Measured value	Screening	N	5	5	5
			Mean (SD)	5.6 (4.9)	10.8 (7.8)	3.4 (2.9)
			Median (Min, Max)	4.0 (1, 14)	10.0 (1, 20)	4.0 (0, 7)

Data based on Full Analysis Set population.

SM17\_02\_A Physical examination tooth status, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson

Table 14.1-10 Physical examination tooth status (FAS) (Part 2)

Assessment	Result Category	Visit Name	Female	Male	Total
Tooth Status (DMFT)	Measured value	Screening	N	20	39
			Mean (SD)	1.9 (2.2)	4.6 (5.2)
			Median (Min, Max)	1.0 (0, 6)	3.0 (0, 20)

Data based on Full Analysis Set population.

SM17\_02\_B Physical examination tooth status, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se  
2018-10-24T13:54:59

*Table 14.1-11 Ratio ZYN<sup>®</sup> products/total nicotin products used (FAS) (Part 2)*

Gender	Study period	N	Mean (SD)	Median (Min, Max)
Female	Visit 2 - Visit 3	20	0.689 (0.240)	0.723 (0.24, 0.98)
	Visit 3 - Visit 4	20	0.825 (0.176)	0.877 (0.40, 1.00)
	Visit 4 - Visit 5	20	0.877 (0.149)	0.935 (0.52, 1.00)
Male	Visit 2 - Visit 3	37	0.732 (0.209)	0.753 (0.21, 1.00)
	Visit 3 - Visit 4	37	0.800 (0.180)	0.836 (0.36, 1.00)
	Visit 4 - Visit 5	37	0.820 (0.171)	0.851 (0.32, 1.00)
Total	Visit 2 - Visit 3	57	0.717 (0.219)	0.745 (0.21, 1.00)
	Visit 3 - Visit 4	57	0.809 (0.178)	0.860 (0.36, 1.00)
	Visit 4 - Visit 5	57	0.840 (0.165)	0.895 (0.32, 1.00)

N is defined as all subjects with self-reported usage in the study period.

Data based on full analysis set population.

SM17\_02\_B Ratio ZYN<sup>®</sup> Products/Total Nicotin Products Used, SAS program:

exposure\_zyn\_frequency.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:56:54

*Table 14.1-12 IP usage per study day (FAS) (Part 2)*

Study period	Product	N	Mean	SD	Min	Median	Max
	Type						
Visit 2 - Visit 3	Snus	57	4.09	4.05	0.00	2.87	19.38
	ZYN <sup>®</sup>	57	10.94	7.16	2.50	8.50	33.82
Visit 3 - Visit 4	Snus	57	2.52	2.45	0.00	1.86	8.40
	ZYN <sup>®</sup>	57	11.93	7.50	2.79	9.58	37.21
Visit 4 - Visit 5	Snus	57	2.17	2.48	0.00	1.77	13.13
	ZYN <sup>®</sup>	57	12.53	7.78	2.91	10.53	37.81

N is defined as all subjects with self-reported usage in the study period.

Data based on full analysis set population.

SM17\_02\_B IP Usage per Study Day, SAS program: IP\_per\_study\_day.sas. Run by: Jerker Linne, jerker.linne@ctc-ab.se 2019-03-15T13:37:22

## 14.2 Demographic data and other baseline characteristics

Reported in-text, see Section 10.4.

## 14.3 Primary and secondary endpoints

*Table 14.3-1 Exposure to study product (Part 1)*

Treatment	Number of subjects
ZYN <sup>®</sup> Smooth 3 mg	18
ZYN <sup>®</sup> Peppermint 3 mg	19
10% sucrose (pos control)	19
10% xylitol (neg control)	18

SM17\_02\_A\_14\_01\_02\_02 Exposure to study product, SAS program: exposure.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:45:16



*Table 14.3-2 Exposure to study product (FAS) (Part 2)*

Gender	Study period	ZYN® Cinnamon 3 mg	ZYN® Cinnamon 6 mg	ZYN® Peppermint 3 mg	ZYN® Peppermint 6 mg	ZYN® Smooth 3 mg	ZYN® Smooth 6 mg	Snus
Female	Visit 2 - Visit 3 (N=20)	4 (20.0%)	4 (20.0%)	6 (30.0%)	7 (35.0%)	4 (20.0%)	7 (35.0%)	20 (100.0%)
	Visit 3 - Visit 4 (N=20)	2 (10.0%)	2 (10.0%)	4 (20.0%)	7 (35.0%)	6 (30.0%)	7 (35.0%)	17 (85.0%)
	Visit 4 - Visit 5 (N=20)	3 (15.0%)	1 (5.0%)	4 (20.0%)	8 (40.0%)	5 (25.0%)	7 (35.0%)	15 (75.0%)
Male	Visit 2 - Visit 3 (N=37)	7 (18.9%)	5 (13.5%)	13 (35.1%)	21 (56.8%)	10 (27.0%)	9 (24.3%)	34 (91.9%)
	Visit 3 - Visit 4 (N=37)	5 (13.5%)	5 (13.5%)	8 (21.6%)	22 (59.5%)	7 (18.9%)	9 (24.3%)	31 (83.8%)
	Visit 4 - Visit 5 (N=37)	5 (13.5%)	2 (5.4%)	7 (18.9%)	21 (56.8%)	5 (13.5%)	7 (18.9%)	33 (89.2%)
Total	Visit 2 - Visit 3 (N=57)	11 (19.3%)	9 (15.8%)	19 (33.3%)	28 (49.1%)	14 (24.6%)	16 (28.1%)	54 (94.7%)
	Visit 3 - Visit 4 (N=57)	7 (12.3%)	7 (12.3%)	12 (21.1%)	29 (50.9%)	13 (22.8%)	16 (28.1%)	48 (84.2%)
	Visit 4 - Visit 5 (N=57)	8 (14.0%)	3 (5.3%)	11 (19.3%)	29 (50.9%)	10 (17.5%)	14 (24.6%)	48 (84.2%)

Subjects are allowed to use multiple products between visits. N is defined as all subjects with self-reported usage in the study period.

Data based on full analysis set population.

SM17\_02\_B Exposure to Study Product, SAS program: exposure\_zyn\_frequency.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:56:54

### 14.3.1 Primary endpoint

Table 14.3-3 Dental plaque acidogenicity between group comparison (PPS) (Part 1)

Subcategory of Measurement	Test Name	ZYN® Smooth 3 mg - ZYN® Peppermint 3 mg	ZYN® Smooth 3 mg - 10% sucrose (pos control)	ZYN® Smooth 3 mg - 10% xylitol (neg control)	ZYN® Peppermint 3 mg - 10% sucrose (pos control)	ZYN® Peppermint 3 mg - 10% xylitol (neg control)	10% sucrose (pos control) - 10% xylitol (neg control)
Mean	AUC Acidogenicity pH 5.5 baseline (min*pH)	0.9118	0.0003	0.2001	0.0001	0.1892	0.0011
Mean	AUC Acidogenicity pH 5.5 baseline (no negative AUC) (min*pH)	1.0000	0.0192	1.0000	0.0192	1.0000	0.0192
Mean	AUC Acidogenicity pH 6.2 baseline (min*pH)	0.9118	0.0003	0.2001	0.0001	0.1892	0.0011
Mean	AUC Acidogenicity pH 6.2 baseline (no negative AUC) (min*pH)	1.0000	<.0001	1.0000	<.0001	1.0000	<.0001
Mean	Max change from baseline dental plaque acidogenicity (pH)	0.7271	<.0001	0.0419	<.0001	0.0109	0.0002
Mean	Min change from baseline dental plaque acidogenicity (pH)	0.4933	<.0001	0.0388	<.0001	0.1042	<.0001
Mean	Min dental plaque acidogenicity (pH)	0.7871	<.0001	0.3658	<.0001	0.4753	<.0001
Site 1	AUC Acidogenicity pH 5.5 baseline (min*pH)	1.0000	0.0003	0.2171	0.0002	0.2232	0.0004
Site 1	AUC Acidogenicity pH 5.5 baseline (no negative AUC) (min*pH)	1.0000	0.0091	1.0000	0.0091	1.0000	0.0091
Site 1	AUC Acidogenicity pH 6.2 baseline (min*pH)	1.0000	0.0003	0.2171	0.0002	0.2232	0.0004
Site 1	AUC Acidogenicity pH 6.2 baseline (no negative AUC) (min*pH)	1.0000	<.0001	1.0000	<.0001	1.0000	<.0001
Site 1	Max change from baseline dental plaque acidogenicity (pH)	0.4549	<.0001	0.0669	<.0001	0.0091	0.0001
Site 1	Min change from baseline dental plaque acidogenicity (pH)	0.8972	<.0001	0.1609	<.0001	0.0524	<.0001
Site 1	Min dental plaque acidogenicity (pH)	0.7260	<.0001	0.6910	<.0001	0.3897	<.0001
Site 2	AUC Acidogenicity pH 5.5 baseline (min*pH)	0.8993	0.0003	0.2114	0.0002	0.1592	0.0018
Site 2	AUC Acidogenicity pH 5.5 baseline (no negative AUC) (min*pH)	1.0000	0.0091	1.0000	0.0091	1.0000	0.0091
Site 2	AUC Acidogenicity pH 6.2 baseline (min*pH)	0.9370	0.0003	0.2114	0.0002	0.1592	0.0018
Site 2	AUC Acidogenicity pH 6.2 baseline (no negative AUC) (min*pH)	1.0000	<.0001	1.0000	<.0001	1.0000	<.0001
Site 2	Max change from baseline dental plaque acidogenicity (pH)	0.7983	<.0001	0.0477	<.0001	0.0086	0.0007
Site 2	Min change from baseline dental plaque acidogenicity (pH)	0.1711	<.0001	0.0170	<.0001	0.2163	<.0001
Site 2	Min dental plaque acidogenicity (pH)	0.8112	<.0001	0.3716	<.0001	0.4071	<.0001

p-values are based on Normal Approximated Two-Sided Wilcoxon Two-Sample Tests.

SM17\_02\_A\_14\_02\_01\_05.rtf Dental Plaque Acidogenicity Between Group Comparisons, PPS, SAS program: dppl\_between\_groups.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:44:44

Table 14.3-4 Dental plaque acidogenicity measurements by timepoint (PPS) (Part 1)

Subcategory of Measurement	Assessment (unit)	Result Category	Planned Timepoint		ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)
Mean	Dental plaque acidogenicity (pH)	Measured value	Pre-Dose	N	18	18	18	18
				Mean (SD)	6.919 (0.328)	6.944 (0.322)	7.089 (0.489)	6.950 (0.291)
				Median (Min, Max)	6.925 (6.35, 7.50)	6.950 (6.35, 7.50)	6.975 (6.40, 8.60)	6.925 (6.40, 7.40)
			00:02	N	18	18	18	18
				Mean (SD)	7.039 (0.305)	7.069 (0.339)	6.392 (0.804)	6.961 (0.309)
				Median (Min, Max)	6.975 (6.50, 7.65)	7.075 (6.50, 7.65)	6.325 (5.35, 9.10)	6.975 (6.35, 7.70)
			00:05	N	18	18	18	18
				Mean (SD)	6.992 (0.334)	7.111 (0.333)	6.017 (0.770)	7.039 (0.320)
				Median (Min, Max)	6.950 (6.35, 7.60)	7.125 (6.60, 7.85)	5.800 (4.90, 8.25)	7.000 (6.55, 7.75)
			00:10	N	18	18	18	18
				Mean (SD)	7.075 (0.347)	7.092 (0.439)	5.981 (0.997)	6.983 (0.296)
				Median (Min, Max)	7.000 (6.45, 7.70)	7.025 (6.35, 7.95)	5.900 (4.75, 9.10)	6.900 (6.55, 7.45)
			00:20	N	18	18	18	18
				Mean (SD)	7.097 (0.383)	7.033 (0.403)	6.139 (0.623)	6.967 (0.257)
				Median (Min, Max)	7.125 (6.45, 7.85)	7.000 (6.35, 7.85)	6.000 (4.90, 7.15)	6.950 (6.50, 7.35)
			00:30	N	18	18	18	18
				Mean (SD)	7.125 (0.397)	7.019 (0.406)	6.450 (0.460)	6.978 (0.273)
				Median (Min, Max)	7.150 (6.40, 7.75)	6.975 (6.25, 7.85)	6.475 (5.80, 7.05)	6.975 (6.45, 7.40)
			00:40	N	18	18	18	18
				Mean (SD)	7.144 (0.427)	7.048 (0.336)	6.608 (0.543)	6.931 (0.278)
				Median (Min, Max)	7.125 (6.40, 8.00)	7.075 (6.35, 7.55)	6.500 (5.80, 7.75)	6.975 (6.40, 7.45)
			00:50	N	18	18	18	18
				Mean (SD)	7.125 (0.396)	7.133 (0.383)	6.667 (0.483)	6.892 (0.313)
				Median (Min, Max)	7.075 (6.45, 7.95)	7.200 (6.30, 7.70)	6.625 (6.05, 7.45)	6.925 (6.40, 7.30)

Subcategory of Measurement	Assessment (unit)	Result Category	Planned Timepoint		ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)
Absolute change from pre-dose baseline			01:00	N	18	18	18	18
				Mean (SD)	7.114 (0.476)	7.194 (0.349)	6.728 (0.427)	6.947 (0.299)
				Median (Min, Max)	7.000 (6.30, 7.95)	7.200 (6.25, 7.70)	6.725 (6.05, 7.40)	6.850 (6.55, 7.50)
			Pre-Dose	N	18	18	18	18
				Mean (SD)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)
				Median (Min, Max)	0.000 (0.00, 0.00)	0.000 (0.00, 0.00)	0.000 (0.00, 0.00)	0.000 (0.00, 0.00)
			00:02	N	18	18	18	18
				Mean (SD)	0.119 (0.136)	0.125 (0.164)	-0.697 (0.462)	0.011 (0.162)
				Median (Min, Max)	0.075 (-0.10, 0.45)	0.100 (-0.20, 0.50)	-0.725 (-1.45, 0.50)	0.025 (-0.35, 0.30)
			00:05	N	18	18	18	18
				Mean (SD)	0.072 (0.130)	0.167 (0.217)	-1.072 (0.478)	0.089 (0.197)
				Median (Min, Max)	0.100 (-0.10, 0.35)	0.125 (-0.05, 0.90)	-1.075 (-2.05, -0.25)	0.150 (-0.45, 0.40)
			00:10	N	18	18	18	18
				Mean (SD)	0.156 (0.201)	0.147 (0.252)	-1.108 (0.621)	0.033 (0.140)
				Median (Min, Max)	0.175 (-0.25, 0.60)	0.100 (-0.20, 1.00)	-1.175 (-1.90, 0.50)	0.050 (-0.20, 0.30)
			00:20	N	18	18	18	18
				Mean (SD)	0.178 (0.272)	0.089 (0.216)	-0.950 (0.492)	0.017 (0.185)
				Median (Min, Max)	0.150 (-0.20, 0.80)	0.075 (-0.15, 0.65)	-1.050 (-1.80, 0.35)	0.025 (-0.40, 0.30)
			00:30	N	18	18	18	18
				Mean (SD)	0.206 (0.301)	0.075 (0.178)	-0.639 (0.389)	0.028 (0.214)
				Median (Min, Max)	0.125 (-0.20, 0.75)	0.050 (-0.25, 0.35)	-0.625 (-1.55, 0.20)	0.025 (-0.30, 0.55)
			00:40	N	18	18	18	18
				Mean (SD)	0.225 (0.282)	0.103 (0.179)	-0.481 (0.273)	-0.019 (0.182)
				Median (Min, Max)	0.175 (-0.15, 0.75)	0.100 (-0.25, 0.55)	-0.525 (-0.90, 0.00)	-0.025 (-0.30, 0.35)
			00:50	N	18	18	18	18

Subcategory of Measurement	Assessment (unit)	Result Category	Planned Timepoint	ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)	
Relative change from pre-dose baseline (%)			01:00	Mean (SD)	0.206 (0.265)	0.189 (0.281)	-0.422 (0.430)	-0.058 (0.171)
				Median (Min, Max)	0.175 (-0.15, 0.75)	0.150 (-0.25, 0.90)	-0.375 (-1.65, 0.15)	0.000 (-0.50, 0.20)
				N	18	18	18	18
			Pre-Dose	Mean (SD)	0.194 (0.314)	0.250 (0.296)	-0.361 (0.362)	-0.003 (0.171)
				Median (Min, Max)	0.075 (-0.25, 0.85)	0.150 (-0.15, 0.90)	-0.275 (-1.35, 0.15)	0.025 (-0.30, 0.30)
				N	18	18	18	18
			00:02	Mean (SD)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
				Median (Min, Max)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 0)
				N	18	18	18	18
			00:05	Mean (SD)	1.8 (1.9)	1.8 (2.4)	-9.9 (6.4)	0.2 (2.3)
				Median (Min, Max)	1.0 (-1, 6)	1.5 (-3, 7)	-9.5 (-20, 6)	0.5 (-5, 4)
				N	18	18	18	18
			00:10	Mean (SD)	1.0 (1.9)	2.5 (3.2)	-15.3 (6.8)	1.3 (2.8)
				Median (Min, Max)	1.0 (-2, 5)	2.0 (-1, 13)	-15.0 (-27, -4)	2.0 (-6, 6)
				N	18	18	18	18
			00:20	Mean (SD)	2.2 (3.0)	2.0 (3.6)	-16.0 (8.8)	0.5 (1.9)
				Median (Min, Max)	2.5 (-4, 9)	1.0 (-3, 14)	-16.5 (-28, 6)	1.0 (-3, 4)
				N	18	18	18	18
			00:30	Mean (SD)	2.6 (3.9)	1.3 (3.0)	-13.4 (7.0)	0.3 (2.6)
				Median (Min, Max)	2.0 (-3, 11)	1.0 (-2, 9)	-15.0 (-27, 5)	0.5 (-5, 4)
				N	18	18	18	18
			00:40	Mean (SD)	2.9 (4.4)	1.1 (2.6)	-8.8 (5.1)	0.6 (3.0)
				Median (Min, Max)	1.5 (-3, 11)	1.0 (-4, 5)	-8.0 (-18, 3)	0.5 (-4, 8)
				N	18	18	18	18
				Mean (SD)	3.3 (4.1)	1.5 (2.7)	-6.7 (3.8)	-0.1 (2.5)

Subcategory of Measurement	Assessment (unit)	Result Category	Planned Timepoint		ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)
			00:50	Median (Min, Max)	2.5 (-2, 11)	1.0 (-4, 8)	-7.5 (-13, 0)	-0.5 (-4, 5)
				N	18	18	18	18
				Mean (SD)	3.1 (3.7)	2.7 (4.2)	-5.8 (5.4)	-0.7 (2.4)
			01:00	Median (Min, Max)	2.5 (-2, 11)	2.0 (-4, 14)	-5.5 (-19, 2)	0.0 (-7, 3)
				N	18	18	18	18
				Mean (SD)	2.8 (4.4)	3.6 (4.5)	-4.9 (4.8)	-0.1 (2.6)
				Median (Min, Max)	1.5 (-3, 12)	2.0 (-2, 14)	-4.0 (-16, 2)	0.5 (-4, 5)
Site 1	Dental plaque acidogenicity (pH)	Measured value	Pre-Dose	N	18	18	18	18
				Mean (SD)	6.883 (0.315)	6.928 (0.348)	7.072 (0.497)	6.922 (0.314)
				Median (Min, Max)	6.900 (6.30, 7.40)	6.900 (6.30, 7.50)	7.000 (6.40, 8.60)	6.900 (6.30, 7.50)
			00:02	N	18	18	18	18
				Mean (SD)	7.000 (0.348)	7.022 (0.359)	6.417 (0.855)	6.967 (0.348)
				Median (Min, Max)	6.950 (6.30, 7.60)	7.050 (6.30, 7.60)	6.350 (5.30, 9.30)	6.950 (6.20, 7.60)
			00:05	N	18	18	18	18
				Mean (SD)	7.011 (0.358)	7.144 (0.396)	5.978 (0.763)	7.011 (0.353)
				Median (Min, Max)	7.000 (6.30, 7.60)	7.100 (6.60, 7.90)	5.850 (4.80, 8.00)	6.950 (6.40, 7.80)
			00:10	N	18	18	18	18
				Mean (SD)	7.056 (0.335)	7.106 (0.483)	6.011 (1.025)	6.950 (0.294)
				Median (Min, Max)	7.100 (6.50, 7.60)	6.950 (6.40, 7.90)	5.900 (4.80, 9.20)	6.950 (6.40, 7.40)
			00:20	N	18	18	18	18
				Mean (SD)	7.044 (0.405)	7.022 (0.424)	6.139 (0.612)	6.917 (0.255)
				Median (Min, Max)	7.050 (6.30, 7.80)	6.900 (6.40, 7.90)	6.050 (4.90, 7.20)	6.950 (6.50, 7.30)
			00:30	N	18	18	18	18
				Mean (SD)	7.100 (0.393)	7.011 (0.440)	6.433 (0.489)	6.972 (0.214)
				Median (Min, Max)	7.150 (6.30, 7.90)	6.900 (6.30, 8.00)	6.550 (5.70, 7.20)	7.000 (6.50, 7.30)

Subcategory of Measurement	Assessment (unit)	Result Category	Planned Timepoint	ZYN® Smooth	ZYN® Peppermint	Sucrose (pos control)	Xylitol (neg control)	
				3 mg	3 mg			
Absolute change from pre-dose baseline			00:40	N	18	18	18	18
			Mean (SD)	7.122 (0.494)	7.001 (0.334)	6.572 (0.462)	6.911 (0.261)	
			Median (Min, Max)	7.200 (6.30, 7.90)	7.050 (6.30, 7.70)	6.550 (5.90, 7.70)	6.950 (6.50, 7.30)	
			00:50	N	18	18	18	18
			Mean (SD)	7.083 (0.449)	7.139 (0.410)	6.617 (0.469)	6.911 (0.310)	
			Median (Min, Max)	7.100 (6.30, 7.80)	7.200 (6.30, 7.70)	6.650 (5.90, 7.30)	6.950 (6.40, 7.30)	
			01:00	N	18	18	18	18
			Mean (SD)	7.106 (0.502)	7.200 (0.428)	6.694 (0.448)	6.928 (0.293)	
			Median (Min, Max)	7.100 (6.20, 8.00)	7.150 (6.30, 8.00)	6.700 (6.10, 7.40)	6.900 (6.50, 7.50)	
			Pre-Dose	N	18	18	18	18
			Mean (SD)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	
			Median (Min, Max)	0.000 (0.00, 0.00)	0.000 (0.00, 0.00)	0.000 (0.00, 0.00)	0.000 (0.00, 0.00)	
			00:02	N	18	18	18	18
			Mean (SD)	0.117 (0.186)	0.094 (0.159)	-0.656 (0.493)	0.044 (0.169)	
			Median (Min, Max)	0.100 (-0.10, 0.50)	0.100 (-0.20, 0.50)	-0.600 (-1.50, 0.70)	0.000 (-0.30, 0.30)	
			00:05	N	18	18	18	18
			Mean (SD)	0.128 (0.174)	0.217 (0.250)	-1.094 (0.467)	0.089 (0.211)	
			Median (Min, Max)	0.100 (-0.10, 0.50)	0.150 (-0.20, 0.70)	-1.200 (-1.70, -0.20)	0.100 (-0.40, 0.40)	
			00:10	N	18	18	18	18
			Mean (SD)	0.172 (0.216)	0.178 (0.271)	-1.061 (0.631)	0.028 (0.164)	
			Median (Min, Max)	0.200 (-0.30, 0.50)	0.150 (-0.40, 0.80)	-1.200 (-1.80, 0.60)	0.000 (-0.20, 0.40)	
			00:20	N	18	18	18	18
			Mean (SD)	0.161 (0.301)	0.094 (0.224)	-0.933 (0.465)	-0.006 (0.221)	
			Median (Min, Max)	0.200 (-0.60, 0.70)	0.100 (-0.20, 0.70)	-0.950 (-1.60, 0.30)	0.000 (-0.30, 0.50)	
			00:30	N	18	18	18	18

Subcategory of Measurement	Assessment (unit)	Result Category	Planned Timepoint		ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)
Relative change from pre-dose baseline (%)			00:40	Mean (SD)	0.217 (0.287)	0.083 (0.223)	-0.639 (0.385)	0.050 (0.248)
				Median (Min, Max)	0.100 (-0.20, 0.80)	0.000 (-0.30, 0.60)	-0.600 (-1.40, 0.10)	0.050 (-0.30, 0.60)
				N	18	18	18	18
			00:50	Mean (SD)	0.239 (0.355)	0.073 (0.252)	-0.500 (0.243)	-0.011 (0.203)
				Median (Min, Max)	0.250 (-0.20, 1.10)	0.000 (-0.30, 0.70)	-0.500 (-0.90, -0.10)	0.050 (-0.40, 0.30)
				N	18	18	18	18
			01:00	Mean (SD)	0.200 (0.334)	0.211 (0.320)	-0.456 (0.466)	-0.011 (0.211)
				Median (Min, Max)	0.100 (-0.40, 1.10)	0.200 (-0.30, 1.00)	-0.350 (-1.70, 0.20)	0.000 (-0.40, 0.40)
				N	18	18	18	18
			Pre-Dose	Mean (SD)	0.222 (0.392)	0.272 (0.349)	-0.378 (0.390)	0.006 (0.207)
				Median (Min, Max)	0.100 (-0.20, 1.30)	0.150 (-0.20, 0.80)	-0.200 (-1.40, 0.20)	0.050 (-0.40, 0.40)
				N	18	18	18	18
			00:02	Mean (SD)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
				Median (Min, Max)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 0)
				N	18	18	18	18
			00:05	Mean (SD)	1.7 (2.7)	1.4 (2.3)	-9.5 (6.6)	0.6 (2.3)
				Median (Min, Max)	1.0 (-2, 8)	1.0 (-3, 7)	-9.0 (-20, 8)	0.0 (-4, 4)
				N	18	18	18	18
			00:10	Mean (SD)	1.8 (2.5)	3.1 (3.7)	-15.6 (7.0)	1.2 (3.1)
				Median (Min, Max)	1.0 (-2, 7)	2.5 (-3, 10)	-16.5 (-26, -3)	1.0 (-6, 5)
				N	18	18	18	18
			00:20	Mean (SD)	2.5 (3.1)	2.6 (3.8)	-15.4 (9.1)	0.6 (2.4)
				Median (Min, Max)	3.0 (-4, 7)	2.5 (-6, 11)	-17.0 (-26, 7)	0.0 (-3, 6)
				N	18	18	18	18
				Mean (SD)	2.4 (4.2)	1.4 (3.1)	-13.2 (6.6)	0.0 (3.3)



Subcategory of Measurement	Assessment (unit)	Result Category	Planned Timepoint		ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)
			00:30	Median (Min, Max)	3.0 (-8, 10)	1.0 (-3, 10)	-14.0 (-25, 4)	0.0 (-4, 8)
				N	18	18	18	18
				Mean (SD)	3.1 (4.2)	1.1 (3.1)	-8.9 (5.0)	0.8 (3.7)
			00:40	Median (Min, Max)	1.0 (-3, 11)	0.0 (-4, 8)	-9.0 (-17, 1)	0.5 (-4, 9)
				N	18	18	18	18
				Mean (SD)	3.4 (5.1)	1.2 (3.6)	-6.9 (3.3)	-0.1 (2.8)
			00:50	Median (Min, Max)	3.5 (-3, 16)	0.0 (-4, 10)	-7.0 (-13, -1)	0.5 (-5, 4)
				N	18	18	18	18
				Mean (SD)	2.8 (4.9)	3.1 (4.7)	-6.2 (6.0)	-0.1 (3.0)
			01:00	Median (Min, Max)	1.5 (-6, 16)	3.0 (-4, 15)	-5.5 (-20, 3)	0.0 (-6, 6)
				N	18	18	18	18
				Mean (SD)	3.2 (5.7)	3.9 (5.2)	-5.1 (5.0)	0.1 (2.8)
				Median (Min, Max)	2.0 (-3, 19)	2.0 (-3, 13)	-3.0 (-16, 3)	0.5 (-5, 6)
Site 2	Dental plaque acidogenicity (pH)	Measured value	Pre-Dose	N	18	18	18	18
				Mean (SD)	6.956 (0.378)	6.961 (0.327)	7.106 (0.503)	6.978 (0.304)
				Median (Min, Max)	7.000 (6.40, 7.80)	7.000 (6.40, 7.60)	7.000 (6.40, 8.60)	7.000 (6.50, 7.50)
			00:02	N	18	18	18	18
				Mean (SD)	7.078 (0.302)	7.117 (0.365)	6.367 (0.775)	6.956 (0.335)
				Median (Min, Max)	6.950 (6.70, 7.80)	7.150 (6.50, 7.70)	6.250 (5.40, 8.90)	6.900 (6.30, 7.80)
			00:05	N	18	18	18	18
				Mean (SD)	6.972 (0.341)	7.078 (0.346)	6.056 (0.810)	7.067 (0.305)
				Median (Min, Max)	6.900 (6.40, 7.80)	7.100 (6.60, 7.90)	5.900 (5.00, 8.50)	7.050 (6.70, 7.80)
			00:10	N	18	18	18	18
				Mean (SD)	7.094 (0.376)	7.078 (0.426)	5.950 (0.976)	7.017 (0.319)
				Median (Min, Max)	7.000 (6.40, 7.80)	7.100 (6.20, 8.00)	5.900 (4.70, 9.00)	6.900 (6.50, 7.50)

Subcategory of Measurement	Assessment (unit)	Result Category	Planned Timepoint		ZYN® Smooth	ZYN® Peppermint	Sucrose (pos control)	Xylitol (neg control)
					3 mg	3 mg		
	Absolute change from pre-dose baseline		00:20	N	18	18	18	18
				Mean (SD)	7.150 (0.444)	7.044 (0.419)	6.139 (0.663)	7.017 (0.283)
				Median (Min, Max)	7.100 (6.40, 8.00)	7.050 (6.20, 7.80)	6.100 (4.90, 7.20)	7.000 (6.50, 7.40)
			00:30	N	18	18	18	18
				Mean (SD)	7.150 (0.460)	7.028 (0.407)	6.467 (0.455)	6.983 (0.350)
				Median (Min, Max)	7.100 (6.50, 7.90)	6.950 (6.20, 7.70)	6.400 (5.90, 7.20)	6.950 (6.40, 7.50)
			00:40	N	18	18	18	18
				Mean (SD)	7.167 (0.412)	7.094 (0.378)	6.644 (0.655)	6.950 (0.319)
				Median (Min, Max)	7.100 (6.50, 8.10)	7.100 (6.40, 7.70)	6.400 (5.70, 7.80)	7.000 (6.20, 7.60)
			00:50	N	18	18	18	18
				Mean (SD)	7.167 (0.450)	7.128 (0.404)	6.717 (0.535)	6.872 (0.344)
				Median (Min, Max)	7.050 (6.50, 8.10)	7.100 (6.30, 7.70)	6.650 (5.90, 7.70)	6.900 (6.40, 7.40)
			01:00	N	18	18	18	18
				Mean (SD)	7.122 (0.504)	7.189 (0.322)	6.761 (0.443)	6.967 (0.345)
				Median (Min, Max)	7.000 (6.40, 8.20)	7.300 (6.20, 7.60)	6.850 (6.00, 7.50)	6.950 (6.40, 7.50)
			Pre-Dose	N	18	18	18	18
				Mean (SD)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)
				Median (Min, Max)	0.000 (0.00, 0.00)	0.000 (0.00, 0.00)	0.000 (0.00, 0.00)	0.000 (0.00, 0.00)
			00:02	N	18	18	18	18
				Mean (SD)	0.122 (0.190)	0.156 (0.257)	-0.739 (0.479)	-0.022 (0.251)
				Median (Min, Max)	0.150 (-0.20, 0.40)	0.100 (-0.20, 0.90)	-0.700 (-1.60, 0.30)	0.000 (-0.60, 0.30)
			00:05	N	18	18	18	18
				Mean (SD)	0.017 (0.154)	0.117 (0.290)	-1.050 (0.558)	0.089 (0.205)
				Median (Min, Max)	0.000 (-0.20, 0.30)	0.100 (-0.30, 1.10)	-1.100 (-2.40, -0.10)	0.100 (-0.50, 0.50)
			00:10	N	18	18	18	18

Subcategory of Measurement	Assessment (unit)	Result Category	Planned Timepoint		ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)		
					Mean (SD)	0.139 (0.266)	0.117 (0.292)	-1.156 (0.638)	0.039 (0.223)	
					Median (Min, Max)	0.100 (-0.30, 0.70)	0.100 (-0.20, 1.20)	-1.150 (-2.10, 0.40)	0.100 (-0.40, 0.50)	
					00:20	N	18	18	18	18
					Mean (SD)	0.194 (0.324)	0.083 (0.283)	-0.967 (0.563)	0.039 (0.235)	
					Median (Min, Max)	0.100 (-0.30, 0.90)	0.100 (-0.40, 0.70)	-1.050 (-2.00, 0.40)	0.100 (-0.50, 0.40)	
					00:30	N	18	18	18	18
					Mean (SD)	0.194 (0.372)	0.067 (0.181)	-0.639 (0.417)	0.006 (0.273)	
					Median (Min, Max)	0.150 (-0.30, 1.10)	0.100 (-0.30, 0.30)	-0.650 (-1.70, 0.30)	0.000 (-0.50, 0.50)	
					00:40	N	18	18	18	18
					Mean (SD)	0.211 (0.297)	0.133 (0.178)	-0.461 (0.378)	-0.028 (0.263)	
					Median (Min, Max)	0.150 (-0.20, 0.80)	0.100 (-0.40, 0.40)	-0.550 (-1.20, 0.10)	-0.050 (-0.70, 0.40)	
					00:50	N	18	18	18	18
					Mean (SD)	0.211 (0.361)	0.167 (0.316)	-0.389 (0.454)	-0.106 (0.236)	
					Median (Min, Max)	0.250 (-0.30, 1.10)	0.100 (-0.30, 0.80)	-0.350 (-1.60, 0.30)	-0.100 (-0.60, 0.30)	
					01:00	N	18	18	18	18
					Mean (SD)	0.167 (0.324)	0.228 (0.295)	-0.344 (0.373)	-0.011 (0.287)	
					Median (Min, Max)	0.100 (-0.30, 0.90)	0.200 (-0.20, 1.00)	-0.250 (-1.30, 0.20)	-0.050 (-0.60, 0.50)	
		Relative change from pre-dose baseline (%)		Pre-Dose	N	18	18	18	18	
					Mean (SD)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	
					Median (Min, Max)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 0)	
				00:02	N	18	18	18	18	
					Mean (SD)	1.9 (2.9)	2.2 (3.8)	-10.5 (6.6)	-0.3 (3.6)	
					Median (Min, Max)	2.0 (-3, 6)	1.0 (-3, 13)	-10.5 (-22, 3)	0.0 (-9, 5)	
				00:05	N	18	18	18	18	
					Mean (SD)	0.3 (2.4)	1.7 (4.2)	-14.9 (7.8)	1.2 (2.9)	

Subcategory of Measurement	Assessment (unit)	Result Category	Planned Timepoint		ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)
				Median (Min, Max)	0.0 (-3, 5)	1.0 (-4, 16)	-15.5 (-31, -1)	1.0 (-7, 7)
			00:10	N	18	18	18	18
				Mean (SD)	2.0 (3.8)	1.6 (4.4)	-16.6 (9.0)	0.6 (3.2)
				Median (Min, Max)	1.0 (-4, 10)	1.0 (-3, 18)	-16.5 (-30, 5)	1.0 (-6, 7)
			00:20	N	18	18	18	18
				Mean (SD)	2.9 (4.7)	1.1 (4.0)	-13.4 (7.9)	0.5 (3.2)
				Median (Min, Max)	1.5 (-4, 13)	1.0 (-6, 10)	-14.5 (-29, 6)	1.0 (-7, 6)
			00:30	N	18	18	18	18
				Mean (SD)	2.8 (5.4)	0.9 (2.5)	-8.8 (5.4)	0.2 (3.9)
				Median (Min, Max)	2.5 (-4, 16)	1.0 (-4, 4)	-8.5 (-20, 4)	0.0 (-7, 7)
			00:40	N	18	18	18	18
				Mean (SD)	3.1 (4.3)	1.8 (2.7)	-6.4 (5.3)	-0.4 (3.8)
				Median (Min, Max)	2.5 (-3, 11)	1.5 (-6, 6)	-8.0 (-17, 1)	-0.5 (-10, 6)
			00:50	N	18	18	18	18
				Mean (SD)	3.1 (5.2)	2.3 (4.7)	-5.3 (5.9)	-1.5 (3.4)
				Median (Min, Max)	3.5 (-4, 16)	1.0 (-4, 12)	-5.0 (-19, 4)	-1.5 (-9, 4)
			01:00	N	18	18	18	18
				Mean (SD)	2.4 (4.6)	3.3 (4.6)	-4.7 (4.9)	0.0 (4.2)
				Median (Min, Max)	1.5 (-4, 13)	3.0 (-3, 16)	-3.5 (-15, 3)	-0.5 (-9, 8)

Data based on Per Protocol Set population.

SM17\_02\_A Dental Plaque Acidogenicity Measurements by timepoint, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:43:54

Table 14.3-5 Dental plaque acidogenicity measurements by timepoint (PPS) (Part 2)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint		Female	Male	Total
Mean	Dental plaque acidogenicity (pH)	Measured value	Screening	Pre-Dose	N	20	36	56
					Mean (SD)	7.125 (0.354)	7.067 (0.358)	7.088 (0.354)
					Median (Min, Max)	7.100 (6.45, 7.70)	7.075 (6.40, 7.65)	7.075 (6.40, 7.70)
					00:02 N	20	36	56
					Mean (SD)	6.493 (0.498)	6.506 (0.486)	6.501 (0.486)
					Median (Min, Max)	6.550 (5.45, 7.45)	6.525 (5.45, 7.30)	6.550 (5.45, 7.45)
					00:05 N	20	36	56
					Mean (SD)	6.233 (0.486)	6.044 (0.706)	6.112 (0.638)
					Median (Min, Max)	6.250 (4.90, 6.95)	6.100 (3.80, 7.05)	6.175 (3.80, 7.05)
					00:10 N	20	36	56
					Mean (SD)	6.058 (0.601)	5.874 (0.637)	5.939 (0.625)
					Median (Min, Max)	6.075 (4.05, 6.95)	5.925 (4.25, 6.95)	6.000 (4.05, 6.95)
					00:20 N	20	36	56
					Mean (SD)	6.423 (0.402)	6.339 (0.669)	6.369 (0.585)
					Median (Min, Max)	6.400 (5.55, 7.15)	6.500 (4.50, 7.40)	6.425 (4.50, 7.40)
					00:30 N	20	36	56
					Mean (SD)	6.560 (0.564)	6.547 (0.563)	6.552 (0.558)
					Median (Min, Max)	6.750 (4.80, 7.25)	6.575 (5.30, 7.45)	6.625 (4.80, 7.45)
					00:40 N	20	36	56
					Mean (SD)	6.808 (0.433)	6.742 (0.500)	6.765 (0.474)
					Median (Min, Max)	6.850 (6.00, 7.65)	6.800 (5.70, 7.65)	6.850 (5.70, 7.65)
					00:50 N	20	36	56
					Mean (SD)	6.833 (0.312)	6.856 (0.412)	6.847 (0.376)
					Median (Min, Max)	6.825 (6.20, 7.30)	6.850 (6.10, 7.55)	6.850 (6.10, 7.55)
					01:00 N	20	36	56

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint		Female	Male	Total	
			Visit 3	Pre-Dose	Mean (SD)	7.010 (0.380)	6.999 (0.418)	7.003 (0.401)	
					Median (Min, Max)	6.975 (6.20, 7.65)	6.950 (6.20, 7.90)	6.950 (6.20, 7.90)	
					00:02	N	20	35	55
						Mean (SD)	7.100 (0.253)	7.136 (0.277)	7.123 (0.267)
						Median (Min, Max)	7.100 (6.75, 7.80)	7.100 (6.55, 7.90)	7.100 (6.55, 7.90)
						N	20	35	55
					00:05	Mean (SD)	6.665 (0.337)	6.544 (0.443)	6.588 (0.409)
						Median (Min, Max)	6.800 (5.70, 7.30)	6.650 (5.40, 7.45)	6.650 (5.40, 7.45)
						N	20	35	55
						Mean (SD)	6.358 (0.318)	6.329 (0.434)	6.339 (0.393)
					00:10	Median (Min, Max)	6.400 (5.55, 6.75)	6.350 (5.25, 7.10)	6.350 (5.25, 7.10)
						N	20	35	55
						Mean (SD)	6.350 (0.354)	6.220 (0.552)	6.267 (0.490)
						Median (Min, Max)	6.350 (5.60, 6.95)	6.300 (5.05, 7.15)	6.350 (5.05, 7.15)
					00:20	N	20	35	55
						Mean (SD)	6.638 (0.399)	6.496 (0.477)	6.547 (0.452)
						Median (Min, Max)	6.750 (5.85, 7.30)	6.550 (5.40, 7.35)	6.600 (5.40, 7.35)
						N	20	35	55
					00:30	Mean (SD)	6.758 (0.324)	6.646 (0.413)	6.686 (0.384)
						Median (Min, Max)	6.850 (6.00, 7.15)	6.700 (5.80, 7.45)	6.750 (5.80, 7.45)
						N	20	35	55
						Mean (SD)	6.865 (0.319)	6.796 (0.404)	6.821 (0.374)
					00:40	Median (Min, Max)	6.950 (6.15, 7.25)	6.850 (5.95, 7.55)	6.850 (5.95, 7.55)
						N	20	35	55
						Mean (SD)	6.945 (0.373)	6.901 (0.363)	6.917 (0.364)
						Median (Min, Max)	6.950 (6.15, 7.50)	6.850 (6.35, 7.65)	6.900 (6.15, 7.65)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total	
				01:00	N	20	35	55
					Mean (SD)	7.003 (0.368)	7.030 (0.349)	7.020 (0.353)
					Median (Min, Max)	7.050 (6.30, 7.65)	7.050 (6.30, 7.80)	7.050 (6.30, 7.80)
			Visit 4	Pre-Dose	N	20	36	56
					Mean (SD)	7.100 (0.172)	7.121 (0.293)	7.113 (0.255)
					Median (Min, Max)	7.100 (6.75, 7.40)	7.150 (6.50, 7.70)	7.150 (6.50, 7.70)
				00:02	N	20	36	56
					Mean (SD)	6.715 (0.239)	6.649 (0.446)	6.672 (0.384)
					Median (Min, Max)	6.750 (6.10, 7.05)	6.650 (5.30, 7.50)	6.725 (5.30, 7.50)
				00:05	N	20	36	56
					Mean (SD)	6.518 (0.390)	6.364 (0.482)	6.419 (0.454)
					Median (Min, Max)	6.475 (5.80, 7.15)	6.475 (5.05, 7.00)	6.475 (5.05, 7.15)
				00:10	N	20	36	56
					Mean (SD)	6.490 (0.451)	6.271 (0.505)	6.349 (0.494)
					Median (Min, Max)	6.525 (5.55, 7.25)	6.300 (5.10, 7.15)	6.400 (5.10, 7.25)
				00:20	N	20	36	56
					Mean (SD)	6.658 (0.384)	6.535 (0.500)	6.579 (0.462)
					Median (Min, Max)	6.750 (5.70, 7.35)	6.550 (5.50, 7.45)	6.675 (5.50, 7.45)
				00:30	N	20	36	56
					Mean (SD)	6.815 (0.345)	6.649 (0.398)	6.708 (0.386)
					Median (Min, Max)	6.850 (5.95, 7.25)	6.700 (5.60, 7.20)	6.750 (5.60, 7.25)
				00:40	N	20	36	56
					Mean (SD)	6.883 (0.368)	6.783 (0.312)	6.819 (0.333)
					Median (Min, Max)	6.925 (5.95, 7.45)	6.850 (6.05, 7.35)	6.900 (5.95, 7.45)
				00:50	N	20	36	56
					Mean (SD)	6.993 (0.273)	6.836 (0.313)	6.892 (0.306)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total
				Median (Min, Max)	6.975 (6.25, 7.55)	6.900 (6.20, 7.35)	6.900 (6.20, 7.55)
				01:00 N	20	36	56
				Mean (SD)	7.098 (0.259)	6.957 (0.328)	7.007 (0.310)
				Median (Min, Max)	7.125 (6.25, 7.55)	7.000 (6.25, 7.55)	7.050 (6.25, 7.55)
			Visit 5	Pre-Dose N	20	35	55
				Mean (SD)	7.093 (0.244)	7.257 (0.287)	7.197 (0.282)
				Median (Min, Max)	7.150 (6.60, 7.50)	7.250 (6.75, 7.75)	7.150 (6.60, 7.75)
				00:02 N	20	35	55
				Mean (SD)	6.745 (0.219)	6.813 (0.287)	6.788 (0.264)
				Median (Min, Max)	6.750 (6.35, 7.15)	6.750 (6.15, 7.40)	6.750 (6.15, 7.40)
				00:05 N	20	35	55
				Mean (SD)	6.595 (0.229)	6.544 (0.318)	6.563 (0.288)
				Median (Min, Max)	6.625 (6.15, 6.95)	6.550 (5.75, 7.20)	6.600 (5.75, 7.20)
				00:10 N	20	35	55
				Mean (SD)	6.368 (0.321)	6.494 (0.356)	6.448 (0.346)
				Median (Min, Max)	6.350 (5.65, 6.85)	6.500 (5.55, 7.20)	6.500 (5.55, 7.20)
				00:20 N	20	35	55
				Mean (SD)	6.585 (0.289)	6.701 (0.298)	6.659 (0.297)
				Median (Min, Max)	6.700 (5.95, 6.95)	6.750 (6.15, 7.55)	6.700 (5.95, 7.55)
				00:30 N	20	35	55
				Mean (SD)	6.743 (0.209)	6.863 (0.266)	6.819 (0.251)
				Median (Min, Max)	6.750 (6.30, 7.10)	6.850 (6.30, 7.45)	6.800 (6.30, 7.45)
				00:40 N	20	35	55
				Mean (SD)	6.873 (0.230)	6.931 (0.262)	6.910 (0.250)
				Median (Min, Max)	6.825 (6.45, 7.45)	6.850 (6.45, 7.45)	6.850 (6.45, 7.45)
				00:50 N	20	35	55



Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint		Female	Male	Total				
Absolute change from baseline	Visit 3			01:00	Mean (SD)	6.978 (0.235)	6.967 (0.290)	6.971 (0.269)				
					Median (Min, Max)	6.950 (6.55, 7.55)	6.950 (6.45, 7.55)	6.950 (6.45, 7.55)				
					N	20	35	55				
				00:02	Mean (SD)	7.018 (0.244)	7.027 (0.298)	7.024 (0.277)				
					Median (Min, Max)	6.975 (6.60, 7.50)	7.000 (6.35, 7.65)	7.000 (6.35, 7.65)				
					N	20	35	55				
				00:05	Mean (SD)	-0.435 (0.244)	-0.591 (0.364)	-0.535 (0.332)				
					Median (Min, Max)	-0.425 (-1.20, -0.10)	-0.500 (-1.50, 0.15)	-0.500 (-1.50, 0.15)				
					N	20	35	55				
				00:10	Mean (SD)	-0.743 (0.295)	-0.807 (0.370)	-0.784 (0.343)				
					Median (Min, Max)	-0.750 (-1.35, -0.30)	-0.750 (-2.00, -0.20)	-0.750 (-2.00, -0.20)				
					N	20	35	55				
				00:20	Mean (SD)	-0.750 (0.315)	-0.916 (0.545)	-0.855 (0.478)				
					Median (Min, Max)	-0.825 (-1.25, -0.15)	-0.800 (-2.35, 0.25)	-0.800 (-2.35, 0.25)				
					N	20	35	55				
				00:30	Mean (SD)	-0.463 (0.295)	-0.640 (0.499)	-0.575 (0.441)				
					Median (Min, Max)	-0.500 (-1.05, 0.15)	-0.600 (-2.00, 0.35)	-0.550 (-2.00, 0.35)				
					N	20	35	55				
				00:40	Mean (SD)	-0.343 (0.246)	-0.490 (0.386)	-0.436 (0.347)				
					Median (Min, Max)	-0.275 (-0.90, 0.05)	-0.500 (-1.45, 0.20)	-0.400 (-1.45, 0.20)				
					N	20	35	55				
				00:50	Mean (SD)	-0.235 (0.271)	-0.340 (0.358)	-0.302 (0.330)				
					Median (Min, Max)	-0.200 (-0.70, 0.15)	-0.300 (-1.30, 0.35)	-0.250 (-1.30, 0.35)				
					N	20	35	55				
									Mean (SD)	-0.155 (0.242)	-0.234 (0.328)	-0.205 (0.299)
									Median (Min, Max)	-0.100 (-0.65, 0.30)	-0.200 (-1.05, 0.65)	-0.150 (-1.05, 0.65)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female		Male	Total
			Visit 4	01:00	N	20	35	55
				Mean (SD)	-0.098 (0.307)	-0.106 (0.331)	-0.103 (0.319)	
				Median (Min, Max)	-0.050 (-0.85, 0.55)	-0.050 (-1.10, 0.55)	-0.050 (-1.10, 0.55)	
				00:02	N	20	36	56
				Mean (SD)	-0.385 (0.239)	-0.472 (0.356)	-0.441 (0.320)	
				Median (Min, Max)	-0.325 (-1.20, -0.10)	-0.350 (-1.80, -0.10)	-0.350 (-1.80, -0.10)	
				00:05	N	20	36	56
				Mean (SD)	-0.583 (0.392)	-0.757 (0.393)	-0.695 (0.398)	
				Median (Min, Max)	-0.550 (-1.40, 0.10)	-0.700 (-2.05, -0.15)	-0.650 (-2.05, 0.10)	
				00:10	N	20	36	56
				Mean (SD)	-0.610 (0.434)	-0.850 (0.468)	-0.764 (0.467)	
				Median (Min, Max)	-0.500 (-1.40, 0.15)	-0.775 (-2.05, -0.05)	-0.700 (-2.05, 0.15)	
				00:20	N	20	36	56
				Mean (SD)	-0.443 (0.374)	-0.586 (0.464)	-0.535 (0.436)	
				Median (Min, Max)	-0.450 (-1.25, 0.20)	-0.525 (-1.60, 0.25)	-0.500 (-1.60, 0.25)	
				00:30	N	20	36	56
				Mean (SD)	-0.285 (0.306)	-0.472 (0.377)	-0.405 (0.362)	
				Median (Min, Max)	-0.250 (-1.00, 0.10)	-0.425 (-1.50, 0.20)	-0.325 (-1.50, 0.20)	
				00:40	N	20	36	56
				Mean (SD)	-0.218 (0.356)	-0.338 (0.316)	-0.295 (0.332)	
				Median (Min, Max)	-0.200 (-1.30, 0.25)	-0.250 (-1.15, 0.15)	-0.250 (-1.30, 0.25)	
				00:50	N	20	36	56
				Mean (SD)	-0.108 (0.254)	-0.285 (0.275)	-0.221 (0.279)	
				Median (Min, Max)	-0.100 (-0.70, 0.30)	-0.225 (-1.00, 0.15)	-0.150 (-1.00, 0.30)	
				01:00	N	20	36	56
				Mean (SD)	-0.003 (0.252)	-0.164 (0.269)	-0.106 (0.272)	

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint		Female	Male	Total
					Median (Min, Max)	0.000 (-0.70, 0.40)	-0.100 (-0.95, 0.30)	-0.100 (-0.95, 0.40)
			Visit 5	00:02	N	20	35	55
					Mean (SD)	-0.348 (0.196)	-0.444 (0.204)	-0.409 (0.205)
					Median (Min, Max)	-0.300 (-0.75, -0.10)	-0.450 (-0.95, -0.05)	-0.400 (-0.95, -0.05)
				00:05	N	20	35	55
					Mean (SD)	-0.498 (0.234)	-0.713 (0.378)	-0.635 (0.347)
					Median (Min, Max)	-0.500 (-1.00, -0.20)	-0.650 (-1.75, -0.15)	-0.600 (-1.75, -0.15)
				00:10	N	20	35	55
					Mean (SD)	-0.725 (0.384)	-0.763 (0.411)	-0.749 (0.398)
					Median (Min, Max)	-0.750 (-1.40, 0.25)	-0.800 (-1.85, 0.00)	-0.750 (-1.85, 0.25)
				00:20	N	20	35	55
					Mean (SD)	-0.508 (0.347)	-0.556 (0.341)	-0.538 (0.341)
					Median (Min, Max)	-0.525 (-1.10, 0.10)	-0.600 (-1.40, 0.10)	-0.550 (-1.40, 0.10)
				00:30	N	20	35	55
					Mean (SD)	-0.350 (0.221)	-0.394 (0.353)	-0.378 (0.310)
					Median (Min, Max)	-0.350 (-0.70, 0.10)	-0.300 (-1.20, 0.15)	-0.350 (-1.20, 0.15)
				00:40	N	20	35	55
					Mean (SD)	-0.220 (0.211)	-0.326 (0.341)	-0.287 (0.303)
					Median (Min, Max)	-0.250 (-0.70, 0.15)	-0.300 (-1.20, 0.30)	-0.250 (-1.20, 0.30)
				00:50	N	20	35	55
					Mean (SD)	-0.115 (0.241)	-0.290 (0.313)	-0.226 (0.299)
					Median (Min, Max)	-0.125 (-0.60, 0.35)	-0.250 (-1.05, 0.40)	-0.200 (-1.05, 0.40)
				01:00	N	20	35	55
					Mean (SD)	-0.075 (0.160)	-0.230 (0.270)	-0.174 (0.246)
					Median (Min, Max)	-0.050 (-0.40, 0.15)	-0.200 (-0.90, 0.30)	-0.150 (-0.90, 0.30)
	Relative change from baseline (%)		Visit 3	00:02	N	20	35	55

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total	
			Visit 4	00:05	Mean (SD)	-6.2 (3.4)	-8.3 (5.2)	-7.5 (4.7)
					Median (Min, Max)	-6.0 (-17, -1)	-7.0 (-22, 2)	-7.0 (-22, 2)
				00:10	N	20	35	55
					Mean (SD)	-10.5 (4.1)	-11.3 (5.1)	-11.0 (4.7)
					Median (Min, Max)	-11.0 (-20, -4)	-10.0 (-27, -3)	-11.0 (-27, -3)
				00:20	N	20	35	55
					Mean (SD)	-10.5 (4.5)	-12.8 (7.6)	-11.9 (6.7)
					Median (Min, Max)	-11.5 (-18, -2)	-11.0 (-32, 4)	-11.0 (-32, 4)
				00:30	N	20	35	55
					Mean (SD)	-6.5 (4.3)	-8.8 (6.9)	-8.0 (6.1)
					Median (Min, Max)	-6.5 (-15, 2)	-8.0 (-27, 5)	-8.0 (-27, 5)
				00:40	N	20	35	55
					Mean (SD)	-4.7 (3.5)	-6.9 (5.4)	-6.1 (4.9)
					Median (Min, Max)	-4.0 (-13, 1)	-7.0 (-20, 3)	-6.0 (-20, 3)
				00:50	N	20	35	55
					Mean (SD)	-3.3 (3.9)	-4.7 (5.0)	-4.2 (4.6)
					Median (Min, Max)	-3.0 (-10, 2)	-4.0 (-18, 5)	-3.0 (-18, 5)
				01:00	N	20	35	55
					Mean (SD)	-2.3 (3.4)	-3.2 (4.5)	-2.9 (4.1)
					Median (Min, Max)	-1.0 (-10, 4)	-3.0 (-14, 9)	-2.0 (-14, 9)
				00:02	N	20	36	56
					Mean (SD)	-5.5 (3.2)	-6.6 (5.0)	-6.2 (4.4)
					Median (Min, Max)	-4.5 (-16, -1)	-5.0 (-25, -2)	-5.0 (-25, -1)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female		Male	Total
			Visit 5	00:05	N	20	36	56
				Mean (SD)	-8.3 (5.4)	-10.6 (5.7)	-9.8 (5.7)	
				Median (Min, Max)	-8.0 (-19, 1)	-9.5 (-29, -2)	-9.0 (-29, 1)	
				00:10	N	20	36	56
				Mean (SD)	-8.6 (6.0)	-11.9 (6.6)	-10.7 (6.5)	
				Median (Min, Max)	-7.0 (-20, 2)	-11.0 (-29, -1)	-10.0 (-29, 2)	
				00:20	N	20	36	56
				Mean (SD)	-6.2 (5.3)	-8.2 (6.6)	-7.5 (6.2)	
				Median (Min, Max)	-6.0 (-18, 3)	-7.0 (-23, 4)	-7.0 (-23, 4)	
				00:30	N	20	36	56
				Mean (SD)	-4.0 (4.3)	-6.5 (5.3)	-5.6 (5.0)	
				Median (Min, Max)	-4.0 (-14, 1)	-6.0 (-21, 3)	-5.0 (-21, 3)	
				00:40	N	20	36	56
				Mean (SD)	-3.1 (4.9)	-4.6 (4.3)	-4.1 (4.6)	
				Median (Min, Max)	-3.0 (-18, 3)	-4.0 (-16, 2)	-3.0 (-18, 3)	
				00:50	N	20	36	56
				Mean (SD)	-1.5 (3.5)	-4.0 (3.8)	-3.1 (3.8)	
				Median (Min, Max)	-1.0 (-10, 4)	-3.0 (-14, 2)	-2.0 (-14, 4)	
				01:00	N	20	36	56
				Mean (SD)	0.1 (3.5)	-2.2 (3.7)	-1.4 (3.8)	
				Median (Min, Max)	0.0 (-10, 6)	-1.0 (-13, 4)	-1.0 (-13, 6)	
				00:02	N	20	35	55
				Mean (SD)	-4.8 (2.7)	-6.1 (2.7)	-5.6 (2.8)	
				Median (Min, Max)	-4.0 (-10, -1)	-6.0 (-13, -1)	-6.0 (-13, -1)	
				00:05	N	20	35	55
				Mean (SD)	-7.0 (3.3)	-9.7 (5.1)	-8.7 (4.7)	

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint		Female	Male	Total
				00:10	Median (Min, Max)	-7.0 (-14, -3)	-9.0 (-23, -2)	-8.0 (-23, -2)
					N	20	35	55
					Mean (SD)	-10.1 (5.4)	-10.4 (5.4)	-10.3 (5.3)
				00:20	Median (Min, Max)	-10.0 (-20, 4)	-11.0 (-24, 0)	-11.0 (-24, 4)
					N	20	35	55
					Mean (SD)	-7.1 (4.9)	-7.5 (4.5)	-7.4 (4.6)
				00:30	Median (Min, Max)	-7.0 (-16, 2)	-8.0 (-18, 1)	-8.0 (-18, 2)
					N	20	35	55
					Mean (SD)	-4.9 (3.1)	-5.3 (4.7)	-5.2 (4.2)
				00:40	Median (Min, Max)	-5.0 (-9, 2)	-4.0 (-16, 2)	-5.0 (-16, 2)
					N	20	35	55
					Mean (SD)	-3.0 (2.8)	-4.4 (4.6)	-3.9 (4.1)
				00:50	Median (Min, Max)	-3.5 (-9, 2)	-4.0 (-16, 4)	-4.0 (-16, 4)
					N	20	35	55
					Mean (SD)	-1.6 (3.4)	-3.9 (4.2)	-3.0 (4.1)
				01:00	Median (Min, Max)	-1.5 (-8, 5)	-3.0 (-14, 6)	-3.0 (-14, 6)
					N	20	35	55
					Mean (SD)	-1.1 (2.3)	-3.0 (3.7)	-2.3 (3.3)
					Median (Min, Max)	-1.0 (-6, 2)	-3.0 (-12, 4)	-2.0 (-12, 4)
Site 1	Dental plaque acidogenicity (pH)	Measured value	Screening	Pre-Dose	N	20	36	56
					Mean (SD)	7.120 (0.399)	7.008 (0.336)	7.048 (0.360)
					Median (Min, Max)	7.050 (6.40, 7.70)	7.050 (6.30, 7.50)	7.050 (6.30, 7.70)
				00:02	N	20	36	56
					Mean (SD)	6.390 (0.599)	6.514 (0.475)	6.470 (0.521)
					Median (Min, Max)	6.450 (5.00, 7.60)	6.600 (5.50, 7.30)	6.600 (5.00, 7.60)
				00:05	N	20	36	56

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total	
			Visit 3	00:10	Mean (SD)	6.150 (0.601)	6.067 (0.672)	6.096 (0.644)
					Median (Min, Max)	6.300 (4.20, 6.90)	6.200 (4.30, 7.10)	6.200 (4.20, 7.10)
					N	20	36	56
				00:20	Mean (SD)	5.990 (0.646)	5.864 (0.594)	5.909 (0.610)
					Median (Min, Max)	6.050 (4.00, 6.90)	5.900 (4.70, 6.90)	6.000 (4.00, 6.90)
					N	20	36	56
				00:30	Mean (SD)	6.405 (0.432)	6.339 (0.681)	6.363 (0.601)
					Median (Min, Max)	6.450 (5.60, 7.00)	6.500 (4.30, 7.50)	6.500 (4.30, 7.50)
					N	20	36	56
				00:40	Mean (SD)	6.525 (0.627)	6.511 (0.549)	6.516 (0.573)
					Median (Min, Max)	6.700 (4.40, 7.20)	6.600 (5.50, 7.60)	6.600 (4.40, 7.60)
					N	20	36	56
				00:50	Mean (SD)	6.795 (0.429)	6.672 (0.524)	6.716 (0.491)
					Median (Min, Max)	6.850 (5.90, 7.60)	6.700 (5.60, 7.50)	6.800 (5.60, 7.60)
					N	20	36	56
				01:00	Mean (SD)	6.750 (0.291)	6.808 (0.423)	6.788 (0.380)
					Median (Min, Max)	6.750 (6.10, 7.20)	6.900 (6.10, 7.50)	6.800 (6.10, 7.50)
					N	20	36	56
				Pre-Dose	Mean (SD)	6.955 (0.350)	6.936 (0.422)	6.943 (0.394)
					Median (Min, Max)	6.900 (6.20, 7.70)	6.900 (6.20, 7.90)	6.900 (6.20, 7.90)
					N	20	35	55
				00:02	Mean (SD)	7.060 (0.260)	7.120 (0.277)	7.098 (0.270)
					Median (Min, Max)	7.000 (6.70, 7.60)	7.100 (6.50, 7.80)	7.000 (6.50, 7.80)
					N	20	35	55
					Mean (SD)	6.645 (0.349)	6.566 (0.463)	6.595 (0.423)
					Median (Min, Max)	6.750 (5.80, 7.10)	6.600 (5.10, 7.30)	6.600 (5.10, 7.30)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total	
			Visit 4	00:05	N	20	35	55
					Mean (SD)	6.355 (0.270)	6.334 (0.438)	6.342 (0.383)
					Median (Min, Max)	6.450 (5.80, 6.70)	6.400 (5.20, 7.00)	6.400 (5.20, 7.00)
				00:10	N	20	35	55
					Mean (SD)	6.390 (0.408)	6.194 (0.622)	6.265 (0.558)
					Median (Min, Max)	6.400 (5.50, 7.00)	6.300 (4.70, 7.50)	6.300 (4.70, 7.50)
				00:20	N	20	35	55
					Mean (SD)	6.625 (0.417)	6.503 (0.524)	6.547 (0.487)
					Median (Min, Max)	6.750 (5.90, 7.40)	6.600 (5.30, 7.30)	6.600 (5.30, 7.40)
				00:30	N	20	35	55
					Mean (SD)	6.775 (0.323)	6.611 (0.425)	6.671 (0.396)
					Median (Min, Max)	6.900 (6.00, 7.30)	6.700 (5.80, 7.50)	6.700 (5.80, 7.50)
				00:40	N	20	35	55
					Mean (SD)	6.855 (0.341)	6.789 (0.388)	6.813 (0.370)
					Median (Min, Max)	6.900 (6.20, 7.30)	6.800 (5.90, 7.60)	6.900 (5.90, 7.60)
				00:50	N	20	35	55
					Mean (SD)	6.965 (0.406)	6.871 (0.427)	6.905 (0.418)
					Median (Min, Max)	7.000 (6.10, 7.60)	6.900 (5.80, 7.60)	6.900 (5.80, 7.60)
				01:00	N	20	35	55
					Mean (SD)	7.000 (0.388)	7.046 (0.391)	7.029 (0.387)
					Median (Min, Max)	7.100 (6.30, 7.60)	7.100 (6.10, 7.80)	7.100 (6.10, 7.80)
				Pre-Dose	N	20	36	56
					Mean (SD)	7.015 (0.184)	7.119 (0.307)	7.082 (0.272)
					Median (Min, Max)	7.000 (6.80, 7.50)	7.200 (6.50, 7.80)	7.000 (6.50, 7.80)
				00:02	N	20	36	56
					Mean (SD)	6.705 (0.188)	6.619 (0.490)	6.650 (0.408)



Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total
				Median (Min, Max)	6.700 (6.20, 7.00)	6.700 (5.20, 7.60)	6.700 (5.20, 7.60)
				N	20	36	56
				Mean (SD)	6.460 (0.469)	6.367 (0.471)	6.400 (0.468)
				Median (Min, Max)	6.550 (5.60, 7.40)	6.500 (5.00, 7.00)	6.500 (5.00, 7.40)
				N	20	36	56
				Mean (SD)	6.475 (0.484)	6.269 (0.527)	6.343 (0.518)
				Median (Min, Max)	6.500 (5.60, 7.40)	6.300 (4.90, 7.00)	6.400 (4.90, 7.40)
				N	20	36	56
				Mean (SD)	6.605 (0.422)	6.503 (0.521)	6.539 (0.487)
				Median (Min, Max)	6.700 (5.60, 7.40)	6.550 (5.30, 7.40)	6.600 (5.30, 7.40)
				N	20	36	56
				Mean (SD)	6.765 (0.377)	6.644 (0.376)	6.688 (0.378)
				Median (Min, Max)	6.800 (5.70, 7.30)	6.700 (5.70, 7.20)	6.800 (5.70, 7.30)
				N	20	36	56
				Mean (SD)	6.870 (0.401)	6.817 (0.300)	6.836 (0.337)
				Median (Min, Max)	6.900 (5.90, 7.60)	6.850 (6.10, 7.40)	6.900 (5.90, 7.60)
				N	20	36	56
				Mean (SD)	6.970 (0.305)	6.828 (0.341)	6.879 (0.333)
				Median (Min, Max)	6.900 (6.10, 7.60)	6.800 (6.10, 7.40)	6.900 (6.10, 7.60)
				N	20	36	56
				Mean (SD)	7.090 (0.290)	6.997 (0.363)	7.030 (0.339)
				Median (Min, Max)	7.100 (6.20, 7.50)	7.100 (6.20, 7.80)	7.100 (6.20, 7.80)
			Visit 5	Pre-Dose N	20	35	55
				Mean (SD)	7.060 (0.268)	7.197 (0.293)	7.147 (0.289)
				Median (Min, Max)	7.100 (6.60, 7.60)	7.200 (6.70, 7.80)	7.100 (6.60, 7.80)
				N	20	35	55

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total	
					Mean (SD)	6.675 (0.240)	6.806 (0.272)	6.758 (0.266)
					Median (Min, Max)	6.700 (6.20, 7.10)	6.800 (6.30, 7.50)	6.700 (6.20, 7.50)
				00:05	N	20	35	55
					Mean (SD)	6.535 (0.248)	6.503 (0.357)	6.515 (0.319)
				00:10	Median (Min, Max)	6.550 (6.00, 7.00)	6.500 (5.60, 7.20)	6.500 (5.60, 7.20)
					N	20	35	55
				00:20	Mean (SD)	6.290 (0.360)	6.454 (0.357)	6.395 (0.363)
					Median (Min, Max)	6.350 (5.60, 6.80)	6.500 (5.80, 7.20)	6.400 (5.60, 7.20)
				00:30	N	20	35	55
					Mean (SD)	6.560 (0.312)	6.637 (0.325)	6.609 (0.320)
				00:40	Median (Min, Max)	6.650 (5.90, 7.00)	6.700 (5.80, 7.50)	6.700 (5.80, 7.50)
					N	20	35	55
				00:50	Mean (SD)	6.710 (0.245)	6.809 (0.268)	6.773 (0.262)
					Median (Min, Max)	6.750 (6.20, 7.10)	6.800 (6.30, 7.40)	6.800 (6.20, 7.40)
				01:00	N	20	35	55
					Mean (SD)	6.855 (0.242)	6.914 (0.253)	6.893 (0.249)
				00:02	Median (Min, Max)	6.800 (6.40, 7.50)	6.900 (6.50, 7.50)	6.800 (6.40, 7.50)
					N	20	35	55
				00:02	Mean (SD)	6.965 (0.246)	6.929 (0.294)	6.942 (0.275)
					Median (Min, Max)	6.900 (6.60, 7.60)	6.900 (6.40, 7.60)	6.900 (6.40, 7.60)
				00:02	N	20	35	55
					Mean (SD)	6.990 (0.263)	6.989 (0.304)	6.989 (0.287)
				00:02	Median (Min, Max)	6.950 (6.60, 7.70)	6.900 (6.40, 7.70)	6.900 (6.40, 7.70)
					N	20	35	55
				00:02	Mean (SD)	-0.415 (0.300)	-0.554 (0.401)	-0.504 (0.371)
					Median (Min, Max)	-0.350 (-1.00, 0.00)	-0.500 (-1.90, 0.10)	-0.400 (-1.90, 0.10)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total	
			Visit 4	00:05	N	20	35	55
				Mean (SD)	-0.705 (0.284)	-0.786 (0.376)	-0.756 (0.345)	
				Median (Min, Max)	-0.750 (-1.10, -0.30)	-0.700 (-2.00, -0.10)	-0.700 (-2.00, -0.10)	
				00:10	N	20	35	55
				Mean (SD)	-0.670 (0.348)	-0.926 (0.615)	-0.833 (0.544)	
				Median (Min, Max)	-0.750 (-1.30, -0.10)	-0.900 (-2.50, 0.70)	-0.800 (-2.50, 0.70)	
				00:20	N	20	35	55
				Mean (SD)	-0.435 (0.317)	-0.617 (0.568)	-0.551 (0.496)	
				Median (Min, Max)	-0.350 (-0.90, 0.10)	-0.600 (-1.90, 0.50)	-0.500 (-1.90, 0.50)	
				00:30	N	20	35	55
				Mean (SD)	-0.285 (0.256)	-0.509 (0.433)	-0.427 (0.391)	
				Median (Min, Max)	-0.300 (-0.80, 0.20)	-0.500 (-1.60, 0.20)	-0.400 (-1.60, 0.20)	
				00:40	N	20	35	55
				Mean (SD)	-0.205 (0.295)	-0.331 (0.391)	-0.285 (0.361)	
				Median (Min, Max)	-0.200 (-0.90, 0.20)	-0.300 (-1.60, 0.30)	-0.200 (-1.60, 0.30)	
				00:50	N	20	35	55
				Mean (SD)	-0.095 (0.312)	-0.249 (0.427)	-0.193 (0.393)	
				Median (Min, Max)	0.000 (-0.70, 0.40)	-0.200 (-1.40, 0.80)	-0.200 (-1.40, 0.80)	
				01:00	N	20	35	55
				Mean (SD)	-0.060 (0.339)	-0.074 (0.392)	-0.069 (0.371)	
				Median (Min, Max)	0.000 (-0.70, 0.40)	0.000 (-1.40, 0.70)	0.000 (-1.40, 0.70)	
				00:02	N	20	36	56
				Mean (SD)	-0.310 (0.229)	-0.500 (0.428)	-0.432 (0.378)	
				Median (Min, Max)	-0.300 (-0.90, 0.00)	-0.400 (-2.00, -0.10)	-0.350 (-2.00, 0.00)	
				00:05	N	20	36	56
				Mean (SD)	-0.555 (0.491)	-0.753 (0.432)	-0.682 (0.460)	

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total
				Median (Min, Max)	-0.400 (-1.60, 0.30)	-0.700 (-2.20, -0.10)	-0.650 (-2.20, 0.30)
				N	20	36	56
				Mean (SD)	-0.540 (0.455)	-0.850 (0.544)	-0.739 (0.531)
				Median (Min, Max)	-0.450 (-1.30, 0.30)	-0.750 (-2.30, 0.10)	-0.650 (-2.30, 0.30)
				N	20	36	56
				Mean (SD)	-0.410 (0.391)	-0.617 (0.522)	-0.543 (0.486)
				Median (Min, Max)	-0.400 (-1.30, 0.20)	-0.600 (-1.80, 0.30)	-0.500 (-1.80, 0.30)
				N	20	36	56
				Mean (SD)	-0.250 (0.350)	-0.475 (0.383)	-0.395 (0.384)
				Median (Min, Max)	-0.200 (-1.20, 0.30)	-0.500 (-1.30, 0.20)	-0.300 (-1.30, 0.30)
				N	20	36	56
				Mean (SD)	-0.145 (0.412)	-0.303 (0.344)	-0.246 (0.374)
				Median (Min, Max)	-0.100 (-1.00, 0.60)	-0.300 (-1.10, 0.20)	-0.200 (-1.10, 0.60)
				N	20	36	56
				Mean (SD)	-0.045 (0.293)	-0.292 (0.334)	-0.204 (0.339)
				Median (Min, Max)	0.000 (-0.80, 0.60)	-0.250 (-1.10, 0.40)	-0.150 (-1.10, 0.60)
				N	20	36	56
				Mean (SD)	0.075 (0.297)	-0.122 (0.323)	-0.052 (0.325)
				Median (Min, Max)	0.100 (-0.70, 0.50)	-0.100 (-0.90, 0.50)	0.000 (-0.90, 0.50)
			Visit 5	N	20	35	55
				Mean (SD)	-0.385 (0.232)	-0.391 (0.201)	-0.389 (0.211)
				Median (Min, Max)	-0.400 (-0.80, -0.10)	-0.400 (-0.80, -0.10)	-0.400 (-0.80, -0.10)
				N	20	35	55
				Mean (SD)	-0.525 (0.326)	-0.694 (0.391)	-0.633 (0.375)
				Median (Min, Max)	-0.450 (-1.30, -0.10)	-0.600 (-1.70, -0.10)	-0.600 (-1.70, -0.10)
				N	20	35	55

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint		Female	Male	Total		
				00:20	Mean (SD)	-0.770 (0.419)	-0.743 (0.422)	-0.753 (0.418)		
					Median (Min, Max)	-0.800 (-1.50, 0.10)	-0.800 (-1.70, 0.00)	-0.800 (-1.70, 0.10)		
				N	20	35	55			
				00:30	Mean (SD)	-0.500 (0.374)	-0.560 (0.407)	-0.538 (0.393)		
					Median (Min, Max)	-0.450 (-1.10, 0.10)	-0.500 (-1.60, 0.10)	-0.500 (-1.60, 0.10)		
				N	20	35	55			
				00:40	Mean (SD)	-0.350 (0.272)	-0.389 (0.386)	-0.375 (0.347)		
					Median (Min, Max)	-0.300 (-0.80, 0.20)	-0.400 (-1.20, 0.30)	-0.400 (-1.20, 0.30)		
				N	20	35	55			
				00:50	Mean (SD)	-0.205 (0.211)	-0.283 (0.319)	-0.255 (0.285)		
					Median (Min, Max)	-0.150 (-0.60, 0.10)	-0.300 (-0.90, 0.20)	-0.200 (-0.90, 0.20)		
				N	20	35	55			
				01:00	Mean (SD)	-0.095 (0.242)	-0.269 (0.333)	-0.205 (0.312)		
					Median (Min, Max)	-0.150 (-0.50, 0.30)	-0.200 (-0.90, 0.30)	-0.200 (-0.90, 0.30)		
				N	20	35	55			
				Relative change from baseline (%)	Visit 3	00:02	N	20	35	55
						00:05	Mean (SD)	-5.8 (4.3)	-7.6 (5.8)	-7.0 (5.3)
		Median (Min, Max)	-5.0 (-15, 0)				-7.0 (-27, 2)	-6.0 (-27, 2)		
		N	20			35	55			
		00:10	Mean (SD)			-9.8 (4.0)	-11.0 (5.3)	-10.5 (4.9)		
			Median (Min, Max)			-10.5 (-15, -4)	-10.0 (-28, -1)	-10.0 (-28, -1)		
		N	20			35	55			
		Mean (SD)	-9.5 (5.0)			-13.0 (8.6)	-11.7 (7.6)			
		Median (Min, Max)	-10.5 (-19, -1)			-12.0 (-35, 10)	-11.0 (-35, 10)			

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female		Male	Total
			Visit 4	00:20	N	20	35	55
				Mean (SD)	-6.1 (4.5)	-8.5 (7.9)	-7.7 (6.9)	
				Median (Min, Max)	-5.0 (-13, 1)	-8.0 (-26, 8)	-7.0 (-26, 8)	
				00:30	N	20	35	55
				Mean (SD)	-3.9 (3.7)	-7.0 (5.9)	-5.8 (5.4)	
				Median (Min, Max)	-4.0 (-12, 3)	-7.0 (-21, 3)	-5.0 (-21, 3)	
				00:40	N	20	35	55
				Mean (SD)	-2.8 (4.2)	-4.6 (5.3)	-3.9 (5.0)	
				Median (Min, Max)	-3.0 (-12, 3)	-4.0 (-21, 4)	-3.0 (-21, 4)	
				00:50	N	20	35	55
				Mean (SD)	-1.3 (4.5)	-3.4 (5.9)	-2.6 (5.5)	
				Median (Min, Max)	0.0 (-10, 6)	-3.0 (-19, 12)	-3.0 (-19, 12)	
				01:00	N	20	35	55
				Mean (SD)	-0.8 (4.7)	-1.0 (5.4)	-0.9 (5.1)	
				Median (Min, Max)	0.0 (-9, 6)	0.0 (-19, 10)	0.0 (-19, 10)	
				00:02	N	20	36	56
				Mean (SD)	-4.3 (3.4)	-7.0 (5.9)	-6.0 (5.3)	
				Median (Min, Max)	-4.0 (-13, 0)	-6.0 (-28, -1)	-4.5 (-28, 0)	
				00:05	N	20	36	56
				Mean (SD)	-7.8 (6.9)	-10.6 (6.1)	-9.6 (6.5)	
				Median (Min, Max)	-6.0 (-22, 4)	-10.0 (-31, -1)	-9.0 (-31, 4)	
				00:10	N	20	36	56
				Mean (SD)	-7.7 (6.5)	-11.9 (7.5)	-10.4 (7.4)	
				Median (Min, Max)	-6.5 (-19, 4)	-11.0 (-32, 1)	-9.5 (-32, 4)	
				00:20	N	20	36	56
				Mean (SD)	-5.8 (5.6)	-8.6 (7.3)	-7.6 (6.8)	

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total
			Visit 5	Median (Min, Max)	-6.0 (-19, 3)	-8.0 (-25, 4)	-7.0 (-25, 4)
				00:30 N	20	36	56
				Mean (SD)	-3.5 (4.9)	-6.6 (5.3)	-5.5 (5.4)
				Median (Min, Max)	-3.0 (-17, 4)	-7.0 (-18, 3)	-4.0 (-18, 4)
				00:40 N	20	36	56
				Mean (SD)	-1.9 (5.8)	-4.2 (4.7)	-3.4 (5.2)
				Median (Min, Max)	-1.0 (-14, 9)	-4.0 (-15, 3)	-3.0 (-15, 9)
				00:50 N	20	36	56
				Mean (SD)	-0.7 (4.3)	-3.9 (4.7)	-2.8 (4.8)
				Median (Min, Max)	0.0 (-12, 9)	-3.5 (-15, 6)	-2.0 (-15, 9)
				01:00 N	20	36	56
				Mean (SD)	1.0 (4.2)	-1.6 (4.5)	-0.7 (4.5)
				Median (Min, Max)	1.0 (-10, 7)	-1.0 (-12, 7)	0.0 (-12, 7)
				00:02 N	20	35	55
				Mean (SD)	-5.4 (3.3)	-5.4 (2.8)	-5.4 (3.0)
				Median (Min, Max)	-5.5 (-11, -1)	-6.0 (-11, -1)	-6.0 (-11, -1)
				00:05 N	20	35	55
				Mean (SD)	-7.3 (4.3)	-9.6 (5.3)	-8.7 (5.0)
				Median (Min, Max)	-6.5 (-17, -2)	-8.0 (-23, -1)	-8.0 (-23, -1)
				00:10 N	20	35	55
				Mean (SD)	-10.8 (5.8)	-10.2 (5.8)	-10.4 (5.7)
				Median (Min, Max)	-11.0 (-21, 1)	-11.0 (-23, 0)	-11.0 (-23, 1)
				00:20 N	20	35	55
				Mean (SD)	-7.0 (5.1)	-7.7 (5.4)	-7.4 (5.3)
				Median (Min, Max)	-6.5 (-15, 1)	-7.0 (-22, 1)	-7.0 (-22, 1)
				00:30 N	20	35	55

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint		Female	Male	Total
				00:40	Mean (SD)	-4.9 (3.8)	-5.3 (5.2)	-5.1 (4.7)
					Median (Min, Max)	-4.0 (-11, 3)	-5.0 (-16, 4)	-5.0 (-16, 4)
					N	20	35	55
				00:50	Mean (SD)	-2.7 (2.8)	-3.8 (4.3)	-3.4 (3.8)
					Median (Min, Max)	-2.0 (-8, 1)	-4.0 (-12, 3)	-3.0 (-12, 3)
					N	20	35	55
				01:00	Mean (SD)	-1.3 (3.5)	-3.6 (4.6)	-2.7 (4.3)
					Median (Min, Max)	-2.0 (-7, 5)	-3.0 (-12, 4)	-3.0 (-12, 5)
					N	20	35	55
					Mean (SD)	-1.0 (2.2)	-2.8 (3.5)	-2.1 (3.2)
					Median (Min, Max)	-0.5 (-4, 3)	-3.0 (-11, 4)	-1.0 (-11, 4)
Site 2	Dental plaque acidogenicity (pH)	Measured value	Screening	Pre-Dose	N	20	36	56
					Mean (SD)	7.130 (0.385)	7.125 (0.429)	7.127 (0.411)
					Median (Min, Max)	7.200 (6.30, 7.70)	7.100 (6.30, 8.00)	7.150 (6.30, 8.00)
				00:02	N	20	36	56
					Mean (SD)	6.595 (0.461)	6.497 (0.565)	6.532 (0.528)
					Median (Min, Max)	6.550 (5.80, 7.40)	6.500 (5.10, 7.40)	6.500 (5.10, 7.40)
				00:05	N	20	36	56
					Mean (SD)	6.315 (0.446)	6.022 (0.779)	6.127 (0.689)
					Median (Min, Max)	6.350 (5.60, 7.00)	6.050 (3.30, 7.10)	6.200 (3.30, 7.10)
				00:10	N	20	36	56
					Mean (SD)	6.125 (0.611)	5.883 (0.720)	5.970 (0.688)
					Median (Min, Max)	6.050 (4.10, 7.00)	5.950 (3.80, 7.00)	6.000 (3.80, 7.00)
				00:20	N	20	36	56
					Mean (SD)	6.440 (0.427)	6.339 (0.684)	6.375 (0.602)
					Median (Min, Max)	6.400 (5.50, 7.30)	6.500 (4.70, 7.50)	6.500 (4.70, 7.50)



Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total	
			Visit 3	00:30	N	20	36	56
				Mean (SD)	6.595 (0.524)	6.583 (0.619)	6.588 (0.582)	
				Median (Min, Max)	6.750 (5.20, 7.40)	6.550 (4.90, 7.60)	6.600 (4.90, 7.60)	
				00:40	N	20	36	56
				Mean (SD)	6.820 (0.473)	6.811 (0.503)	6.814 (0.488)	
				Median (Min, Max)	6.900 (6.00, 7.70)	6.900 (5.80, 7.80)	6.900 (5.80, 7.80)	
				00:50	N	20	36	56
				Mean (SD)	6.915 (0.384)	6.903 (0.453)	6.907 (0.426)	
				Median (Min, Max)	6.950 (6.00, 7.50)	6.900 (6.10, 7.70)	6.900 (6.00, 7.70)	
				01:00	N	20	36	56
				Mean (SD)	7.065 (0.450)	7.061 (0.448)	7.063 (0.445)	
				Median (Min, Max)	7.050 (6.20, 7.80)	7.000 (6.10, 7.90)	7.000 (6.10, 7.90)	
				Pre-Dose	N	20	35	55
				Mean (SD)	7.140 (0.312)	7.151 (0.315)	7.147 (0.311)	
				Median (Min, Max)	7.050 (6.70, 8.00)	7.100 (6.60, 8.00)	7.100 (6.60, 8.00)	
				00:02	N	20	35	55
				Mean (SD)	6.685 (0.394)	6.523 (0.518)	6.582 (0.479)	
				Median (Min, Max)	6.700 (5.60, 7.60)	6.600 (5.00, 7.60)	6.700 (5.00, 7.60)	
				00:05	N	20	35	55
				Mean (SD)	6.360 (0.404)	6.323 (0.458)	6.336 (0.436)	
				Median (Min, Max)	6.450 (5.30, 6.80)	6.400 (5.10, 7.20)	6.400 (5.10, 7.20)	
				00:10	N	20	35	55
				Mean (SD)	6.310 (0.370)	6.246 (0.535)	6.269 (0.479)	
				Median (Min, Max)	6.350 (5.60, 7.00)	6.300 (5.30, 7.00)	6.300 (5.30, 7.00)	
				00:20	N	20	35	55
				Mean (SD)	6.650 (0.422)	6.489 (0.491)	6.547 (0.470)	

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint		Female	Male	Total
			Visit 4	00:30	Median (Min, Max)	6.750 (5.80, 7.30)	6.500 (5.40, 7.40)	6.600 (5.40, 7.40)
					N	20	35	55
					Mean (SD)	6.740 (0.350)	6.680 (0.423)	6.702 (0.396)
				00:40	Median (Min, Max)	6.800 (6.00, 7.10)	6.700 (5.80, 7.50)	6.800 (5.80, 7.50)
					N	20	35	55
					Mean (SD)	6.875 (0.337)	6.803 (0.451)	6.829 (0.412)
				00:50	Median (Min, Max)	7.000 (6.10, 7.30)	6.800 (5.90, 7.50)	6.900 (5.90, 7.50)
					N	20	35	55
					Mean (SD)	6.925 (0.378)	6.931 (0.368)	6.929 (0.369)
				01:00	Median (Min, Max)	6.950 (6.20, 7.50)	6.900 (6.30, 7.70)	6.900 (6.20, 7.70)
					N	20	35	55
					Mean (SD)	7.005 (0.375)	7.014 (0.371)	7.011 (0.369)
				Pre-Dose	Median (Min, Max)	7.000 (6.30, 7.70)	7.000 (6.30, 7.80)	7.000 (6.30, 7.80)
					N	20	36	56
					Mean (SD)	7.185 (0.221)	7.122 (0.317)	7.145 (0.286)
				00:02	Median (Min, Max)	7.200 (6.70, 7.50)	7.100 (6.50, 7.70)	7.200 (6.50, 7.70)
					N	20	36	56
					Mean (SD)	6.725 (0.326)	6.678 (0.461)	6.695 (0.415)
				00:05	Median (Min, Max)	6.800 (6.00, 7.30)	6.700 (5.40, 7.40)	6.700 (5.40, 7.40)
					N	20	36	56
					Mean (SD)	6.575 (0.399)	6.361 (0.550)	6.438 (0.508)
				00:10	Median (Min, Max)	6.550 (5.80, 7.20)	6.500 (4.90, 7.20)	6.500 (4.90, 7.20)
					N	20	36	56
					Mean (SD)	6.505 (0.458)	6.272 (0.538)	6.355 (0.519)
				00:20	Median (Min, Max)	6.600 (5.50, 7.10)	6.400 (5.10, 7.30)	6.400 (5.10, 7.30)
					N	20	36	56

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint		Female	Male	Total
			Visit 5	00:30	Mean (SD)	6.710 (0.395)	6.567 (0.496)	6.618 (0.464)
					Median (Min, Max)	6.800 (5.80, 7.30)	6.600 (5.50, 7.50)	6.700 (5.50, 7.50)
					N	20	36	56
				00:40	Mean (SD)	6.865 (0.353)	6.653 (0.454)	6.729 (0.430)
					Median (Min, Max)	6.900 (6.20, 7.50)	6.600 (5.30, 7.40)	6.700 (5.30, 7.50)
					N	20	36	56
				00:50	Mean (SD)	6.895 (0.380)	6.750 (0.363)	6.802 (0.372)
					Median (Min, Max)	6.900 (5.70, 7.30)	6.800 (5.90, 7.30)	6.900 (5.70, 7.30)
					N	20	36	56
				01:00	Mean (SD)	7.015 (0.270)	6.844 (0.332)	6.905 (0.319)
					Median (Min, Max)	7.000 (6.40, 7.50)	6.850 (6.10, 7.60)	6.900 (6.10, 7.60)
					N	20	36	56
				Pre-Dose	Mean (SD)	7.105 (0.263)	6.917 (0.331)	6.984 (0.319)
					Median (Min, Max)	7.100 (6.30, 7.60)	6.950 (6.30, 7.60)	7.000 (6.30, 7.60)
					N	20	35	55
				00:02	Mean (SD)	7.125 (0.269)	7.317 (0.310)	7.247 (0.308)
					Median (Min, Max)	7.150 (6.50, 7.60)	7.400 (6.80, 7.80)	7.200 (6.50, 7.80)
					N	20	35	55
				00:05	Mean (SD)	6.815 (0.230)	6.820 (0.340)	6.818 (0.303)
					Median (Min, Max)	6.800 (6.40, 7.20)	6.800 (6.00, 7.60)	6.800 (6.00, 7.60)
					N	20	35	55
				00:10	Mean (SD)	6.655 (0.305)	6.586 (0.320)	6.611 (0.314)
					Median (Min, Max)	6.700 (6.10, 7.20)	6.600 (5.90, 7.20)	6.600 (5.90, 7.20)
					N	20	35	55
					Mean (SD)	6.445 (0.325)	6.534 (0.396)	6.502 (0.371)
					Median (Min, Max)	6.500 (5.60, 6.90)	6.600 (5.30, 7.20)	6.500 (5.30, 7.20)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female		Male	Total
				00:20	N	20	35	55
					Mean (SD)	6.610 (0.299)	6.766 (0.334)	6.709 (0.328)
					Median (Min, Max)	6.600 (5.90, 7.00)	6.800 (6.00, 7.60)	6.700 (5.90, 7.60)
				00:30	N	20	35	55
					Mean (SD)	6.775 (0.205)	6.917 (0.309)	6.865 (0.282)
					Median (Min, Max)	6.700 (6.40, 7.10)	6.900 (6.30, 7.60)	6.800 (6.30, 7.60)
				00:40	N	20	35	55
					Mean (SD)	6.890 (0.253)	6.949 (0.298)	6.927 (0.282)
					Median (Min, Max)	6.800 (6.50, 7.40)	6.900 (6.30, 7.50)	6.900 (6.30, 7.50)
				00:50	N	20	35	55
					Mean (SD)	6.990 (0.253)	7.006 (0.317)	7.000 (0.293)
					Median (Min, Max)	6.900 (6.50, 7.50)	7.000 (6.40, 7.70)	7.000 (6.40, 7.70)
				01:00	N	20	35	55
					Mean (SD)	7.045 (0.261)	7.066 (0.326)	7.058 (0.302)
					Median (Min, Max)	7.000 (6.60, 7.50)	7.100 (6.30, 7.70)	7.100 (6.30, 7.70)
		Absolute change from baseline	Visit 3	00:02	N	20	35	55
					Mean (SD)	-0.455 (0.307)	-0.629 (0.418)	-0.565 (0.387)
					Median (Min, Max)	-0.400 (-1.40, -0.10)	-0.500 (-1.90, 0.20)	-0.500 (-1.90, 0.20)
				00:05	N	20	35	55
					Mean (SD)	-0.780 (0.396)	-0.829 (0.404)	-0.811 (0.398)
					Median (Min, Max)	-0.700 (-1.70, -0.30)	-0.800 (-2.00, -0.20)	-0.800 (-2.00, -0.20)
				00:10	N	20	35	55
					Mean (SD)	-0.830 (0.383)	-0.906 (0.543)	-0.878 (0.488)
					Median (Min, Max)	-0.900 (-1.40, -0.10)	-0.700 (-2.20, -0.10)	-0.800 (-2.20, -0.10)
				00:20	N	20	35	55
					Mean (SD)	-0.490 (0.352)	-0.663 (0.501)	-0.600 (0.457)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total
				Median (Min, Max)	-0.400 (-1.20, 0.20)	-0.700 (-2.20, 0.40)	-0.600 (-2.20, 0.40)
				N	20	35	55
				Mean (SD)	-0.400 (0.351)	-0.471 (0.383)	-0.445 (0.370)
				Median (Min, Max)	-0.300 (-1.00, 0.10)	-0.400 (-1.50, 0.20)	-0.400 (-1.50, 0.20)
				N	20	35	55
				Mean (SD)	-0.265 (0.336)	-0.349 (0.396)	-0.318 (0.374)
				Median (Min, Max)	-0.200 (-1.00, 0.20)	-0.300 (-1.40, 0.40)	-0.200 (-1.40, 0.40)
				N	20	35	55
				Mean (SD)	-0.215 (0.315)	-0.220 (0.301)	-0.218 (0.303)
				Median (Min, Max)	-0.250 (-0.60, 0.50)	-0.200 (-1.20, 0.50)	-0.200 (-1.20, 0.50)
				N	20	35	55
				Mean (SD)	-0.135 (0.353)	-0.137 (0.335)	-0.136 (0.338)
				Median (Min, Max)	-0.100 (-1.00, 0.70)	-0.100 (-1.30, 0.50)	-0.100 (-1.30, 0.70)
			Visit 4	N	20	36	56
				Mean (SD)	-0.460 (0.332)	-0.444 (0.332)	-0.450 (0.329)
				Median (Min, Max)	-0.400 (-1.50, -0.10)	-0.350 (-1.60, -0.10)	-0.400 (-1.60, -0.10)
				N	20	36	56
				Mean (SD)	-0.610 (0.444)	-0.761 (0.430)	-0.707 (0.437)
				Median (Min, Max)	-0.500 (-1.70, 0.30)	-0.700 (-1.90, -0.10)	-0.600 (-1.90, 0.30)
				N	20	36	56
				Mean (SD)	-0.680 (0.470)	-0.850 (0.474)	-0.789 (0.475)
				Median (Min, Max)	-0.650 (-1.50, 0.10)	-0.800 (-1.90, -0.10)	-0.700 (-1.90, 0.10)
				N	20	36	56
				Mean (SD)	-0.475 (0.418)	-0.556 (0.458)	-0.527 (0.442)
				Median (Min, Max)	-0.450 (-1.20, 0.20)	-0.450 (-1.40, 0.20)	-0.450 (-1.40, 0.20)
				N	20	36	56

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint		Female	Male	Total
			Visit 5	00:40	Mean (SD)	-0.320 (0.346)	-0.469 (0.432)	-0.416 (0.407)
					Median (Min, Max)	-0.300 (-0.90, 0.30)	-0.400 (-1.70, 0.20)	-0.400 (-1.70, 0.30)
					N	20	36	56
				00:50	Mean (SD)	-0.290 (0.395)	-0.372 (0.370)	-0.343 (0.377)
					Median (Min, Max)	-0.250 (-1.70, 0.20)	-0.350 (-1.60, 0.20)	-0.300 (-1.70, 0.20)
					N	20	36	56
				01:00	Mean (SD)	-0.170 (0.308)	-0.278 (0.323)	-0.239 (0.319)
					Median (Min, Max)	-0.150 (-0.80, 0.30)	-0.200 (-1.00, 0.50)	-0.200 (-1.00, 0.50)
					N	20	36	56
				00:02	Mean (SD)	-0.080 (0.261)	-0.206 (0.291)	-0.161 (0.285)
					Median (Min, Max)	0.000 (-0.70, 0.30)	-0.200 (-1.10, 0.50)	-0.150 (-1.10, 0.50)
					N	20	35	55
				00:05	Mean (SD)	-0.310 (0.205)	-0.497 (0.294)	-0.429 (0.278)
					Median (Min, Max)	-0.250 (-0.80, -0.10)	-0.500 (-1.20, 0.00)	-0.400 (-1.20, 0.00)
					N	20	35	55
				00:10	Mean (SD)	-0.470 (0.315)	-0.731 (0.418)	-0.636 (0.401)
					Median (Min, Max)	-0.500 (-1.10, 0.00)	-0.700 (-1.80, 0.00)	-0.600 (-1.80, 0.00)
					N	20	35	55
				00:20	Mean (SD)	-0.680 (0.399)	-0.783 (0.459)	-0.745 (0.437)
					Median (Min, Max)	-0.700 (-1.40, 0.40)	-0.800 (-2.10, 0.00)	-0.800 (-2.10, 0.40)
					N	20	35	55
				00:30	Mean (SD)	-0.515 (0.356)	-0.551 (0.373)	-0.538 (0.364)
					Median (Min, Max)	-0.600 (-1.10, 0.20)	-0.600 (-1.50, 0.10)	-0.600 (-1.50, 0.20)
					N	20	35	55
					Mean (SD)	-0.350 (0.228)	-0.400 (0.399)	-0.382 (0.345)
					Median (Min, Max)	-0.300 (-0.80, 0.10)	-0.400 (-1.40, 0.40)	-0.300 (-1.40, 0.40)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total	
		Relative change from baseline (%)	Visit 3	00:40	N	20	35	55
				Mean (SD)	-0.235 (0.276)	-0.369 (0.412)	-0.320 (0.371)	
				Median (Min, Max)	-0.200 (-0.80, 0.30)	-0.300 (-1.50, 0.50)	-0.300 (-1.50, 0.50)	
				00:50	N	20	35	55
				Mean (SD)	-0.135 (0.301)	-0.311 (0.346)	-0.247 (0.339)	
				Median (Min, Max)	-0.200 (-0.70, 0.50)	-0.300 (-1.30, 0.50)	-0.200 (-1.30, 0.50)	
				01:00	N	20	35	55
				Mean (SD)	-0.080 (0.185)	-0.251 (0.332)	-0.189 (0.297)	
				Median (Min, Max)	0.000 (-0.50, 0.20)	-0.200 (-1.10, 0.40)	-0.100 (-1.10, 0.40)	
				00:02	N	20	35	55
				Mean (SD)	-6.3 (4.4)	-8.8 (6.0)	-7.9 (5.5)	
				Median (Min, Max)	-6.0 (-20, -1)	-7.0 (-28, 3)	-7.0 (-28, 3)	
				00:05	N	20	35	55
				Mean (SD)	-10.9 (5.3)	-11.5 (5.6)	-11.3 (5.5)	
				Median (Min, Max)	-10.0 (-24, -4)	-11.0 (-26, -3)	-11.0 (-26, -3)	
				00:10	N	20	35	55
				Mean (SD)	-11.4 (5.3)	-12.6 (7.4)	-12.1 (6.7)	
				Median (Min, Max)	-12.0 (-20, -1)	-10.0 (-29, -2)	-12.0 (-29, -1)	
				00:20	N	20	35	55
				Mean (SD)	-6.8 (4.9)	-9.1 (6.9)	-8.3 (6.3)	
				Median (Min, Max)	-5.5 (-17, 3)	-9.0 (-29, 6)	-8.0 (-29, 6)	
				00:30	N	20	35	55
				Mean (SD)	-5.6 (4.8)	-6.5 (5.2)	-6.2 (5.0)	
				Median (Min, Max)	-4.0 (-14, 1)	-6.0 (-20, 3)	-6.0 (-20, 3)	
				00:40	N	20	35	55
				Mean (SD)	-3.7 (4.6)	-4.8 (5.4)	-4.4 (5.1)	

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint		Female	Male	Total
					Median (Min, Max)	-3.0 (-13, 3)	-4.0 (-18, 6)	-3.0 (-18, 6)
				00:50	N	20	35	55
					Mean (SD)	-3.1 (4.5)	-3.1 (4.1)	-3.1 (4.2)
					Median (Min, Max)	-3.5 (-9, 7)	-3.0 (-16, 7)	-3.0 (-16, 7)
				01:00	N	20	35	55
					Mean (SD)	-1.9 (4.9)	-1.8 (4.6)	-1.8 (4.6)
					Median (Min, Max)	-1.0 (-13, 10)	-1.0 (-17, 7)	-1.0 (-17, 10)
			Visit 4	00:02	N	20	36	56
					Mean (SD)	-6.4 (4.5)	-6.2 (4.8)	-6.3 (4.6)
					Median (Min, Max)	-6.0 (-20, -1)	-4.5 (-23, -1)	-5.0 (-23, -1)
				00:05	N	20	36	56
					Mean (SD)	-8.5 (6.0)	-10.7 (6.3)	-9.9 (6.2)
					Median (Min, Max)	-7.0 (-23, 4)	-9.0 (-27, -1)	-9.0 (-27, 4)
				00:10	N	20	36	56
					Mean (SD)	-9.6 (6.4)	-12.0 (6.7)	-11.1 (6.7)
					Median (Min, Max)	-9.5 (-21, 1)	-11.0 (-27, -2)	-10.0 (-27, 1)
				00:20	N	20	36	56
					Mean (SD)	-6.6 (5.8)	-7.7 (6.4)	-7.3 (6.2)
					Median (Min, Max)	-6.5 (-17, 3)	-6.5 (-20, 3)	-6.5 (-20, 3)
				00:30	N	20	36	56
					Mean (SD)	-4.3 (4.8)	-6.6 (6.0)	-5.8 (5.7)
					Median (Min, Max)	-4.0 (-12, 4)	-6.0 (-24, 3)	-5.0 (-24, 4)
				00:40	N	20	36	56
					Mean (SD)	-4.0 (5.4)	-5.1 (5.1)	-4.7 (5.2)
					Median (Min, Max)	-3.5 (-23, 3)	-4.5 (-21, 3)	-4.0 (-23, 3)
				00:50	N	20	36	56



Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint		Female	Male	Total				
			Visit 5	01:00	Mean (SD)	-2.4 (4.2)	-3.8 (4.4)	-3.3 (4.4)				
					Median (Min, Max)	-2.0 (-11, 4)	-3.0 (-13, 7)	-3.0 (-13, 7)				
					N	20	36	56				
				00:02	Mean (SD)	-1.2 (3.6)	-2.8 (4.0)	-2.2 (3.9)				
					Median (Min, Max)	0.0 (-10, 4)	-3.0 (-15, 7)	-2.0 (-15, 7)				
					N	20	35	55				
				00:05	Mean (SD)	-4.3 (2.8)	-6.7 (4.0)	-5.8 (3.8)				
					Median (Min, Max)	-3.5 (-11, -1)	-6.0 (-17, 0)	-5.0 (-17, 0)				
					N	20	35	55				
				00:10	Mean (SD)	-6.6 (4.3)	-9.9 (5.5)	-8.7 (5.3)				
					Median (Min, Max)	-7.0 (-15, 0)	-10.0 (-23, 0)	-8.0 (-23, 0)				
					N	20	35	55				
				00:20	Mean (SD)	-9.5 (5.6)	-10.6 (6.0)	-10.2 (5.9)				
					Median (Min, Max)	-10.0 (-20, 6)	-11.0 (-27, 0)	-11.0 (-27, 6)				
					N	20	35	55				
				00:30	Mean (SD)	-7.1 (5.0)	-7.4 (4.9)	-7.3 (4.9)				
					Median (Min, Max)	-8.0 (-16, 3)	-8.0 (-19, 1)	-8.0 (-19, 3)				
					N	20	35	55				
				00:40	Mean (SD)	-4.9 (3.2)	-5.3 (5.3)	-5.2 (4.7)				
					Median (Min, Max)	-4.0 (-11, 2)	-5.0 (-18, 6)	-4.0 (-18, 6)				
					N	20	35	55				
				00:50	Mean (SD)	-3.3 (3.7)	-4.8 (5.4)	-4.2 (4.9)				
					Median (Min, Max)	-3.0 (-11, 4)	-4.0 (-19, 7)	-4.0 (-19, 7)				
					N	20	35	55				

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Planned Timepoint	Female	Male	Total	
				01:00	N	20	35	55
					Mean (SD)	-1.2 (2.6)	-3.3 (4.4)	-2.5 (4.0)
					Median (Min, Max)	0.0 (-7, 3)	-3.0 (-14, 6)	-1.0 (-14, 6)

Data based on Per Protocol Set population.

SM17\_02\_B Dental Plaque Acidogenicity Measurements by timepoint, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:54:59

### 14.3.1.1 Dental plaque acedogenicity

Table 14.3-6 Minimum and maximum dental plaque acidogenicity measurements (PPS) (Part 1)

				ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)
Subcategory of Measurement	Assessment (unit)	Result Category					
Mean	Min change from baseline dental plaque acidogenicity (pH)	Measured value	N	18	18	18	18
		Mean (SD)		-0.039 (0.153)	-0.081 (0.109)	-1.311 (0.458)	-0.169 (0.168)
		Median (Min, Max)		-0.075 (-0.25, 0.30)	-0.075 (-0.25, 0.10)	-1.325 (-2.05, -0.40)	-0.175 (-0.50, 0.10)
	Min dental plaque acidogenicity (pH)	Measured value	N	18	18	18	18
		Mean (SD)		6.881 (0.312)	6.864 (0.336)	5.778 (0.636)	6.781 (0.288)
		Median (Min, Max)		6.825 (6.30, 7.35)	6.825 (6.25, 7.55)	5.775 (4.75, 6.95)	6.750 (6.35, 7.25)
	Max change from baseline dental plaque acidogenicity (pH)	Measured value	N	18	18	18	18
		Mean (SD)		0.406 (0.272)	0.450 (0.281)	-0.178 (0.326)	0.217 (0.157)
		Median (Min, Max)		0.400 (0.00, 0.85)	0.375 (0.10, 1.00)	-0.100 (-0.65, 0.50)	0.200 (-0.10, 0.55)
Site 1	Min change from baseline dental plaque acidogenicity (pH)	Measured value	N	18	18	18	18
		Mean (SD)		-0.222 (0.306)	-0.194 (0.126)	-1.372 (0.504)	-0.294 (0.151)
		Median (Min, Max)		-0.200 (-1.20, 0.20)	-0.150 (-0.40, 0.00)	-1.400 (-2.30, -0.30)	-0.300 (-0.60, -0.10)
	Min dental plaque acidogenicity (pH)	Measured value	N	18	18	18	18
		Mean (SD)		6.778 (0.352)	6.828 (0.316)	5.778 (0.613)	6.733 (0.279)
		Median (Min, Max)		6.750 (6.20, 7.30)	6.800 (6.30, 7.40)	5.800 (4.80, 6.90)	6.750 (6.20, 7.20)

				ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)
Subcategory of Measurement	Assessment (unit)	Result Category					
Site 2	Max change from baseline dental plaque acidogenicity (pH)	Measured value	N	18	18	18	18
			Mean (SD)	0.500 (0.327)	0.578 (0.317)	-0.122 (0.326)	0.306 (0.224)
			Median (Min, Max)	0.500 (0.00, 1.30)	0.550 (0.00, 1.10)	-0.150 (-0.60, 0.70)	0.300 (-0.10, 0.80)
	Min change from baseline dental plaque acidogenicity (pH)	Measured value	N	18	18	18	18
			Mean (SD)	-0.111 (0.153)	-0.194 (0.166)	-1.406 (0.509)	-0.283 (0.212)
			Median (Min, Max)	-0.100 (-0.40, 0.10)	-0.200 (-0.50, 0.00)	-1.400 (-2.40, -0.60)	-0.250 (-0.70, 0.00)
	Min dental plaque acidogenicity (pH)	Measured value	N	18	18	18	18
			Mean (SD)	6.889 (0.361)	6.828 (0.325)	5.744 (0.646)	6.744 (0.315)
			Median (Min, Max)	6.800 (6.40, 7.80)	6.850 (6.20, 7.40)	5.750 (4.70, 7.10)	6.800 (6.20, 7.30)
	Max change from baseline dental plaque acidogenicity (pH)	Measured value	N	18	18	18	18
			Mean (SD)	0.539 (0.322)	0.561 (0.279)	-0.044 (0.324)	0.311 (0.200)
			Median (Min, Max)	0.450 (-0.10, 1.10)	0.500 (0.20, 1.20)	-0.050 (-0.50, 0.50)	0.350 (0.00, 0.60)

Data based on Per Protocol Set population.

SM17\_02\_A Minimum and Maximum Dental Plaque Acidogenicity Measurements, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:43:54

Table 14.3-7 Minimum and maximum dental plaque acidogenicity measurements (PPS) (Part 2)

				Female	Male	Total	
Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name				
Mean	Min change from baseline dental plaque acidogenicity (pH)	Measured value	Screening	N	20	36	56
				Mean (SD)	-1.220 (0.538)	-1.289 (0.594)	-1.264 (0.571)
				Median (Min, Max)	-1.150 (-2.60, -0.55)	-1.225 (-3.15, -0.05)	-1.200 (-3.15, -0.05)
			Visit 3	N	20	35	55
				Mean (SD)	-0.890 (0.266)	-1.019 (0.465)	-0.972 (0.406)
				Median (Min, Max)	-0.925 (-1.35, -0.35)	-0.900 (-2.35, -0.25)	-0.900 (-2.35, -0.25)
			Visit 4	N	20	36	56

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Female	Male	Total	
		Absolute change from baseline	Visit 5	Mean (SD)	-0.793 (0.376)	-0.978 (0.444)	-0.912 (0.427)
				Median (Min, Max)	-0.750 (-1.40, -0.20)	-1.000 (-2.05, -0.20)	-0.850 (-2.05, -0.20)
				N	20	35	55
			Visit 3	Mean (SD)	-0.783 (0.325)	-0.889 (0.371)	-0.850 (0.356)
				Median (Min, Max)	-0.750 (-1.40, -0.25)	-0.850 (-1.85, -0.20)	-0.850 (-1.85, -0.20)
				N	20	35	55
			Visit 4	Mean (SD)	0.330 (0.556)	0.283 (0.643)	0.300 (0.608)
				Median (Min, Max)	0.350 (-0.60, 1.80)	0.250 (-1.45, 1.95)	0.250 (-1.45, 1.95)
				Within group p-value	0.0164	0.0068	0.0002
			Visit 5	N	20	36	56
				Mean (SD)	0.428 (0.555)	0.311 (0.665)	0.353 (0.625)
				Median (Min, Max)	0.400 (-0.55, 1.80)	0.275 (-1.50, 1.85)	0.300 (-1.50, 1.85)
				Within group p-value	0.0009	0.0017	0.0000
		Relative change from baseline (%)	Visit 5	N	20	35	55
				Mean (SD)	0.438 (0.525)	0.416 (0.636)	0.424 (0.593)
				Median (Min, Max)	0.325 (-0.20, 1.65)	0.300 (-0.60, 2.50)	0.300 (-0.60, 2.50)
				Within group p-value	0.0005	0.0002	0.0000
			Visit 3	N	20	35	55
				Mean (SD)	-15.9 (44.1)	66.1 (494.3)	36.3 (395.1)
				Median (Min, Max)	-28.5 (-69, 91)	-16.0 (-87, 2900)	-21.0 (-87, 2900)
				Within group p-value	0.0797	0.0215	0.0025
			Visit 4	N	20	36	56
				Mean (SD)	-28.5 (39.8)	64.1 (504.8)	31.1 (405.9)
				Median (Min, Max)	-29.0 (-79, 79)	-25.0 (-82, 3000)	-25.5 (-82, 3000)
				Within group p-value	0.0033	0.0115	0.0001
			Visit 5	N	20	35	55

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
				Mean (SD)	-29.6 (30.4)	10.9 (210.2)	-3.9 (168.9)
				Median (Min, Max)	-35.0 (-80, 25)	-24.0 (-81, 1200)	-25.0 (-81, 1200)
				Within group p-value	0.0005	0.0054	0.0000
Min dental plaque acidogenicity (pH)	Measured value	Screening	N		20	36	56
				Mean (SD)	5.905 (0.677)	5.778 (0.673)	5.823 (0.671)
				Median (Min, Max)	6.025 (4.05, 6.95)	5.900 (3.80, 6.80)	5.950 (3.80, 6.95)
		Visit 3	N		20	35	55
				Mean (SD)	6.210 (0.275)	6.117 (0.484)	6.151 (0.420)
				Median (Min, Max)	6.300 (5.55, 6.60)	6.150 (5.05, 6.80)	6.250 (5.05, 6.80)
		Visit 4	N		20	36	56
				Mean (SD)	6.308 (0.366)	6.143 (0.494)	6.202 (0.456)
				Median (Min, Max)	6.275 (5.55, 6.90)	6.250 (5.05, 7.00)	6.250 (5.05, 7.00)
		Visit 5	N		20	35	55
				Mean (SD)	6.310 (0.275)	6.369 (0.311)	6.347 (0.297)
				Median (Min, Max)	6.350 (5.65, 6.75)	6.450 (5.55, 7.10)	6.350 (5.55, 7.10)
	Absolute change from baseline	Visit 3	N		20	35	55
				Mean (SD)	0.305 (0.624)	0.360 (0.635)	0.340 (0.626)
				Median (Min, Max)	0.400 (-0.85, 1.50)	0.350 (-1.30, 1.80)	0.350 (-1.30, 1.80)
		Visit 4		Within group p-value	0.0207	0.0008	0.0000
			N		20	36	56
				Mean (SD)	0.403 (0.635)	0.365 (0.663)	0.379 (0.648)
				Median (Min, Max)	0.375 (-0.50, 2.15)	0.300 (-0.85, 2.05)	0.325 (-0.85, 2.15)
		Visit 5		Within group p-value	0.0062	0.0025	0.0000
			N		20	35	55
				Mean (SD)	0.405 (0.757)	0.594 (0.750)	0.525 (0.752)
				Median (Min, Max)	0.175 (-0.60, 2.55)	0.550 (-0.80, 2.80)	0.500 (-0.80, 2.80)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
	Relative change from baseline (%)		Visit 3	Within group p-value	0.0616	0.0000	0.0000
				N	20	35	55
				Mean (SD)	6.5 (12.4)	7.5 (12.7)	7.1 (12.5)
			Visit 4	Median (Min, Max)	7.0 (-13, 37)	6.0 (-19, 39)	6.0 (-19, 39)
				Within group p-value	0.0208	0.0007	0.0000
				N	20	36	56
			Visit 5	Mean (SD)	8.2 (13.9)	7.5 (13.7)	7.7 (13.6)
				Median (Min, Max)	6.5 (-8, 53)	4.5 (-13, 46)	5.5 (-13, 53)
				Within group p-value	0.0047	0.0022	0.0000
			Visit 5	N	20	35	55
				Mean (SD)	8.5 (16.8)	12.0 (16.3)	10.7 (16.4)
				Median (Min, Max)	3.0 (-9, 63)	10.0 (-12, 74)	8.0 (-12, 74)
				Within group p-value	0.0583	0.0000	0.0000
	Max change from baseline dental plaque acidogenicity (pH)	Measured value	Screening	N	20	36	56
				Mean (SD)	-0.045 (0.242)	-0.010 (0.375)	-0.022 (0.331)
				Median (Min, Max)	-0.050 (-0.75, 0.40)	0.000 (-0.75, 0.90)	-0.025 (-0.75, 0.90)
			Visit 3	N	20	35	55
				Mean (SD)	-0.035 (0.251)	-0.044 (0.298)	-0.041 (0.279)
				Median (Min, Max)	0.050 (-0.60, 0.55)	-0.050 (-0.85, 0.65)	0.000 (-0.85, 0.65)
			Visit 4	N	20	36	56
				Mean (SD)	0.045 (0.220)	-0.099 (0.240)	-0.047 (0.241)
				Median (Min, Max)	0.050 (-0.55, 0.40)	-0.075 (-0.90, 0.30)	-0.025 (-0.90, 0.40)
			Visit 5	N	20	35	55
				Mean (SD)	-0.030 (0.183)	-0.074 (0.209)	-0.058 (0.199)
				Median (Min, Max)	-0.050 (-0.40, 0.35)	-0.100 (-0.45, 0.40)	-0.050 (-0.45, 0.40)
		Absolute change from baseline	Visit 3	N	20	35	55

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
		Relative change from baseline (%)	Visit 4	Mean (SD)	0.010 (0.410)	-0.029 (0.300)	-0.015 (0.341)
				Median (Min, Max)	0.125 (-1.00, 0.80)	0.050 (-0.60, 0.40)	0.050 (-1.00, 0.80)
				Within group p-value	0.6155	0.7126	0.8889
			Visit 5	N	20	36	56
				Mean (SD)	0.090 (0.290)	-0.089 (0.462)	-0.025 (0.415)
				Median (Min, Max)	0.100 (-0.55, 0.60)	-0.050 (-1.75, 0.70)	0.050 (-1.75, 0.70)
				Within group p-value	0.0772	0.3884	0.8947
			Visit 3	N	20	35	55
				Mean (SD)	0.015 (0.272)	-0.071 (0.381)	-0.040 (0.345)
				Median (Min, Max)	0.050 (-0.45, 0.55)	-0.100 (-0.75, 0.80)	-0.050 (-0.75, 0.80)
				Within group p-value	0.8671	0.2570	0.4254
			Visit 4	N	17	31	48
				Mean (SD)	-163.2 (132.5)	-50.5 (200.3)	-90.4 (185.8)
				Median (Min, Max)	-175.0 (-400, 100)	-86.0 (-400, 700)	-94.5 (-400, 700)
				Within group p-value	0.0003	0.0209	0.0000
			Visit 5	N	17	32	49
				Mean (SD)	-144.8 (147.9)	-115.7 (147.7)	-125.8 (146.9)
				Median (Min, Max)	-100.0 (-400, 100)	-89.5 (-700, 100)	-94.0 (-700, 100)
				Within group p-value	0.0006	0.0000	0.0000
			Visit 5	N	17	31	48
				Mean (SD)	-103.2 (216.8)	-111.7 (136.1)	-108.7 (166.9)
				Median (Min, Max)	-150.0 (-400, 500)	-100.0 (-450, 150)	-112.0 (-450, 500)
				Within group p-value	0.0301	0.0000	0.0000
Site 1	Min change from baseline dental plaque acidogenicity (pH)	Measured value	Screening	N	20	36	56
				Mean (SD)	-1.445 (0.696)	-1.428 (0.643)	-1.434 (0.656)
				Median (Min, Max)	-1.300 (-3.20, -0.70)	-1.400 (-2.80, -0.10)	-1.400 (-3.20, -0.10)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Female		Male	Total	
			Visit 3	N	20	35	55	
				Mean (SD)	-0.985 (0.318)	-1.151 (0.543)	-1.091 (0.477)	
				Median (Min, Max)	-1.000 (-1.50, -0.30)	-1.000 (-2.90, -0.30)	-1.000 (-2.90, -0.30)	
			Visit 4	N	20	36	56	
				Mean (SD)	-0.975 (0.422)	-1.092 (0.488)	-1.050 (0.465)	
				Median (Min, Max)	-0.950 (-1.60, -0.30)	-0.900 (-2.30, -0.20)	-0.900 (-2.30, -0.20)	
			Visit 5	N	20	35	55	
				Mean (SD)	-0.955 (0.366)	-1.037 (0.435)	-1.007 (0.410)	
				Median (Min, Max)	-1.000 (-1.60, -0.40)	-1.000 (-2.00, -0.20)	-1.000 (-2.00, -0.20)	
			Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	0.460 (0.709)	0.291 (0.706)	0.353 (0.705)
					Median (Min, Max)	0.400 (-0.60, 2.10)	0.200 (-1.20, 2.10)	0.300 (-1.20, 2.10)
					Within group p-value	0.0097	0.0348	0.0009
				Visit 4	N	20	36	56
					Mean (SD)	0.470 (0.663)	0.336 (0.772)	0.384 (0.732)
					Median (Min, Max)	0.500 (-0.60, 2.20)	0.300 (-2.10, 2.20)	0.300 (-2.10, 2.20)
					Within group p-value	0.0049	0.0026	0.0000
				Visit 5	N	20	35	55
					Mean (SD)	0.490 (0.707)	0.411 (0.618)	0.440 (0.646)
					Median (Min, Max)	0.350 (-0.50, 2.20)	0.400 (-0.80, 1.90)	0.400 (-0.80, 2.20)
					Within group p-value	0.0073	0.0004	0.0000
			Relative change from baseline (%)	Visit 3	N	20	35	55
					Mean (SD)	-19.7 (41.1)	23.3 (209.7)	7.6 (169.4)
					Median (Min, Max)	-30.0 (-75, 67)	-20.0 (-83, 1200)	-21.0 (-83, 1200)
					Within group p-value	0.0451	0.1777	0.0203
				Visit 4	N	20	36	56
Mean (SD)	-19.7 (41.1)	23.3 (209.7)			7.6 (169.4)			
Median (Min, Max)	-30.0 (-75, 67)	-20.0 (-83, 1200)			-21.0 (-83, 1200)			
Within group p-value	0.0451	0.1777			0.0203			



Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Visit 5	Mean (SD)	-23.4 (41.1)	42.4 (356.0)	18.9 (286.7)
				Median (Min, Max)	-33.0 (-71, 86)	-27.0 (-81, 2100)	-29.5 (-81, 2100)
				Within group p-value	0.0155	0.0619	0.0034
				N	20	35	55
				Mean (SD)	-23.0 (41.1)	-2.5 (112.3)	-10.0 (92.9)
				Median (Min, Max)	-33.0 (-76, 71)	-29.0 (-80, 600)	-30.0 (-80, 600)
				Within group p-value	0.0395	0.0275	0.0023
	Min dental plaque acidogenicity (pH)	Measured value	Screening	N	20	36	56
				Mean (SD)	5.810 (0.789)	5.756 (0.635)	5.775 (0.687)
				Median (Min, Max)	5.950 (4.00, 6.90)	5.900 (4.30, 6.70)	5.900 (4.00, 6.90)
			Visit 3	N	20	35	55
				Mean (SD)	6.220 (0.309)	6.071 (0.551)	6.125 (0.480)
				Median (Min, Max)	6.250 (5.50, 6.70)	6.200 (4.70, 6.80)	6.200 (4.70, 6.80)
			Visit 4	N	20	36	56
				Mean (SD)	6.240 (0.395)	6.111 (0.509)	6.157 (0.472)
				Median (Min, Max)	6.300 (5.60, 6.90)	6.200 (4.90, 6.90)	6.250 (4.90, 6.90)
			Visit 5	N	20	35	55
				Mean (SD)	6.220 (0.302)	6.303 (0.343)	6.273 (0.328)
				Median (Min, Max)	6.300 (5.60, 6.70)	6.400 (5.60, 7.10)	6.300 (5.60, 7.10)
		Absolute change from baseline	Visit 3	N	20	35	55
				Mean (SD)	0.410 (0.700)	0.337 (0.608)	0.364 (0.638)
				Median (Min, Max)	0.450 (-0.80, 1.70)	0.300 (-1.10, 1.80)	0.300 (-1.10, 1.80)
				Within group p-value	0.0171	0.0020	0.0001
			Visit 4	N	20	36	56
				Mean (SD)	0.430 (0.678)	0.356 (0.685)	0.382 (0.677)
				Median (Min, Max)	0.400 (-0.60, 2.10)	0.300 (-1.40, 2.20)	0.300 (-1.40, 2.20)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
		Relative change from baseline (%)	Visit 5	Within group p-value	0.0099	0.0018	0.0000
				N	20	35	55
				Mean (SD)	0.410 (0.848)	0.554 (0.696)	0.502 (0.750)
				Median (Min, Max)	0.100 (-0.50, 2.30)	0.600 (-0.60, 2.30)	0.500 (-0.60, 2.30)
			Visit 3	Within group p-value	0.0851	0.0000	0.0000
				N	20	35	55
				Mean (SD)	9.0 (15.3)	6.7 (11.8)	7.5 (13.1)
				Median (Min, Max)	7.5 (-12, 43)	5.0 (-16, 40)	5.0 (-16, 43)
			Visit 4	Within group p-value	0.0154	0.0012	0.0000
				N	20	36	56
				Mean (SD)	9.2 (15.0)	7.2 (13.4)	7.9 (13.9)
				Median (Min, Max)	6.0 (-9, 48)	5.0 (-21, 51)	5.0 (-21, 51)
			Visit 5	Within group p-value	0.0093	0.0015	0.0000
				N	20	35	55
				Mean (SD)	9.5 (19.1)	11.0 (14.0)	10.5 (15.9)
				Median (Min, Max)	2.0 (-8, 58)	10.0 (-9, 53)	8.0 (-9, 58)
				Within group p-value	0.0853	0.0000	0.0000
	Max change from baseline dental plaque acidogenicity (pH)	Measured value	Screening	N	20	36	56
				Mean (SD)	0.070 (0.260)	0.100 (0.398)	0.089 (0.352)
				Median (Min, Max)	0.000 (-0.60, 0.50)	0.150 (-0.60, 1.10)	0.100 (-0.60, 1.10)
			Visit 3	N	20	35	55
				Mean (SD)	0.110 (0.261)	0.077 (0.322)	0.089 (0.299)
				Median (Min, Max)	0.150 (-0.50, 0.60)	0.100 (-0.60, 0.80)	0.100 (-0.60, 0.80)
			Visit 4	N	20	36	56
				Mean (SD)	0.180 (0.265)	0.031 (0.251)	0.084 (0.263)
				Median (Min, Max)	0.200 (-0.50, 0.60)	0.000 (-0.60, 0.50)	0.100 (-0.60, 0.60)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female		Male	Total
Absolute change from baseline			Visit 5	N	20		35	55
				Mean (SD)	0.040 (0.239)		-0.014 (0.261)	0.005 (0.253)
				Median (Min, Max)	0.050 (-0.30, 0.60)		0.000 (-0.50, 0.60)	0.000 (-0.50, 0.60)
			Visit 3	N	20		35	55
				Mean (SD)	0.040 (0.415)		-0.014 (0.401)	0.005 (0.403)
				Median (Min, Max)	0.100 (-0.90, 0.60)		0.000 (-0.70, 1.00)	0.100 (-0.90, 1.00)
				Within group p-value	0.5210		0.7589	0.7281
			Visit 4	N	20		36	56
				Mean (SD)	0.110 (0.357)		-0.069 (0.480)	-0.005 (0.445)
				Median (Min, Max)	0.200 (-0.90, 0.60)		0.000 (-1.60, 0.60)	0.000 (-1.60, 0.60)
				Within group p-value	0.1048		0.5864	0.6403
			Visit 5	N	20		35	55
				Mean (SD)	-0.030 (0.321)		-0.117 (0.445)	-0.085 (0.403)
				Median (Min, Max)	-0.050 (-0.70, 0.60)		-0.100 (-1.00, 0.90)	-0.100 (-1.00, 0.90)
				Within group p-value	0.7298		0.0974	0.1129
Relative change from baseline (%)			Visit 3	N	15		33	48
				Mean (SD)	-139.4 (175.9)		-67.5 (137.3)	-90.0 (152.3)
				Median (Min, Max)	-100.0 (-500, 200)		-75.0 (-350, 300)	-100.0 (-500, 300)
				Within group p-value	0.0112		0.0023	0.0000
			Visit 4	N	15		34	49
				Mean (SD)	-72.6 (190.8)		-113.1 (164.0)	-100.7 (171.6)
				Median (Min, Max)	-67.0 (-500, 300)		-100.0 (-600, 400)	-100.0 (-600, 400)
				Within group p-value	0.1406		0.0000	0.0000
			Visit 5	N	15		34	49
				Mean (SD)	-77.9 (151.3)		-84.9 (98.6)	-82.8 (115.6)
				Median (Min, Max)	-100.0 (-300, 200)		-80.0 (-300, 150)	-80.0 (-300, 200)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Female				Male				Total			
				Within group p-value		0.0703		0.0000		0.0000					
Site 2	Min change from baseline dental plaque acidogenicity (pH)	Measured value	Screening	N		20		36		56					
				Mean (SD)		-1.305 (0.508)		-1.453 (0.682)		-1.400 (0.625)					
				Median (Min, Max)		-1.200 (-2.40, -0.70)		-1.400 (-3.80, -0.10)		-1.300 (-3.80, -0.10)					
			Visit 3	N		20		35		55					
				Mean (SD)		-1.040 (0.338)		-1.137 (0.500)		-1.102 (0.447)					
				Median (Min, Max)		-1.100 (-1.70, -0.40)		-0.900 (-2.20, -0.20)		-1.100 (-2.20, -0.20)					
			Visit 4	N		20		36		56					
				Mean (SD)		-0.870 (0.440)		-1.083 (0.486)		-1.007 (0.477)					
				Median (Min, Max)		-0.800 (-1.70, -0.20)		-1.050 (-2.10, -0.30)		-0.900 (-2.10, -0.20)					
		Visit 5	N		20		35		55						
			Mean (SD)		-0.805 (0.291)		-0.951 (0.413)		-0.898 (0.377)						
			Median (Min, Max)		-0.750 (-1.50, -0.30)		-0.900 (-2.10, -0.30)		-0.800 (-2.10, -0.30)						
		Absolute change from baseline	Visit 3	N		20		35		55					
				Mean (SD)		0.265 (0.612)		0.331 (0.745)		0.307 (0.694)					
				Median (Min, Max)		0.150 (-0.90, 1.70)		0.200 (-1.80, 2.20)		0.200 (-1.80, 2.20)					
					Within group p-value		0.0674		0.0024		0.0003				
			Visit 4	N		20		36		56					
				Mean (SD)		0.435 (0.621)		0.369 (0.741)		0.393 (0.696)					
	Median (Min, Max)				0.450 (-0.70, 1.90)		0.250 (-1.50, 2.10)		0.300 (-1.50, 2.10)						
				Within group p-value		0.0051		0.0023		0.0000					
	Visit 5		N		20		35		55						
		Mean (SD)		0.500 (0.512)		0.517 (0.729)		0.511 (0.653)							
		Median (Min, Max)		0.300 (-0.10, 1.50)		0.500 (-0.70, 2.80)		0.400 (-0.70, 2.80)							
			Within group p-value		0.0001		0.0001		0.0000						
	Relative change from baseline (%)	Visit 3	N		20		35		55						

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Visit 4	Mean (SD)	-8.0 (49.9)	33.5 (309.3)	18.4 (248.0)
				Median (Min, Max)	-13.0 (-71, 129)	-18.0 (-91, 1800)	-18.0 (-91, 1800)
				Within group p-value	0.2884	0.0095	0.0065
			Visit 5	N	20	36	56
				Mean (SD)	-26.8 (41.2)	21.6 (256.4)	4.3 (207.3)
				Median (Min, Max)	-32.5 (-86, 70)	-23.5 (-83, 1500)	-27.5 (-86, 1500)
				Within group p-value	0.0145	0.0155	0.0005
				N	20	35	55
				Mean (SD)	-32.1 (28.6)	-6.5 (129.1)	-15.8 (104.6)
				Median (Min, Max)	-29.0 (-75, 14)	-33.0 (-83, 700)	-33.0 (-83, 700)
				Within group p-value	0.0001	0.0040	0.0000
	Min dental plaque acidogenicity (pH)	Measured value	Screening	N	20	36	56
				Mean (SD)	5.950 (0.612)	5.731 (0.749)	5.809 (0.705)
				Median (Min, Max)	6.000 (4.10, 7.00)	5.850 (3.30, 7.00)	5.950 (3.30, 7.00)
			Visit 3	N	20	35	55
				Mean (SD)	6.165 (0.327)	6.086 (0.502)	6.115 (0.444)
				Median (Min, Max)	6.200 (5.30, 6.60)	6.100 (5.00, 6.80)	6.200 (5.00, 6.80)
			Visit 4	N	20	36	56
				Mean (SD)	6.345 (0.427)	6.119 (0.544)	6.200 (0.513)
				Median (Min, Max)	6.400 (5.50, 6.90)	6.250 (4.90, 7.10)	6.300 (4.90, 7.10)
			Visit 5	N	20	35	55
				Mean (SD)	6.370 (0.283)	6.389 (0.359)	6.382 (0.331)
				Median (Min, Max)	6.400 (5.60, 6.80)	6.400 (5.30, 7.10)	6.400 (5.30, 7.10)
		Absolute change from baseline	Visit 3	N	20	35	55
				Mean (SD)	0.215 (0.586)	0.377 (0.754)	0.318 (0.696)
				Median (Min, Max)	0.350 (-0.80, 1.30)	0.300 (-1.70, 1.80)	0.300 (-1.70, 1.80)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
		Relative change from baseline (%)	Visit 4	Within group p-value	0.1246	0.0014	0.0004
				N	20	36	56
				Mean (SD)	0.395 (0.706)	0.389 (0.715)	0.391 (0.705)
				Median (Min, Max)	0.300 (-0.70, 2.60)	0.350 (-0.80, 1.90)	0.300 (-0.80, 2.60)
			Visit 5	Within group p-value	0.0103	0.0029	0.0001
				N	20	35	55
				Mean (SD)	0.420 (0.727)	0.660 (0.825)	0.573 (0.793)
				Median (Min, Max)	0.400 (-0.80, 2.60)	0.600 (-1.00, 3.20)	0.500 (-1.00, 3.20)
			Visit 3	Within group p-value	0.0099	0.0000	0.0000
				N	20	35	55
				Mean (SD)	4.6 (10.7)	8.3 (15.7)	6.9 (14.1)
				Median (Min, Max)	6.0 (-12, 29)	5.0 (-25, 55)	5.0 (-25, 55)
			Visit 4	Within group p-value	0.0952	0.0016	0.0003
				N	20	36	56
				Mean (SD)	7.9 (15.4)	8.3 (15.5)	8.2 (15.3)
				Median (Min, Max)	5.0 (-11, 63)	6.5 (-12, 55)	5.0 (-12, 63)
			Visit 5	Within group p-value	0.0110	0.0020	0.0001
				N	20	35	55
				Mean (SD)	8.4 (15.5)	13.9 (19.9)	11.9 (18.5)
				Median (Min, Max)	7.0 (-11, 63)	11.0 (-14, 97)	8.0 (-14, 97)
				Within group p-value	0.0086	0.0000	0.0000
Max change from baseline dental plaque acidogenicity (pH)	Measured value		Screening	N	20	36	56
				Mean (SD)	0.160 (0.223)	0.164 (0.386)	0.163 (0.335)
				Median (Min, Max)	0.200 (-0.40, 0.50)	0.200 (-0.90, 1.20)	0.200 (-0.90, 1.20)
			Visit 3	N	20	35	55
				Mean (SD)	0.105 (0.286)	0.054 (0.294)	0.073 (0.290)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
		Absolute change from baseline	Visit 4	Median (Min, Max)	0.100 (-0.50, 0.70)	0.000 (-0.50, 0.70)	0.100 (-0.50, 0.70)
				N	20	36	56
				Mean (SD)	0.190 (0.213)	-0.008 (0.275)	0.063 (0.270)
			Visit 5	Median (Min, Max)	0.200 (-0.30, 0.60)	0.000 (-0.80, 0.50)	0.050 (-0.80, 0.60)
				N	20	35	55
				Mean (SD)	0.120 (0.228)	0.071 (0.204)	0.089 (0.212)
			Visit 3	Median (Min, Max)	0.100 (-0.30, 0.50)	0.100 (-0.40, 0.50)	0.100 (-0.40, 0.50)
				N	20	35	55
				Mean (SD)	-0.055 (0.359)	-0.111 (0.325)	-0.091 (0.336)
			Visit 4	Median (Min, Max)	0.000 (-0.90, 0.50)	-0.100 (-0.90, 0.80)	-0.100 (-0.90, 0.80)
				Within group p-value	0.7915	0.0409	0.0780
				N	20	36	56
			Visit 5	Mean (SD)	0.030 (0.270)	-0.172 (0.504)	-0.100 (0.443)
				Median (Min, Max)	0.100 (-0.40, 0.40)	-0.150 (-1.60, 0.90)	0.000 (-1.60, 0.90)
				Within group p-value	0.6123	0.0628	0.1660
			Visit 3	N	20	35	55
				Mean (SD)	-0.040 (0.312)	-0.109 (0.400)	-0.084 (0.369)
				Median (Min, Max)	-0.100 (-0.40, 0.60)	-0.200 (-0.90, 1.10)	-0.100 (-0.90, 1.10)
			Visit 4	Within group p-value	0.4223	0.0622	0.0558
				N	17	34	51
				Mean (SD)	-76.8 (176.8)	-44.2 (105.7)	-55.1 (132.7)
			Visit 3	Median (Min, Max)	-50.0 (-600, 200)	-69.0 (-200, 400)	-63.0 (-600, 400)
				Within group p-value	0.0729	0.0007	0.0001
			Visit 4	N	17	35	52
				Mean (SD)	-17.1 (165.5)	-102.1 (137.7)	-74.3 (151.2)
				Median (Min, Max)	-60.0 (-400, 400)	-100.0 (-400, 400)	-100.0 (-400, 400)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Female	Male	Total
			Within group p-value	0.3367	0.0000	0.0000
			Visit 5 N	17	34	51
			Mean (SD)	-111.2 (203.5)	-89.0 (89.0)	-96.4 (136.3)
			Median (Min, Max)	-100.0 (-600, 200)	-100.0 (-300, 100)	-100.0 (-600, 200)
			Within group p-value	0.0145	0.0000	0.0000

Data based on Per Protocol Set population.

SM17\_02\_B Minimum and Maximum Dental Plaque Acidogenicity Measurements, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:54:59

Table 14.3-8 AUC dental plaque acidogenicity (PPS) (Part 1)

				ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)
Subcategory of Measurement	Assessment (unit)	Result Category					
Mean	AUC Acidogenicity pH 6.2 baseline (min*pH)	Measured value	N	18	18	18	18
			Mean (SD)	-54.0 (21.7)	-55.3 (24.3)	-12.3 (32.7)	-45.3 (15.4)
			Median (Min, Max)	-54.5 (-91, -20)	-52.5 (-111, -12)	-11.5 (-85, 41)	-45.3 (-72, -22)
	AUC Acidogenicity pH 5.5 baseline (min*pH)	Measured value	N	18	18	18	18
			Mean (SD)	-96.0 (21.7)	-99.0 (28.8)	-54.3 (32.7)	-87.3 (15.4)
			Median (Min, Max)	-96.5 (-133, -62)	-94.5 (-182, -54)	-53.5 (-127, -1)	-87.3 (-114, -64)
Site 1	AUC Acidogenicity pH 6.2 baseline (min*pH)	Measured value	N	18	18	18	18
			Mean (SD)	-52.4 (22.0)	-55.2 (28.0)	-11.2 (32.4)	-44.3 (14.3)
			Median (Min, Max)	-52.7 (-89, -15)	-51.3 (-131, -9)	-13.7 (-87, 40)	-46.0 (-68, -17)
	AUC Acidogenicity pH 5.5 baseline (min*pH)	Measured value	N	18	18	18	18
			Mean (SD)	-94.4 (22.0)	-98.9 (33.1)	-53.2 (32.4)	-86.3 (14.3)
			Median (Min, Max)	-94.7 (-131, -57)	-93.3 (-203, -51)	-55.7 (-129, -3)	-88.0 (-110, -59)
Site 2	AUC Acidogenicity pH 6.2 baseline (min*pH)	Measured value	N	18	18	18	18
			Mean (SD)	-55.7 (23.5)	-55.4 (22.1)	-13.4 (33.8)	-46.3 (17.1)



			ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)
Subcategory of Measurement	Assessment (unit)	Result Category				
		Median (Min, Max)	-54.3 (-107, -21)	-55.4 (-91, -13)	-10.6 (-83, 42)	-43.0 (-75, -21)
AUC Acidogenicity pH 5.5 baseline (min*pH)	Measured value	N	18	18	18	18
		Mean (SD)	-97.7 (23.5)	-99.1 (25.6)	-55.4 (33.8)	-88.3 (17.1)
		Median (Min, Max)	-96.3 (-149, -63)	-97.4 (-162, -55)	-52.6 (-125, 0)	-85.0 (-117, -63)

Data based on Per Protocol Set population.

SM17\_02\_A AUC Dental Plaque Acidogenicity, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:43:54

*Table 14.3-9 AUC dental plaque acidogenicity (values over baseline set to zero) (PPS) (Part 1)*

				ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)
Subcategory of Measurement	Assessment (unit)	Result Category					
Mean	AUC Acidogenicity pH 6.2 baseline (no negative AUC) (min*pH)	Measured value	N	18	18	18	18
			Mean (SD)	0.0 (0.0)	0.0 (0.0)	9.7 (12.1)	0.0 (0.0)
			Median (Min, Max)	0.0 (0, 0)	0.0 (0, 0)	5.7 (0, 41)	0.0 (0, 0)
			Geometric Mean (CV%)	(%)	(%)	6.8 (125.5%)	(%)
	AUC Acidogenicity pH 5.5 baseline (no negative AUC) (min*pH)	Measured value	N	18	18	18	18
			Mean (SD)	0.0 (0.0)	0.0 (0.0)	1.5 (3.6)	0.0 (0.0)
			Median (Min, Max)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 13)	0.0 (0, 0)
			Geometric Mean (CV%)	(%)	(%)	3.2 (232.3%)	(%)
Site 1	AUC Acidogenicity pH 6.2 baseline (no negative AUC) (min*pH)	Measured value	N	18	18	18	18
			Mean (SD)	0.0 (0.0)	0.0 (0.0)	10.1 (12.1)	0.0 (0.0)
			Median (Min, Max)	0.0 (0, 0)	0.0 (0, 0)	5.6 (0, 40)	0.0 (0, 0)
			Geometric Mean (CV%)	(%)	(%)	8.6 (120.8%)	(%)
	AUC Acidogenicity pH 5.5 baseline (no negative AUC) (min*pH)	Measured value	N	18	18	18	18
			Mean (SD)	0.0 (0.0)	0.0 (0.0)	1.6 (3.7)	0.0 (0.0)
			Median (Min, Max)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 14)	0.0 (0, 0)

				ZYN® Smooth 3 mg	ZYN® Peppermint 3 mg	Sucrose (pos control)	Xylitol (neg control)
Subcategory of Measurement	Assessment (unit)	Result Category					
			Geometric Mean (CV%)	(%)	(%)	2.3 (236.2%)	(%)
Site 2	AUC Acidogenicity pH 6.2 baseline (no negative AUC) (min*pH)	Measured value	N	18	18	18	18
			Mean (SD)	0.0 (0.0)	0.0 (0.0)	9.8 (12.4)	0.0 (0.0)
			Median (Min, Max)	0.0 (0, 0)	0.0 (0, 0)	5.8 (0, 42)	0.0 (0, 0)
			Geometric Mean (CV%)	(%)	(%)	8.9 (126.2%)	(%)
	AUC Acidogenicity pH 5.5 baseline (no negative AUC) (min*pH)	Measured value	N	18	18	18	18
			Mean (SD)	0.0 (0.0)	0.0 (0.0)	1.6 (3.5)	0.0 (0.0)
			Median (Min, Max)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 12)	0.0 (0, 0)
			Geometric Mean (CV%)	(%)	(%)	1.5 (220.3%)	(%)

Data based on Per Protocol Set population.

SM17\_02\_A AUC Dental Plaque Acidogenicity (values over baseline set to zero), SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:43:54

Table 14.3-10 AUC dental plaque acidogenicity (PPS) (Part 2)

					Female	Male	Total
Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name				
Mean	AUC Acidogenicity pH 6.2 baseline (min*pH)	Measured value	Screening	N	20	36	56
				Mean (SD)	-23.0 (21.0)	-19.4 (26.8)	-20.7 (24.8)
				Median (Min, Max)	-23.3 (-61, 12)	-23.2 (-67, 28)	-23.2 (-67, 28)
			Visit 3	N	20	35	55
				Mean (SD)	-31.9 (18.8)	-27.0 (22.2)	-28.8 (21.0)
				Median (Min, Max)	-38.2 (-57, 10)	-28.2 (-63, 21)	-33.6 (-63, 21)
			Visit 4	N	20	36	56
				Mean (SD)	-35.6 (16.6)	-27.1 (20.8)	-30.1 (19.7)
				Median (Min, Max)	-36.1 (-58, 12)	-29.3 (-61, 22)	-32.6 (-61, 22)
			Visit 5	N	20	35	55

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
	Absolute change from baseline		Visit 3	Mean (SD)	-33.0 (11.4)	-37.0 (12.3)	-35.5 (12.0)
				Median (Min, Max)	-33.7 (-53, -9)	-37.3 (-74, -7)	-36.3 (-74, -7)
				N	20	35	55
			Visit 4	Mean (SD)	-8.9 (22.5)	-8.6 (25.0)	-8.7 (23.9)
				Median (Min, Max)	-9.0 (-37, 59)	-6.6 (-70, 36)	-9.0 (-70, 59)
				Within group p-value	0.0320	0.0709	0.0061
			Visit 5	N	20	36	56
				Mean (SD)	-12.6 (23.9)	-7.7 (27.7)	-9.4 (26.3)
				Median (Min, Max)	-16.4 (-65, 24)	-5.8 (-62, 55)	-8.6 (-65, 55)
				Within group p-value	0.0266	0.1137	0.0100
	Relative change from baseline (%)		Visit 3	N	20	35	55
				Mean (SD)	-10.0 (23.9)	-16.9 (30.2)	-14.4 (28.0)
				Median (Min, Max)	-6.9 (-64, 26)	-18.3 (-70, 41)	-15.4 (-70, 41)
			Visit 4	Within group p-value	0.1327	0.0030	0.0008
				N	20	35	55
				Mean (SD)	-15.6 (299.2)	-690.4 (3617.5)	-445.0 (2894.6)
			Visit 5	Median (Min, Max)	19.0 (-935, 481)	-28.0 (-21400, 358)	-6.0 (-21400, 481)
				Within group p-value	0.4358	0.0678	0.2821
			Visit 3	N	20	36	56
				Mean (SD)	-69.7 (390.2)	-571.5 (2689.3)	-392.3 (2171.1)
				Median (Min, Max)	-1.0 (-1323, 450)	-32.5 (-16100, 365)	-23.5 (-16100, 450)
			Visit 4	Within group p-value	0.7285	0.0299	0.1283
				N	20	35	55
				Mean (SD)	-122.4 (391.1)	-419.8 (1377.1)	-311.6 (1126.4)
			Visit 5	Median (Min, Max)	-17.5 (-1342, 301)	-33.0 (-7500, 500)	-23.0 (-7500, 500)
				Within group p-value	0.3934	0.0824	0.0616

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
AUC Acidogenicity pH 5.5 baseline (min*pH)	Measured value	Screening	N		20	36	56
			Mean (SD)		-65.0 (21.0)	-61.4 (26.8)	-62.7 (24.8)
			Median (Min, Max)		-65.3 (-103, -30)	-65.2 (-109, -14)	-65.2 (-109, -14)
			Visit 3	N	20	35	55
				Mean (SD)	-73.9 (18.8)	-69.0 (22.1)	-70.8 (20.9)
				Median (Min, Max)	-80.2 (-99, -32)	-70.2 (-105, -21)	-75.6 (-105, -21)
			Visit 4	N	20	36	56
				Mean (SD)	-77.6 (16.6)	-69.1 (20.8)	-72.1 (19.7)
				Median (Min, Max)	-78.1 (-100, -31)	-71.3 (-103, -20)	-74.6 (-103, -20)
			Visit 5	N	20	35	55
				Mean (SD)	-75.0 (11.4)	-79.0 (12.3)	-77.5 (12.0)
				Median (Min, Max)	-75.7 (-95, -51)	-79.3 (-116, -49)	-78.3 (-116, -49)
	Absolute change from baseline	Visit 3	N		20	35	55
			Mean (SD)		-8.9 (22.5)	-8.6 (24.9)	-8.7 (23.9)
			Median (Min, Max)		-9.0 (-37, 59)	-6.5 (-70, 36)	-9.0 (-70, 59)
			Within group p-value		0.0320	0.0709	0.0061
		Visit 4	N		20	36	56
			Mean (SD)		-12.6 (23.9)	-7.7 (27.7)	-9.4 (26.3)
			Median (Min, Max)		-16.4 (-65, 24)	-5.8 (-62, 55)	-8.6 (-65, 55)
			Within group p-value		0.0266	0.1137	0.0100
		Visit 5	N		20	35	55
			Mean (SD)		-10.0 (23.9)	-16.9 (30.2)	-14.4 (28.0)
			Median (Min, Max)		-6.9 (-64, 26)	-18.3 (-70, 41)	-15.4 (-70, 41)
			Within group p-value		0.1327	0.0030	0.0008
	Relative change from baseline (%)	Visit 3	N		20	35	55
			Mean (SD)		21.3 (34.7)	40.3 (88.1)	33.4 (73.5)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Visit 4	Median (Min, Max)	17.5 (-63, 75)	16.0 (-64, 351)	16.0 (-64, 351)
				Within group p-value	0.0091	0.0147	0.0004
				N	20	36	56
				Mean (SD)	31.6 (55.1)	42.3 (93.4)	38.5 (81.4)
			Visit 5	Median (Min, Max)	24.5 (-26, 208)	8.5 (-73, 317)	13.0 (-73, 317)
				Within group p-value	0.0140	0.0332	0.0012
				N	20	35	55
				Mean (SD)	30.7 (58.9)	72.3 (125.4)	57.2 (107.4)
				Median (Min, Max)	9.5 (-30, 202)	31.0 (-37, 456)	25.0 (-37, 456)
				Within group p-value	0.0842	0.0004	0.0001
	AUC Acidogenicity pH 6.2 baseline (no negative AUC) (min*pH)	Measured value	Screening	N	20	36	56
				Mean (SD)	4.3 (6.2)	7.9 (11.1)	6.6 (9.7)
				Median (Min, Max)	0.9 (0, 19)	1.6 (0, 39)	1.1 (0, 39)
			Visit 3	N	20	35	55
				Mean (SD)	1.4 (3.5)	3.2 (6.2)	2.6 (5.4)
				Median (Min, Max)	0.0 (0, 13)	0.3 (0, 25)	0.0 (0, 25)
			Visit 4	N	20	36	56
				Mean (SD)	1.0 (3.1)	3.1 (6.6)	2.4 (5.7)
				Median (Min, Max)	0.0 (0, 14)	0.0 (0, 26)	0.0 (0, 26)
			Visit 5	N	20	35	55
				Mean (SD)	0.6 (1.5)	0.4 (1.3)	0.5 (1.4)
				Median (Min, Max)	0.0 (0, 6)	0.0 (0, 7)	0.0 (0, 7)
		Absolute change from baseline	Visit 3	N	20	35	55
				Mean (SD)	-2.9 (5.4)	-5.0 (10.8)	-4.2 (9.2)
				Median (Min, Max)	-0.9 (-14, 9)	-0.5 (-39, 14)	-0.7 (-39, 14)
				Within group p-value	0.0045	0.0049	0.0001

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
		Relative change from baseline (%)	Visit 4	N	20	36	56
				Mean (SD)	-3.2 (5.8)	-4.8 (11.1)	-4.3 (9.5)
				Median (Min, Max)	-0.5 (-19, 2)	-0.6 (-39, 16)	-0.6 (-39, 16)
				Within group p-value	0.0065	0.0042	0.0001
			Visit 5	N	20	35	55
				Mean (SD)	-3.7 (6.7)	-7.6 (11.2)	-6.2 (9.9)
				Median (Min, Max)	-0.8 (-19, 5)	-1.4 (-37, 3)	-1.1 (-37, 5)
				Within group p-value	0.0282	0.0000	0.0000
			Visit 3	N	14	26	40
				Mean (SD)	-91.7 (20.8)	-11.3 (188.7)	-39.5 (156.4)
				Median (Min, Max)	-100.0 (-100, -32)	-85.0 (-100, 667)	-100.0 (-100, 667)
				Within group p-value	0.0001	0.0125	0.0000
			Visit 4	N	14	26	40
				Mean (SD)	-36.0 (178.7)	-56.6 (78.2)	-49.4 (121.1)
				Median (Min, Max)	-100.0 (-100, 575)	-100.0 (-100, 162)	-100.0 (-100, 575)
				Within group p-value	0.0107	0.0014	0.0000
			Visit 5	N	14	25	39
				Mean (SD)	63.6 (340.2)	-77.9 (67.8)	-27.1 (217.3)
				Median (Min, Max)	-100.0 (-100, 925)	-100.0 (-100, 227)	-100.0 (-100, 925)
				Within group p-value	0.4119	0.0000	0.0002
AUC Acidogenicity pH 5.5 baseline (no negative AUC) (min*pH)	Measured value		Screening	N	20	36	56
				Mean (SD)	0.7 (1.9)	1.6 (3.6)	1.3 (3.1)
				Median (Min, Max)	0.0 (0, 8)	0.0 (0, 14)	0.0 (0, 14)
			Visit 3	N	20	35	55
				Mean (SD)	0.0 (0.0)	0.3 (0.9)	0.2 (0.8)
				Median (Min, Max)	0.0 (0, 0)	0.0 (0, 4)	0.0 (0, 4)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
		Absolute change from baseline	Visit 4	N	20	36	56
				Mean (SD)	0.0 (0.0)	0.2 (0.7)	0.1 (0.6)
				Median (Min, Max)	0.0 (0, 0)	0.0 (0, 4)	0.0 (0, 4)
			Visit 5	N	20	35	55
				Mean (SD)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
				Median (Min, Max)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 0)
			Visit 3	N	20	35	55
				Mean (SD)	-0.7 (1.9)	-1.4 (3.5)	-1.1 (3.0)
				Median (Min, Max)	0.0 (-8, 0)	0.0 (-14, 4)	0.0 (-14, 4)
				Within group p-value	0.2500	0.0137	0.0031
			Visit 4	N	20	36	56
				Mean (SD)	-0.7 (1.9)	-1.4 (3.6)	-1.1 (3.1)
				Median (Min, Max)	0.0 (-8, 0)	0.0 (-14, 2)	0.0 (-14, 2)
				Within group p-value	0.2500	0.0220	0.0027
		Relative change from baseline (%)	Visit 5	N	20	35	55
				Mean (SD)	-0.7 (1.9)	-1.7 (3.6)	-1.3 (3.1)
				Median (Min, Max)	0.0 (-8, 0)	0.0 (-14, 0)	0.0 (-14, 0)
				Within group p-value	0.2500	0.0010	0.0001
			Visit 3	N	3	11	14
				Mean (SD)	-100.0 (0.0)	288.2 (1264.3)	205.0 (1121.1)
				Median (Min, Max)	-100.0 (-100, -100)	-100.0 (-100, 4100)	-100.0 (-100, 4100)
				Within group p-value	0.2500	0.0498	0.0096
			Visit 4	N	3	11	14
				Mean (SD)	-100.0 (0.0)	69.0 (479.7)	32.8 (426.9)
				Median (Min, Max)	-100.0 (-100, -100)	-100.0 (-100, 1500)	-100.0 (-100, 1500)
				Within group p-value	0.2500	0.2920	0.1147

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
Site 1	AUC Acidogenicity pH 6.2 baseline (min*pH)	Measured value	Visit 5	N	3	11	14
				Mean (SD)	-100.0 (0.0)	-100.0 (0.0)	-100.0 (0.0)
				Median (Min, Max)	-100.0 (-100, -100)	-100.0 (-100, -100)	-100.0 (-100, -100)
				Within group p-value	0.2500	0.0010	0.0001
			Screening	N	20	36	56
				Mean (SD)	-20.2 (21.4)	-17.5 (26.1)	-18.5 (24.4)
				Median (Min, Max)	-26.4 (-55, 14)	-22.1 (-56, 31)	-23.6 (-56, 31)
			Visit 3	N	20	35	55
				Mean (SD)	-32.2 (19.2)	-26.3 (23.0)	-28.5 (21.7)
				Median (Min, Max)	-37.0 (-60, 10)	-27.5 (-62, 27)	-30.7 (-62, 27)
			Visit 4	N	20	36	56
				Mean (SD)	-33.8 (17.5)	-27.1 (20.6)	-29.5 (19.7)
				Median (Min, Max)	-33.2 (-58, 20)	-31.9 (-58, 23)	-32.1 (-58, 23)
			Visit 5	N	20	35	55
				Mean (SD)	-30.9 (11.8)	-34.5 (12.1)	-33.2 (12.0)
				Median (Min, Max)	-32.0 (-52, -7)	-34.7 (-73, -11)	-34.3 (-73, -7)
		Absolute change from baseline	Visit 3	N	20	35	55
				Mean (SD)	-12.1 (23.0)	-9.9 (26.4)	-10.7 (25.1)
				Median (Min, Max)	-14.3 (-49, 55)	-6.7 (-77, 41)	-13.6 (-77, 55)
				Within group p-value	0.0110	0.0379	0.0011
			Visit 4	N	20	36	56
				Mean (SD)	-13.6 (24.6)	-9.5 (27.6)	-11.0 (26.4)
				Median (Min, Max)	-14.4 (-67, 17)	-13.1 (-67, 56)	-13.1 (-67, 56)
				Within group p-value	0.0328	0.0409	0.0029
			Visit 5	N	20	35	55
				Mean (SD)	-10.8 (25.0)	-16.5 (28.4)	-14.4 (27.1)



Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
	Relative change from baseline (%)			Median (Min, Max)	-7.9 (-65, 21)	-16.7 (-66, 35)	-14.6 (-66, 35)
				Within group p-value	0.1429	0.0022	0.0004
			Visit 3	N	20	35	55
				Mean (SD)	121.7 (3519.4)	-39.9 (350.1)	18.8 (2107.5)
				Median (Min, Max)	13.0 (-9300, 12175)	-4.0 (-1700, 660)	-2.0 (-9300, 12175)
				Within group p-value	0.7080	0.6187	0.8785
			Visit 4	N	20	36	56
				Mean (SD)	330.6 (3619.0)	-60.4 (314.3)	79.2 (2150.1)
				Median (Min, Max)	-8.0 (-6575, 14375)	-14.0 (-1364, 808)	-14.0 (-6575, 14375)
				Within group p-value	0.9636	0.2253	0.2874
			Visit 5	N	20	35	55
				Mean (SD)	131.6 (2775.1)	-38.7 (352.0)	23.2 (1671.7)
				Median (Min, Max)	-34.0 (-5825, 10550)	-17.0 (-879, 1476)	-33.0 (-5825, 10550)
				Within group p-value	0.2732	0.3329	0.1418
AUC Acidogenicity pH 5.5 baseline (min*pH)	Measured value		Screening	N	20	36	56
				Mean (SD)	-62.2 (21.4)	-59.6 (26.1)	-60.5 (24.4)
				Median (Min, Max)	-68.4 (-97, -28)	-64.1 (-98, -11)	-65.6 (-98, -11)
			Visit 3	N	20	35	55
				Mean (SD)	-74.3 (19.2)	-68.3 (23.0)	-70.5 (21.7)
				Median (Min, Max)	-79.0 (-102, -32)	-69.5 (-104, -15)	-72.7 (-104, -15)
			Visit 4	N	20	36	56
				Mean (SD)	-75.8 (17.5)	-69.1 (20.6)	-71.5 (19.6)
				Median (Min, Max)	-75.2 (-100, -22)	-73.9 (-100, -19)	-74.1 (-100, -19)
			Visit 5	N	20	35	55
				Mean (SD)	-72.9 (11.8)	-76.5 (12.1)	-75.2 (12.0)
				Median (Min, Max)	-74.0 (-94, -49)	-76.7 (-115, -53)	-76.3 (-115, -49)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
	Absolute change from baseline		Visit 3	N	20	35	55
				Mean (SD)	-12.1 (23.0)	-9.9 (26.4)	-10.7 (25.0)
				Median (Min, Max)	-14.3 (-49, 55)	-6.7 (-76, 41)	-13.6 (-76, 55)
				Within group p-value	0.0110	0.0379	0.0011
			Visit 4	N	20	36	56
				Mean (SD)	-13.6 (24.6)	-9.5 (27.6)	-11.0 (26.4)
				Median (Min, Max)	-14.4 (-67, 17)	-13.1 (-67, 56)	-13.1 (-67, 56)
				Within group p-value	0.0328	0.0409	0.0029
			Visit 5	N	20	35	55
				Mean (SD)	-10.8 (24.9)	-16.5 (28.3)	-14.4 (27.1)
				Median (Min, Max)	-7.9 (-65, 21)	-16.7 (-65, 35)	-14.6 (-65, 35)
				Within group p-value	0.1429	0.0022	0.0005
	Relative change from baseline (%)		Visit 3	N	20	35	55
				Mean (SD)	30.0 (42.8)	46.2 (100.5)	40.3 (84.0)
				Median (Min, Max)	22.5 (-61, 115)	10.0 (-65, 426)	21.0 (-65, 426)
				Within group p-value	0.0037	0.0115	0.0001
			Visit 4	N	20	36	56
				Mean (SD)	37.0 (65.8)	46.6 (94.9)	43.2 (85.1)
				Median (Min, Max)	20.5 (-22, 229)	19.5 (-74, 399)	19.5 (-74, 399)
				Within group p-value	0.0336	0.0121	0.0007
			Visit 5	N	20	35	55
				Mean (SD)	36.8 (68.4)	74.3 (132.7)	60.7 (114.3)
				Median (Min, Max)	13.5 (-25, 222)	28.0 (-36, 579)	22.0 (-36, 579)
				Within group p-value	0.0914	0.0003	0.0000
AUC Acidogenicity pH 6.2 baseline (no negative AUC) (min*pH)	Measured value		Screening	N	20	36	56
				Mean (SD)	5.6 (8.2)	8.0 (11.0)	7.1 (10.1)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Visit 3	Median (Min, Max)	1.2 (0, 21)	1.9 (0, 37)	1.5 (0, 37)
				N	20	35	55
				Mean (SD)	1.4 (3.3)	3.9 (7.3)	3.0 (6.2)
			Visit 4	Median (Min, Max)	0.0 (0, 11)	0.0 (0, 30)	0.0 (0, 30)
				N	20	36	56
				Mean (SD)	1.6 (4.7)	3.2 (6.7)	2.7 (6.1)
			Visit 5	Median (Min, Max)	0.0 (0, 21)	0.0 (0, 27)	0.0 (0, 27)
				N	20	35	55
				Mean (SD)	0.9 (1.8)	0.6 (1.2)	0.7 (1.5)
		Absolute change from baseline	Visit 3	Median (Min, Max)	0.0 (0, 6)	0.0 (0, 5)	0.0 (0, 6)
				N	20	35	55
				Mean (SD)	-4.2 (7.5)	-4.4 (11.2)	-4.3 (10.0)
			Visit 4	Median (Min, Max)	-1.2 (-21, 9)	-0.4 (-36, 18)	-0.6 (-36, 18)
				Within group p-value	0.0058	0.0242	0.0004
				N	20	36	56
			Visit 5	Mean (SD)	-4.0 (7.7)	-4.8 (11.0)	-4.5 (9.9)
				Median (Min, Max)	-0.2 (-21, 3)	-0.7 (-37, 16)	-0.6 (-37, 16)
				Within group p-value	0.0432	0.0028	0.0003
		Relative change from baseline (%)	Visit 3	N	20	35	55
				Mean (SD)	-4.7 (8.9)	-7.6 (11.1)	-6.5 (10.3)
				Median (Min, Max)	-0.2 (-21, 6)	-1.3 (-35, 3)	-0.8 (-35, 6)
				Within group p-value	0.0730	0.0000	0.0000
			Visit 4	N	12	28	40
				Mean (SD)	-91.6 (17.5)	-13.6 (191.1)	-37.0 (163.4)
				Median (Min, Max)	-100.0 (-100, -45)	-91.0 (-100, 885)	-99.0 (-100, 885)
				Within group p-value	0.0005	0.0259	0.0001

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
AUC Acidogenicity pH 5.5 baseline (no negative AUC) (min*pH)	Measured value		Visit 4	N	12	28	40
				Mean (SD)	-66.4 (58.8)	-54.4 (85.9)	-58.0 (78.2)
				Median (Min, Max)	-96.5 (-100, 86)	-99.5 (-100, 224)	-99.5 (-100, 224)
				Within group p-value	0.0049	0.0050	0.0001
			Visit 5	N	12	27	39
				Mean (SD)	-28.4 (193.0)	-48.8 (132.3)	-42.5 (151.1)
				Median (Min, Max)	-100.0 (-100, 571)	-100.0 (-100, 486)	-100.0 (-100, 571)
				Within group p-value	0.0205	0.0130	0.0008
			Screening	N	20	36	56
				Mean (SD)	1.2 (2.8)	1.4 (3.2)	1.3 (3.0)
				Median (Min, Max)	0.0 (0, 8)	0.0 (0, 15)	0.0 (0, 15)
			Visit 3	N	20	35	55
				Mean (SD)	0.0 (0.0)	0.5 (1.5)	0.3 (1.2)
				Median (Min, Max)	0.0 (0, 0)	0.0 (0, 8)	0.0 (0, 8)
			Visit 4	N	20	36	56
				Mean (SD)	0.0 (0.0)	0.3 (1.3)	0.2 (1.0)
				Median (Min, Max)	0.0 (0, 0)	0.0 (0, 8)	0.0 (0, 8)
			Visit 5	N	20	35	55
				Mean (SD)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
				Median (Min, Max)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 0)
	Absolute change from baseline		Visit 3	N	20	35	55
				Mean (SD)	-1.2 (2.8)	-1.0 (3.2)	-1.1 (3.0)
				Median (Min, Max)	0.0 (-8, 0)	0.0 (-15, 6)	0.0 (-15, 6)
				Within group p-value	0.1250	0.0342	0.0028
			Visit 4	N	20	36	56
				Mean (SD)	-1.2 (2.8)	-1.1 (3.3)	-1.1 (3.1)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
		Relative change from baseline (%)	Visit 5	Median (Min, Max)	0.0 (-8, 0)	0.0 (-15, 5)	0.0 (-15, 5)
				Within group p-value	0.1250	0.0415	0.0040
				N	20	35	55
				Mean (SD)	-1.2 (2.8)	-1.5 (3.2)	-1.4 (3.1)
			Visit 3	Median (Min, Max)	0.0 (-8, 0)	0.0 (-15, 0)	0.0 (-15, 0)
				Within group p-value	0.1250	0.0010	0.0001
				N	4	11	15
				Mean (SD)	-100.0 (0.0)	-30.6 (188.1)	-49.1 (162.1)
			Visit 4	Median (Min, Max)	-100.0 (-100, -100)	-100.0 (-100, 533)	-100.0 (-100, 533)
				Within group p-value	0.1250	0.0498	0.0059
				N	4	11	15
				Mean (SD)	-100.0 (0.0)	-60.7 (91.7)	-71.2 (79.6)
			Visit 5	Median (Min, Max)	-100.0 (-100, -100)	-100.0 (-100, 192)	-100.0 (-100, 192)
				Within group p-value	0.1250	0.0371	0.0033
				N	4	11	15
				Mean (SD)	-100.0 (0.0)	-100.0 (0.0)	-100.0 (0.0)
				Median (Min, Max)	-100.0 (-100, -100)	-100.0 (-100, -100)	-100.0 (-100, -100)
				Within group p-value	0.1250	0.0010	0.0001
Site 2	AUC Acidogenicity pH 6.2 baseline (min*pH)	Measured value	Screening	N	20	36	56
				Mean (SD)	-25.9 (22.0)	-21.3 (28.5)	-22.9 (26.2)
				Median (Min, Max)	-29.5 (-67, 10)	-22.4 (-77, 31)	-24.5 (-77, 31)
			Visit 3	N	20	35	55
				Mean (SD)	-31.6 (19.2)	-27.7 (22.4)	-29.1 (21.2)
				Median (Min, Max)	-37.7 (-53, 10)	-26.2 (-66, 23)	-29.7 (-66, 23)
			Visit 4	N	20	36	56
				Mean (SD)	-37.5 (16.9)	-27.1 (21.6)	-30.8 (20.5)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
		Absolute change from baseline	Visit 5	Median (Min, Max)	-39.5 (-61, 3)	-28.9 (-64, 27)	-33.8 (-64, 27)
				N	20	35	55
				Mean (SD)	-35.0 (11.9)	-39.4 (13.7)	-37.8 (13.1)
			Visit 3	Median (Min, Max)	-34.5 (-55, -12)	-40.3 (-75, -4)	-39.6 (-75, -4)
				N	20	35	55
				Mean (SD)	-5.7 (23.3)	-7.3 (24.8)	-6.7 (24.1)
			Visit 4	Median (Min, Max)	-10.9 (-36, 63)	-5.4 (-69, 38)	-6.1 (-69, 63)
				Within group p-value	0.1327	0.1113	0.0283
				N	20	36	56
			Visit 5	Mean (SD)	-11.6 (25.2)	-5.8 (29.0)	-7.9 (27.6)
				Median (Min, Max)	-13.3 (-64, 32)	-7.2 (-59, 54)	-8.5 (-64, 54)
				Within group p-value	0.0583	0.2604	0.0424
		Relative change from baseline (%)	Visit 5	N	20	35	55
				Mean (SD)	-9.2 (24.5)	-17.3 (32.8)	-14.4 (30.1)
				Median (Min, Max)	-11.7 (-62, 32)	-21.2 (-79, 50)	-17.7 (-79, 50)
			Visit 3	Within group p-value	0.1429	0.0045	0.0013
				N	20	35	55
				Mean (SD)	45.5 (175.5)	-11.6 (481.7)	9.2 (397.1)
			Visit 4	Median (Min, Max)	20.0 (-449, 393)	-14.0 (-1983, 1583)	-6.0 (-1983, 1583)
				Within group p-value	0.1678	0.3089	0.9769
				N	20	36	56
			Visit 5	Mean (SD)	17.1 (291.3)	-243.5 (1401.6)	-150.5 (1138.1)
				Median (Min, Max)	5.5 (-751, 574)	-38.5 (-8250, 1092)	-24.0 (-8250, 1092)
				Within group p-value	0.4900	0.0727	0.3253
			Visit 5	N	20	35	55
				Mean (SD)	-37.3 (298.7)	-205.1 (1526.8)	-144.1 (1227.1)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
				Median (Min, Max)	-8.0 (-798, 441)	-21.0 (-8683, 1385)	-15.0 (-8683, 1385)
				Within group p-value	0.9491	0.7484	0.8331
AUC Acidogenicity pH 5.5 baseline (min*pH)	Measured value		Screening	N	20	36	56
				Mean (SD)	-67.9 (22.0)	-63.3 (28.5)	-64.9 (26.2)
				Median (Min, Max)	-71.5 (-109, -32)	-64.4 (-119, -11)	-66.5 (-119, -11)
			Visit 3	N	20	35	55
				Mean (SD)	-73.6 (19.2)	-69.7 (22.4)	-71.1 (21.2)
				Median (Min, Max)	-79.7 (-95, -32)	-68.2 (-108, -19)	-71.7 (-108, -19)
			Visit 4	N	20	36	56
				Mean (SD)	-79.5 (16.9)	-69.1 (21.6)	-72.8 (20.5)
				Median (Min, Max)	-81.5 (-103, -39)	-70.9 (-106, -16)	-75.8 (-106, -16)
			Visit 5	N	20	35	55
				Mean (SD)	-77.0 (11.9)	-81.4 (13.7)	-79.8 (13.1)
				Median (Min, Max)	-76.5 (-97, -54)	-82.3 (-117, -46)	-81.6 (-117, -46)
	Absolute change from baseline		Visit 3	N	20	35	55
				Mean (SD)	-5.7 (23.3)	-7.3 (24.8)	-6.7 (24.1)
				Median (Min, Max)	-10.9 (-36, 63)	-5.4 (-69, 38)	-6.1 (-69, 63)
			Visit 4	N	20	36	56
				Mean (SD)	-11.6 (25.2)	-5.8 (28.9)	-7.9 (27.6)
				Median (Min, Max)	-13.3 (-64, 32)	-7.2 (-59, 54)	-8.5 (-64, 54)
			Visit 5	N	20	35	55
				Mean (SD)	-9.1 (24.5)	-17.3 (32.8)	-14.3 (30.0)
				Median (Min, Max)	-11.7 (-62, 32)	-21.2 (-79, 50)	-17.7 (-79, 50)
			Visit 5	N	20	35	55
				Mean (SD)	-9.1 (24.5)	-17.3 (32.8)	-14.3 (30.0)
				Median (Min, Max)	-11.7 (-62, 32)	-21.2 (-79, 50)	-17.7 (-79, 50)
				Within group p-value	0.1429	0.0045	0.0013

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
	Relative change from baseline (%)		Visit 3	N	20	35	55
				Mean (SD)	15.1 (32.7)	41.1 (96.3)	31.7 (79.8)
				Median (Min, Max)	18.5 (-65, 70)	6.0 (-62, 370)	15.0 (-65, 370)
				Within group p-value	0.0473	0.0230	0.0023
			Visit 4	N	20	36	56
				Mean (SD)	29.2 (52.2)	46.4 (121.2)	40.3 (101.8)
				Median (Min, Max)	23.5 (-32, 190)	10.5 (-72, 532)	19.5 (-72, 532)
				Within group p-value	0.0265	0.0560	0.0032
			Visit 5	N	20	35	55
				Mean (SD)	27.6 (54.4)	82.9 (169.5)	62.8 (140.9)
				Median (Min, Max)	15.0 (-34, 185)	34.0 (-42, 709)	28.0 (-42, 709)
				Within group p-value	0.0623	0.0013	0.0001
AUC Acidogenicity pH 6.2 baseline (no negative AUC) (min*pH)	Measured value		Screening	N	20	36	56
				Mean (SD)	3.7 (5.2)	8.2 (11.7)	6.6 (10.1)
				Median (Min, Max)	0.9 (0, 19)	1.8 (0, 40)	1.1 (0, 40)
			Visit 3	N	20	35	55
				Mean (SD)	1.7 (3.9)	3.2 (6.1)	2.7 (5.4)
				Median (Min, Max)	0.0 (0, 15)	0.0 (0, 26)	0.0 (0, 26)
			Visit 4	N	20	36	56
				Mean (SD)	1.1 (2.5)	3.3 (6.9)	2.5 (5.8)
				Median (Min, Max)	0.0 (0, 10)	0.0 (0, 28)	0.0 (0, 28)
			Visit 5	N	20	35	55
				Mean (SD)	0.5 (1.5)	0.5 (1.6)	0.5 (1.6)
				Median (Min, Max)	0.0 (0, 7)	0.0 (0, 9)	0.0 (0, 9)
		Absolute change from baseline	Visit 3	N	20	35	55
				Mean (SD)	-2.0 (4.2)	-5.2 (11.2)	-4.0 (9.4)



Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
		Relative change from baseline (%)	Visit 4	Median (Min, Max)	-0.9 (-10, 9)	-1.3 (-40, 13)	-1.0 (-40, 13)
				Within group p-value	0.0185	0.0009	0.0000
				N	20	36	56
				Mean (SD)	-2.6 (5.2)	-4.9 (11.7)	-4.1 (9.9)
			Visit 5	Median (Min, Max)	-0.4 (-19, 3)	-0.5 (-40, 16)	-0.4 (-40, 16)
				Within group p-value	0.0302	0.0118	0.0008
				N	20	35	55
				Mean (SD)	-3.2 (5.7)	-7.7 (12.0)	-6.0 (10.3)
			Visit 3	Median (Min, Max)	-0.6 (-19, 6)	-0.9 (-40, 3)	-0.8 (-40, 6)
				Within group p-value	0.0256	0.0000	0.0000
				N	14	26	40
				Mean (SD)	-69.1 (68.5)	79.1 (733.1)	27.2 (592.6)
			Visit 4	Median (Min, Max)	-100.0 (-100, 150)	-94.5 (-100, 3650)	-99.0 (-100, 3650)
				Within group p-value	0.0120	0.0005	0.0000
				N	14	26	40
				Mean (SD)	-52.6 (97.8)	29.5 (285.3)	0.8 (238.6)
			Visit 5	Median (Min, Max)	-100.0 (-100, 180)	-100.0 (-100, 1150)	-100.0 (-100, 1150)
				Within group p-value	0.1024	0.0888	0.0176
				N	14	25	39
				Mean (SD)	-8.5 (289.9)	-79.7 (79.2)	-54.1 (184.1)
			Visit 3	Median (Min, Max)	-100.0 (-100, 983)	-100.0 (-100, 290)	-100.0 (-100, 983)
				Within group p-value	0.0061	0.0000	0.0000
AUC Acidogenicity pH 5.5 baseline (no negative AUC) (min*pH)	Measured value		Screening	N	20	36	56
				Mean (SD)	0.4 (1.7)	2.1 (4.6)	1.5 (3.9)
				Median (Min, Max)	0.0 (0, 8)	0.0 (0, 18)	0.0 (0, 18)
			Visit 3	N	20	35	55

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
		Absolute change from baseline	Visit 4	Mean (SD)	0.0 (0.1)	0.2 (0.6)	0.1 (0.5)
				Median (Min, Max)	0.0 (0, 1)	0.0 (0, 3)	0.0 (0, 3)
				N	20	36	56
				Mean (SD)	0.0 (0.0)	0.3 (0.7)	0.2 (0.6)
			Visit 5	Median (Min, Max)	0.0 (0, 0)	0.0 (0, 3)	0.0 (0, 3)
				N	20	35	55
				Mean (SD)	0.0 (0.0)	0.0 (0.1)	0.0 (0.1)
				Median (Min, Max)	0.0 (0, 0)	0.0 (0, 0)	0.0 (0, 0)
			Visit 3	N	20	35	55
				Mean (SD)	-0.4 (1.6)	-1.9 (4.4)	-1.4 (3.7)
				Median (Min, Max)	0.0 (-7, 0)	0.0 (-15, 1)	0.0 (-15, 1)
				Within group p-value	0.5000	0.0105	0.0036
			Visit 4	N	20	36	56
				Mean (SD)	-0.4 (1.7)	-1.8 (4.4)	-1.3 (3.7)
				Median (Min, Max)	0.0 (-8, 0)	0.0 (-15, 2)	0.0 (-15, 2)
				Within group p-value	0.5000	0.0161	0.0067
			Visit 5	N	20	35	55
				Mean (SD)	-0.4 (1.7)	-2.1 (4.7)	-1.5 (3.9)
				Median (Min, Max)	0.0 (-8, 0)	0.0 (-18, 0)	0.0 (-18, 0)
				Within group p-value	0.5000	0.0039	0.0010
		Relative change from baseline (%)	Visit 3	N	2	10	12
				Mean (SD)	NC	-94.6 (8.5)	-95.0 (7.8)
				Median (Min, Max)	NC (-100, -94)	-100.0 (-100, -76)	-100.0 (-100, -76)
				Within group p-value	0.5000	0.0020	0.0005
			Visit 4	N	2	10	12
				Mean (SD)	NC	-72.3 (67.8)	-76.9 (62.3)

Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Female	Male	Total
			Median (Min, Max)	NC (-100, -100)	-100.0 (-100, 118)	-100.0 (-100, 118)
			Within group p-value	0.5000	0.0762	0.0278
			Visit 5 N	2	10	12
			Mean (SD)	NC	-86.7 (42.1)	-88.9 (38.4)
			Median (Min, Max)	NC (-100, -100)	-100.0 (-100, 33)	-100.0 (-100, 33)
			Within group p-value	0.5000	0.0039	0.0010

Data based on Per Protocol Set population. NC: Not calculated - number of non-missing observations less than 3.

SM17\_02\_B AUC Dental Plaque Acidogenicity, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:54:59

### 14.3.1 Secondary endpoints

Table 14.3-11 Plaque amount (Silness-Löe index) (PPS) (Part 2)

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Female	Male	Total
T16	Buccal	Plaque Amount Assessment	Measured value	Screening N	20	36	56
				Mean (SD)	0.60 (0.60)	0.81 (0.62)	0.73 (0.62)
				Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
				Visit 3 N	20	35	55
				Mean (SD)	0.65 (0.67)	0.74 (0.70)	0.71 (0.69)
				Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)
				Visit 4 N	20	36	56
				Mean (SD)	0.80 (0.52)	0.67 (0.63)	0.71 (0.59)
				Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
				Visit 5 N	20	36	56
				Mean (SD)	0.80 (0.62)	0.78 (0.76)	0.79 (0.71)
				Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	0.05 (0.76)	-0.06 (0.80)	-0.02 (0.78)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)
					Within group p-value	1.0000	0.8331	0.8652
				Visit 4	N	20	36	56
					Mean (SD)	0.20 (0.70)	-0.14 (0.72)	-0.02 (0.73)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)
					Within group p-value	0.3438	0.3593	0.8564
				Visit 5	N	20	36	56
					Mean (SD)	0.20 (0.70)	-0.03 (0.81)	0.05 (0.77)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)
					Within group p-value	0.3438	1.0000	0.6034
	Disto-Buccal	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
					Mean (SD)	0.60 (0.68)	0.75 (0.81)	0.70 (0.76)
					Median (Min, Max)	0.50 (0.0, 2.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.90 (0.64)	0.80 (0.72)	0.84 (0.69)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.85 (0.67)	1.03 (0.74)	0.96 (0.71)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.75 (0.55)	1.00 (0.68)	0.91 (0.64)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)
			Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	0.30 (0.73)	0.09 (0.82)	0.16 (0.79)

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total	
				Visit 4	Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)	
					Within group p-value	0.1484	0.5079	0.1254	
					N	20	36	56	
					Mean (SD)	0.25 (0.91)	0.28 (0.94)	0.27 (0.92)	
				Visit 5	Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)	
					Within group p-value	0.2695	0.0883	0.0326	
					N	20	36	56	
					Mean (SD)	0.15 (0.81)	0.25 (1.05)	0.21 (0.97)	
					Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-2.0, 3.0)	0.00 (-2.0, 3.0)	
					Within group p-value	0.5898	0.1929	0.1280	
	Disto-Lingual	Plaque Amount Assessment	Measured value	Screening	N	20	36	56	
					Mean (SD)	0.15 (0.49)	0.19 (0.40)	0.18 (0.43)	
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	
				Visit 3	N	20	35	55	
					Mean (SD)	0.30 (0.47)	0.31 (0.53)	0.31 (0.50)	
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	
				Visit 4	N	20	36	56	
					Mean (SD)	0.35 (0.59)	0.42 (0.50)	0.39 (0.53)	
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	
				Visit 5	N	20	36	56	
					Mean (SD)	0.20 (0.41)	0.42 (0.55)	0.34 (0.51)	
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	
		Absolute change from baseline		Visit 3	N	20	35	55	
					Mean (SD)	0.15 (0.67)	0.14 (0.69)	0.15 (0.68)	
					Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-2.0, 2.0)	
					Within group p-value	0.5313	0.3367	0.1686	

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Female			Male			Total			
Lingual	Plaque Amount Assessment	Measured value	Screening	Visit 4	N	20	36	56						
				Mean (SD)	0.20 (0.70)	0.22 (0.59)	0.21 (0.62)							
				Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)							
				Within group p-value	0.3594	0.0574	0.0104							
				Visit 5	N	20	36	56						
				Mean (SD)	0.05 (0.60)	0.22 (0.64)	0.16 (0.63)							
				Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-2.0, 2.0)							
				Within group p-value	1.0000	0.0762	0.0930							
				Visit 3	N	20	35	55						
				Mean (SD)	0.10 (0.31)	0.17 (0.38)	0.15 (0.36)							
				Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)							
				Visit 4	N	20	36	56						
				Mean (SD)	0.25 (0.44)	0.17 (0.38)	0.20 (0.40)							
				Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)							
				Visit 5	N	20	36	56						
				Mean (SD)	0.20 (0.41)	0.17 (0.38)	0.18 (0.39)							
				Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)							
				Absolute change from baseline	Visit 3	N	20	35	55					
				Mean (SD)	-0.10 (0.55)	-0.09 (0.61)	-0.09 (0.59)							
				Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)							
				Within group p-value	0.7500	0.5811	0.3629							
				Visit 4	N	20	36	56						
				Mean (SD)	0.05 (0.76)	-0.11 (0.62)	-0.05 (0.67)							

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
Mesio-Buccal	Plaque Amount Assessment	Measured value		Visit 5	Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	1.0000	0.4240	0.5608
					N	20	36	56
					Mean (SD)	0.00 (0.65)	-0.11 (0.52)	-0.07 (0.57)
					Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	1.0000	0.3438	0.4850
			Screening	N	20	36	56	
					Mean (SD)	0.60 (0.50)	0.86 (0.68)	0.77 (0.63)
					Median (Min, Max)	1.00 (0.0, 1.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.90 (0.45)	0.97 (0.62)	0.95 (0.56)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.65 (0.49)	0.81 (0.62)	0.75 (0.58)
					Median (Min, Max)	1.00 (0.0, 1.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.70 (0.57)	0.97 (0.65)	0.88 (0.63)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)
	Absolute change from baseline	Visit 3	N	20	35	55		
			Mean (SD)	0.30 (0.57)	0.14 (0.69)	0.20 (0.65)		
			Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)		
			Within group p-value	0.0703	0.2695	0.0370		
		Visit 4	N	20	36	56		
			Mean (SD)	0.05 (0.51)	-0.06 (0.71)	-0.02 (0.65)		
			Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)		
			Within group p-value	1.0000	0.8167	1.0000		

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
Mesio-Lingual	Plaque Amount Assessment	Measured value		Visit 5	N	20	36	56
				Mean (SD)	0.10 (0.79)	0.11 (0.85)	0.11 (0.82)	
				Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)	
				Within group p-value	0.7744	0.4230	0.3348	
				Screening	N	20	36	56
				Mean (SD)	0.40 (0.75)	0.28 (0.57)	0.32 (0.64)	
				Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	
				Visit 3	N	20	35	55
				Mean (SD)	0.10 (0.31)	0.34 (0.48)	0.25 (0.44)	
				Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	
				Visit 4	N	20	36	56
				Mean (SD)	0.25 (0.55)	0.28 (0.45)	0.27 (0.49)	
				Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	
				Visit 5	N	20	36	56
				Mean (SD)	0.30 (0.57)	0.28 (0.45)	0.29 (0.49)	
				Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	
			Absolute change from baseline	Visit 3	N	20	35	55
				Mean (SD)	-0.30 (0.73)	0.09 (0.74)	-0.05 (0.76)	
				Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	
				Within group p-value	0.1563	0.6536	0.4896	
				Visit 4	N	20	36	56
				Mean (SD)	-0.15 (0.59)	0.00 (0.68)	-0.05 (0.64)	
				Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	
				Within group p-value	0.5000	1.0000	0.5079	
			Visit 5	N	20	36	56	
				Mean (SD)	-0.10 (0.97)	0.00 (0.79)	-0.04 (0.85)	



Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
					Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	0.5156	0.8953	0.6654
	Total index	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
					Mean (SD)	0.43 (0.38)	0.53 (0.39)	0.49 (0.39)
					Median (Min, Max)	0.30 (0.0, 1.3)	0.40 (0.0, 1.3)	0.30 (0.0, 1.3)
				Visit 3	N	20	35	55
					Mean (SD)	0.49 (0.24)	0.56 (0.32)	0.53 (0.30)
					Median (Min, Max)	0.50 (0.0, 1.0)	0.50 (0.0, 1.3)	0.50 (0.0, 1.3)
				Visit 4	N	20	36	56
					Mean (SD)	0.54 (0.25)	0.56 (0.33)	0.55 (0.30)
					Median (Min, Max)	0.50 (0.0, 1.0)	0.50 (0.0, 1.2)	0.50 (0.0, 1.2)
				Visit 5	N	20	36	56
					Mean (SD)	0.50 (0.29)	0.61 (0.37)	0.57 (0.35)
					Median (Min, Max)	0.50 (0.0, 1.0)	0.50 (0.0, 1.7)	0.50 (0.0, 1.7)
		Absolute change from baseline		Visit 3	N	20	35	55
					Mean (SD)	0.06 (0.38)	0.06 (0.39)	0.06 (0.38)
					Median (Min, Max)	0.10 (-1.0, 0.5)	0.00 (-0.7, 1.0)	0.00 (-1.0, 1.0)
					Within group p-value	0.3039	0.4074	0.1723
				Visit 4	N	20	36	56
					Mean (SD)	0.11 (0.32)	0.04 (0.43)	0.06 (0.39)
					Median (Min, Max)	0.20 (-0.5, 0.7)	0.00 (-1.0, 0.9)	0.05 (-1.0, 0.9)
					Within group p-value	0.1713	0.5454	0.1935
				Visit 5	N	20	36	56
					Mean (SD)	0.07 (0.46)	0.08 (0.51)	0.08 (0.49)
					Median (Min, Max)	0.20 (-1.3, 0.7)	0.10 (-0.9, 1.4)	0.20 (-1.3, 1.4)
					Within group p-value	0.2445	0.3153	0.1393

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
T21	Buccal	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
					Mean (SD)	0.35 (0.49)	0.36 (0.64)	0.36 (0.59)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.25 (0.44)	0.23 (0.55)	0.24 (0.51)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.25 (0.55)	0.11 (0.32)	0.16 (0.42)
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.25 (0.55)	0.14 (0.42)	0.18 (0.47)
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
			Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	-0.10 (0.64)	-0.11 (0.58)	-0.11 (0.60)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	0.7266	0.3984	0.2657
				Visit 4	N	20	36	56
					Mean (SD)	-0.10 (0.72)	-0.25 (0.69)	-0.20 (0.70)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	0.7539	0.0571	0.0376
				Visit 5	N	20	36	56
					Mean (SD)	-0.10 (0.64)	-0.22 (0.59)	-0.18 (0.61)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	0.7266	0.0557	0.0519
	Disto-Buccal	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
					Mean (SD)	0.30 (0.66)	0.42 (0.73)	0.38 (0.70)

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total	
				Visit 3	Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	
					N	20	35	55	
					Mean (SD)	0.25 (0.44)	0.31 (0.58)	0.29 (0.53)	
				Visit 4	Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	
					N	20	36	56	
					Mean (SD)	0.40 (0.75)	0.22 (0.54)	0.29 (0.62)	
				Visit 5	Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	
					N	20	36	56	
					Mean (SD)	0.30 (0.47)	0.31 (0.52)	0.30 (0.50)	
				Absolute change from baseline	Visit 3	Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
						N	20	35	55
						Mean (SD)	-0.05 (0.69)	-0.11 (0.58)	-0.09 (0.62)
					Visit 4	Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
						Within group p-value	1.0000	0.3984	0.2970
						N	20	36	56
					Visit 5	Mean (SD)	0.10 (0.91)	-0.19 (0.67)	-0.09 (0.77)
						Median (Min, Max)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
						Within group p-value	0.7656	0.1484	0.5056
					Visit 5	N	20	36	56
						Mean (SD)	0.00 (0.79)	-0.11 (0.71)	-0.07 (0.74)
						Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
				Within group p-value		0.8125	0.4850	0.4539	
Disto-Lingual	Plaque Amount Assessment	Measured value		Screening	N	20	36	56	
					Mean (SD)	0.20 (0.41)	0.22 (0.48)	0.21 (0.46)	
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	
				Visit 3	N	20	35	55	

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total				
			Absolute change from baseline	Visit 4	Mean (SD)	0.00 (0.00)	0.11 (0.40)	0.07 (0.33)				
					Median (Min, Max)	0.00 (0.0, 0.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)				
					N	20	36	56				
				Visit 5	Mean (SD)	0.10 (0.31)	0.17 (0.45)	0.14 (0.40)				
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)				
					N	20	36	56				
				Visit 3	Mean (SD)	0.05 (0.22)	0.03 (0.17)	0.04 (0.19)				
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)				
					N	20	35	55				
				Visit 4	Mean (SD)	-0.20 (0.41)	-0.11 (0.47)	-0.15 (0.45)				
					Median (Min, Max)	0.00 (-1.0, 0.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)				
					Within group p-value	0.1250	0.2891	0.0386				
				Visit 5	N	20	36	56				
					Mean (SD)	-0.10 (0.55)	-0.06 (0.63)	-0.07 (0.60)				
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)				
				Visit 5	Within group p-value	0.6875	0.7891	0.5018				
					N	20	36	56				
					Mean (SD)	-0.15 (0.37)	-0.19 (0.52)	-0.18 (0.47)				
				Lingual	Plaque Amount Assessment	Measured value		Screening	N	20	36	56
									Mean (SD)	0.30 (0.47)	0.17 (0.38)	0.21 (0.41)
Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)									
Visit 3	N	20	35					55				
	Mean (SD)	0.15 (0.37)	0.09 (0.37)					0.11 (0.37)				
	Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)					0.00 (0.0, 2.0)				

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Absolute change from baseline	Visit 4	N	20	36	56
					Mean (SD)	0.20 (0.41)	0.22 (0.54)	0.21 (0.49)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.20 (0.41)	0.11 (0.32)	0.14 (0.35)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
				Visit 3	N	20	35	55
					Mean (SD)	-0.15 (0.59)	-0.06 (0.54)	-0.09 (0.55)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)
					Within group p-value	0.4531	0.7656	0.3367
				Visit 4	N	20	36	56
					Mean (SD)	-0.10 (0.45)	0.06 (0.71)	0.00 (0.63)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)
					Within group p-value	0.6250	0.5913	0.8953
				Visit 5	N	20	36	56
					Mean (SD)	-0.10 (0.55)	-0.06 (0.41)	-0.07 (0.46)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)
					Within group p-value	0.6875	0.6875	0.3877
Mesio-Buccal	Plaque Amount Assessment	Measured value	Screening	N	20	36	56	
				Mean (SD)	0.25 (0.44)	0.25 (0.44)	0.25 (0.44)	
				Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	
			Visit 3	N	20	35	55	
				Mean (SD)	0.30 (0.57)	0.31 (0.58)	0.31 (0.57)	
				Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	
			Visit 4	N	20	36	56	
				Mean (SD)	0.45 (0.76)	0.11 (0.32)	0.23 (0.54)	

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Absolute change from baseline	Visit 5	Median (Min, Max)	0.00 (0.0, 3.0)	0.00 (0.0, 1.0)	0.00 (0.0, 3.0)
					N	20	36	56
					Mean (SD)	0.50 (0.61)	0.33 (0.53)	0.39 (0.56)
				Visit 3	Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
					N	20	35	55
					Mean (SD)	0.05 (0.69)	0.06 (0.64)	0.05 (0.65)
				Visit 4	Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)
					Within group p-value	1.0000	0.7949	0.5079
					N	20	36	56
				Visit 5	Mean (SD)	0.20 (0.89)	-0.14 (0.49)	-0.02 (0.67)
					Median (Min, Max)	0.00 (-1.0, 3.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 3.0)
					Within group p-value	0.5625	0.1797	0.8254
				Visit 5	N	20	36	56
					Mean (SD)	0.25 (0.72)	0.08 (0.55)	0.14 (0.62)
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)
					Within group p-value	0.2344	0.5488	0.1344
Mesio-Lingual	Plaque Amount Assessment	Measured value		Screening	N	20	36	56
					Mean (SD)	0.25 (0.44)	0.17 (0.45)	0.20 (0.44)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.05 (0.22)	0.06 (0.24)	0.05 (0.23)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.10 (0.31)	0.17 (0.45)	0.14 (0.40)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 5	N	20	36	56

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total				
			Absolute change from baseline	Visit 3	Mean (SD)	0.05 (0.22)	0.06 (0.23)	0.05 (0.23)				
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)				
					N	20	35	55				
					Mean (SD)	-0.20 (0.52)	-0.11 (0.40)	-0.15 (0.45)				
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)				
					Within group p-value	0.2188	0.2188	0.0386				
				Visit 4	N	20	36	56				
					Mean (SD)	-0.15 (0.49)	0.00 (0.53)	-0.05 (0.52)				
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)				
					Within group p-value	0.3750	1.0000	0.6133				
					Visit 5	N	20	36	56			
						Mean (SD)	-0.20 (0.41)	-0.11 (0.46)	-0.14 (0.44)			
				Median (Min, Max)		0.00 (-1.0, 0.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)				
					Within group p-value	0.1250	0.3125	0.0352				
					Total index	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
									Mean (SD)	0.28 (0.30)	0.27 (0.27)	0.27 (0.28)
				Median (Min, Max)					0.20 (0.0, 1.0)	0.20 (0.0, 1.0)	0.20 (0.0, 1.0)	
								Visit 3	N	20	35	55
									Mean (SD)	0.17 (0.22)	0.19 (0.34)	0.18 (0.30)
									Median (Min, Max)	0.00 (0.0, 0.5)	0.00 (0.0, 1.5)	0.00 (0.0, 1.5)
								Visit 4	N	20	36	56
Mean (SD)	0.26 (0.36)	0.17 (0.26)	0.20 (0.30)									
Median (Min, Max)	0.20 (0.0, 1.2)	0.00 (0.0, 1.2)	0.00 (0.0, 1.2)									
				Visit 5	N	20	36	56				
					Mean (SD)	0.23 (0.29)	0.16 (0.24)	0.19 (0.26)				
					Median (Min, Max)	0.20 (0.0, 1.2)	0.00 (0.0, 1.0)	0.20 (0.0, 1.2)				

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	-0.11 (0.31)	-0.08 (0.25)	-0.09 (0.27)
					Median (Min, Max)	0.00 (-0.8, 0.5)	0.00 (-0.6, 0.8)	0.00 (-0.8, 0.8)
					Within group p-value	0.1553	0.0253	0.0048
				Visit 4	N	20	36	56
					Mean (SD)	-0.02 (0.44)	-0.09 (0.30)	-0.07 (0.35)
					Median (Min, Max)	0.00 (-0.8, 0.8)	-0.05 (-0.8, 1.0)	0.00 (-0.8, 1.0)
					Within group p-value	0.7963	0.0248	0.1030
				Visit 5	N	20	36	56
					Mean (SD)	-0.05 (0.26)	-0.10 (0.24)	-0.08 (0.25)
					Median (Min, Max)	0.00 (-0.6, 0.5)	-0.05 (-0.6, 0.6)	0.00 (-0.6, 0.6)
					Within group p-value	0.4849	0.0111	0.0322
T24	Buccal	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
					Mean (SD)	0.50 (0.51)	0.53 (0.61)	0.52 (0.57)
					Median (Min, Max)	0.50 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.50 (0.51)	0.37 (0.60)	0.42 (0.57)
					Median (Min, Max)	0.50 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.40 (0.60)	0.42 (0.60)	0.41 (0.60)
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.40 (0.60)	0.44 (0.65)	0.43 (0.63)
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
			Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	0.00 (0.79)	-0.14 (0.77)	-0.09 (0.78)



Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total	
Disto-Buccal	Plaque Amount Assessment	Measured value	Measured value	Screening	Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)	
					Within group p-value	1.0000	0.3843	0.3965	
					N	20	36	56	
					Mean (SD)	-0.10 (0.79)	-0.11 (0.67)	-0.11 (0.71)	
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)	
					Within group p-value	0.7744	0.4545	0.2643	
					N	20	36	56	
					Mean (SD)	-0.10 (0.79)	-0.08 (0.81)	-0.09 (0.79)	
				Visit 4	Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	
					Within group p-value	0.7744	0.6796	0.4066	
					N	20	36	56	
					Mean (SD)	0.60 (0.68)	1.06 (0.92)	0.89 (0.87)	
				Visit 3	Median (Min, Max)	0.50 (0.0, 2.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)	
					N	20	35	55	
					Mean (SD)	0.85 (0.75)	0.69 (0.68)	0.75 (0.70)	
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	
				Visit 4	N	20	36	56	
					Mean (SD)	0.65 (0.49)	0.83 (0.77)	0.77 (0.69)	
					Median (Min, Max)	1.00 (0.0, 1.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)	
				Visit 5	N	20	36	56	
					Mean (SD)	0.90 (0.72)	0.78 (0.68)	0.82 (0.69)	
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)	
				Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	0.25 (1.02)	-0.40 (0.91)	-0.16 (1.00)	
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)	
					Within group p-value	0.2554	0.0220	0.2717	

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
Disto-Lingual	Plaque Amount Assessment	Measured value		Visit 4	N	20	36	56
					Mean (SD)	0.05 (0.76)	-0.22 (0.99)	-0.13 (0.92)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	1.0000	0.1713	0.2964
				Visit 5	N	20	36	56
					Mean (SD)	0.30 (1.03)	-0.28 (0.94)	-0.07 (1.01)
					Median (Min, Max)	0.00 (-2.0, 2.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 2.0)
					Within group p-value	0.2832	0.0828	0.6007
				Screening	N	20	36	56
					Mean (SD)	0.20 (0.41)	0.28 (0.51)	0.25 (0.48)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.25 (0.44)	0.14 (0.43)	0.18 (0.43)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.25 (0.44)	0.14 (0.35)	0.18 (0.39)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.15 (0.37)	0.33 (0.48)	0.27 (0.45)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
Absolute change from baseline	Visit 3	N	20	35	55			
		Mean (SD)	0.05 (0.60)	-0.14 (0.65)	-0.07 (0.63)			
		Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)			
		Within group p-value	1.0000	0.3071	0.5262			
Visit 4	N	20	36	56				
	Mean (SD)	0.05 (0.60)	-0.14 (0.59)	-0.07 (0.60)				

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
Lingual	Plaque Amount Assessment	Measured value		Visit 5	Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	1.0000	0.2734	0.5069
					N	20	36	56
					Mean (SD)	-0.05 (0.51)	0.06 (0.71)	0.02 (0.65)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)
					Within group p-value	1.0000	0.8145	0.8401
				Screening	N	20	36	56
					Mean (SD)	0.00 (0.00)	0.08 (0.37)	0.05 (0.30)
					Median (Min, Max)	0.00 (0.0, 0.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.15 (0.37)	0.11 (0.32)	0.13 (0.34)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.10 (0.31)	0.08 (0.28)	0.09 (0.29)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.00 (0.00)	0.03 (0.17)	0.02 (0.13)
					Median (Min, Max)	0.00 (0.0, 0.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
			Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	0.15 (0.37)	0.03 (0.38)	0.07 (0.38)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)
				Visit 4	Within group p-value	0.2500	1.0000	0.2891
					N	20	36	56
					Mean (SD)	0.10 (0.31)	0.00 (0.48)	0.04 (0.42)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	0.5000	1.0000	0.7656

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
Mesio-Buccal	Plaque Amount Assessment	Measured value		Visit 5	N	20	36	56
				Mean (SD)	0.00 (0.00)	-0.06 (0.41)	-0.04 (0.33)	
				Median (Min, Max)	0.00 (0.0, 0.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	
				Within group p-value	NA	0.7500	0.7500	
				Screening	N	20	36	56
				Mean (SD)	0.50 (0.51)	0.69 (0.79)	0.63 (0.70)	
				Median (Min, Max)	0.50 (0.0, 1.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)	
				Visit 3	N	20	35	55
			Mean (SD)		0.85 (0.75)	0.77 (0.69)	0.80 (0.70)	
			Median (Min, Max)		1.00 (0.0, 3.0)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)	
			Visit 4	N	20	36	56	
				Mean (SD)	0.80 (0.52)	0.75 (0.50)	0.77 (0.50)	
				Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	
			Visit 5	N	20	36	56	
				Mean (SD)	0.75 (0.55)	0.89 (0.52)	0.84 (0.53)	
				Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	
			Absolute change from baseline	Visit 3	N	20	35	55
				Mean (SD)	0.35 (0.75)	0.09 (0.56)	0.18 (0.64)	
				Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	
				Within group p-value	0.0918	0.5488	0.0378	
				Visit 4	N	20	36	56
				Mean (SD)	0.30 (0.57)	0.06 (0.89)	0.14 (0.80)	
				Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)	
				Within group p-value	0.0703	0.8455	0.1983	
			Visit 5	N	20	36	56	
				Mean (SD)	0.25 (0.72)	0.19 (0.92)	0.21 (0.85)	

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
					Within group p-value	0.2266	0.2179	0.0639
	Mesio-Lingual	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
					Mean (SD)	0.20 (0.52)	0.22 (0.54)	0.21 (0.53)
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.20 (0.41)	0.23 (0.43)	0.22 (0.42)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.30 (0.47)	0.17 (0.38)	0.21 (0.41)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.05 (0.22)	0.22 (0.42)	0.16 (0.37)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
		Absolute change from baseline		Visit 3	N	20	35	55
					Mean (SD)	0.00 (0.46)	0.00 (0.64)	0.00 (0.58)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	1.0000	1.0000	1.0000
				Visit 4	N	20	36	56
					Mean (SD)	0.10 (0.64)	-0.06 (0.67)	0.00 (0.66)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	0.7266	0.5742	0.9018
				Visit 5	N	20	36	56
					Mean (SD)	-0.15 (0.59)	0.00 (0.59)	-0.05 (0.59)
					Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	0.5000	1.0000	0.4790

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
	Total index	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
					Mean (SD)	0.34 (0.24)	0.48 (0.37)	0.43 (0.34)
					Median (Min, Max)	0.30 (0.0, 0.8)	0.50 (0.0, 1.3)	0.50 (0.0, 1.3)
				Visit 3	N	20	35	55
					Mean (SD)	0.47 (0.34)	0.38 (0.37)	0.41 (0.36)
					Median (Min, Max)	0.30 (0.0, 1.2)	0.30 (0.0, 1.3)	0.30 (0.0, 1.3)
				Visit 4	N	20	36	56
					Mean (SD)	0.42 (0.25)	0.40 (0.27)	0.40 (0.26)
					Median (Min, Max)	0.30 (0.0, 0.8)	0.30 (0.0, 1.0)	0.30 (0.0, 1.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.37 (0.26)	0.45 (0.32)	0.42 (0.30)
					Median (Min, Max)	0.30 (0.0, 1.0)	0.30 (0.0, 1.3)	0.30 (0.0, 1.3)
			Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	0.13 (0.39)	-0.10 (0.35)	-0.02 (0.38)
					Median (Min, Max)	0.00 (-0.5, 0.9)	0.00 (-0.7, 0.6)	0.00 (-0.7, 0.9)
					Within group p-value	0.2011	0.0932	0.5566
				Visit 4	N	20	36	56
					Mean (SD)	0.08 (0.27)	-0.08 (0.33)	-0.03 (0.32)
					Median (Min, Max)	0.00 (-0.3, 0.7)	0.00 (-0.7, 0.7)	0.00 (-0.7, 0.7)
					Within group p-value	0.3264	0.1388	0.5643
				Visit 5	N	20	36	56
					Mean (SD)	0.04 (0.36)	-0.03 (0.46)	-0.01 (0.42)
					Median (Min, Max)	0.00 (-0.7, 0.7)	-0.05 (-0.8, 1.0)	0.00 (-0.8, 1.0)
					Within group p-value	0.7995	0.5452	0.6059
T36	Buccal	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
					Mean (SD)	0.50 (0.51)	0.42 (0.55)	0.45 (0.54)

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total			
			Absolute change from baseline	Visit 3	Median (Min, Max)	0.50 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)			
					N	20	35	55			
					Mean (SD)	0.45 (0.76)	0.51 (0.56)	0.49 (0.63)			
				Visit 4	Median (Min, Max)	0.00 (0.0, 3.0)	0.00 (0.0, 2.0)	0.00 (0.0, 3.0)			
					N	20	36	56			
					Mean (SD)	0.45 (0.60)	0.53 (0.70)	0.50 (0.66)			
				Visit 5	Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 3.0)	0.00 (0.0, 3.0)			
					N	20	36	56			
					Mean (SD)	0.40 (0.68)	0.50 (0.61)	0.46 (0.63)			
				Visit 3	Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)			
					N	20	35	55			
					Mean (SD)	-0.05 (0.76)	0.11 (0.80)	0.05 (0.78)			
				Visit 4	Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)			
					Within group p-value	1.0000	0.5176	0.6073			
					N	20	36	56			
				Visit 5	Mean (SD)	-0.05 (0.83)	0.11 (0.92)	0.05 (0.88)			
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-1.0, 3.0)	0.00 (-1.0, 3.0)			
					Within group p-value	1.0000	0.5608	0.7443			
							Visit 5	N	20	36	56
								Mean (SD)	-0.10 (0.64)	0.08 (0.94)	0.02 (0.84)
								Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
								Within group p-value	0.7266	0.5968	0.8686
Disto-Buccal	Plaque Amount Assessment	Measured value		Screening	N	20	36	56			
					Mean (SD)	0.50 (0.61)	0.75 (0.73)	0.66 (0.69)			
					Median (Min, Max)	0.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)			
				Visit 3	N	20	35	55			

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Absolute change from baseline	Visit 4	Mean (SD)	0.85 (0.75)	0.63 (0.55)	0.71 (0.63)
					Median (Min, Max)	1.00 (0.0, 3.0)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)
					N	20	36	56
				Visit 5	Mean (SD)	0.65 (0.75)	0.67 (0.53)	0.66 (0.61)
					Median (Min, Max)	1.00 (0.0, 3.0)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)
					N	20	36	56
				Visit 3	Mean (SD)	0.65 (0.67)	0.86 (0.64)	0.79 (0.65)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)
					N	20	35	55
				Visit 4	Mean (SD)	0.35 (0.88)	-0.11 (0.83)	0.05 (0.87)
					Median (Min, Max)	0.00 (-2.0, 2.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 2.0)
					Within group p-value	0.1465	0.4095	0.6801
				Visit 5	N	20	36	56
					Mean (SD)	0.15 (0.93)	-0.08 (0.91)	0.00 (0.91)
					Median (Min, Max)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
				Visit 5	Within group p-value	0.6279	0.5912	1.0000
					N	20	36	56
					Mean (SD)	0.15 (0.75)	0.11 (1.04)	0.13 (0.94)
				Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 3.0)	0.00 (-2.0, 3.0)	
				Within group p-value	0.5488	0.6439	0.3863	
Disto-Lingual	Plaque Amount Assessment	Measured value	Screening	N	20	36	56	
				Mean (SD)	0.30 (0.57)	0.72 (0.70)	0.57 (0.68)	
				Median (Min, Max)	0.00 (0.0, 2.0)	1.00 (0.0, 2.0)	0.00 (0.0, 2.0)	
				Visit 3	N	20	35	55
					Mean (SD)	0.45 (0.51)	0.66 (0.68)	0.58 (0.63)
					Median (Min, Max)	0.00 (0.0, 1.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)



Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total			
			Absolute change from baseline	Visit 4	N	20	36	56			
					Mean (SD)	0.85 (0.59)	0.72 (0.61)	0.77 (0.60)			
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)			
				Visit 5	N	20	36	56			
					Mean (SD)	0.60 (0.68)	0.67 (0.63)	0.64 (0.64)			
					Median (Min, Max)	0.50 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)			
				Visit 3	N	20	35	55			
					Mean (SD)	0.15 (0.49)	-0.09 (0.85)	0.00 (0.75)			
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)			
					Within group p-value	0.3750	0.6695	1.0000			
				Visit 4	N	20	36	56			
					Mean (SD)	0.55 (0.51)	0.00 (0.93)	0.20 (0.84)			
					Median (Min, Max)	1.00 (0.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)			
					Within group p-value	0.0010	0.9855	0.0870			
				Visit 5	N	20	36	56			
					Mean (SD)	0.30 (0.92)	-0.06 (0.75)	0.07 (0.83)			
					Median (Min, Max)	0.00 (-2.0, 2.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 2.0)			
					Within group p-value	0.2432	0.6066	0.5654			
				Lingual	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
								Mean (SD)	0.20 (0.41)	0.47 (0.61)	0.38 (0.56)
								Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
							Visit 3	N	20	35	55
								Mean (SD)	0.25 (0.44)	0.43 (0.56)	0.36 (0.52)
								Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
							Visit 4	N	20	36	56
								Mean (SD)	0.65 (0.75)	0.31 (0.58)	0.43 (0.66)

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Absolute change from baseline	Visit 5	Median (Min, Max)	0.50 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
					N	20	36	56
					Mean (SD)	0.40 (0.68)	0.61 (0.64)	0.54 (0.66)
				Visit 3	Median (Min, Max)	0.00 (0.0, 2.0)	1.00 (0.0, 2.0)	0.00 (0.0, 2.0)
					N	20	35	55
					Mean (SD)	0.05 (0.69)	-0.06 (0.84)	-0.02 (0.78)
				Visit 4	Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
					Within group p-value	1.0000	0.6934	0.8652
					N	20	36	56
				Visit 5	Mean (SD)	0.45 (0.83)	-0.17 (0.70)	0.05 (0.80)
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 2.0)
					Within group p-value	0.0449	0.2407	0.6171
				Visit 5	N	20	36	56
					Mean (SD)	0.20 (0.89)	0.14 (0.68)	0.16 (0.76)
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)
					Within group p-value	0.3535	0.3367	0.1140
Mesio-Buccal	Plaque Amount Assessment	Measured value		Screening	N	20	36	56
					Mean (SD)	0.70 (0.73)	0.89 (0.78)	0.82 (0.77)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	1.00 (0.73)	0.74 (0.56)	0.84 (0.63)
					Median (Min, Max)	1.00 (0.0, 3.0)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.95 (0.69)	0.92 (0.55)	0.93 (0.60)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)
				Visit 5	N	20	36	56

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Absolute change from baseline	Visit 3	Mean (SD)	0.90 (0.72)	0.97 (0.45)	0.95 (0.55)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
					N	20	35	55
					Mean (SD)	0.30 (0.98)	-0.14 (0.91)	0.02 (0.95)
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
				Visit 4	Within group p-value	0.2130	0.4614	0.8491
					N	20	36	56
					Mean (SD)	0.25 (1.07)	0.03 (0.91)	0.11 (0.97)
					Median (Min, Max)	0.00 (-2.0, 2.0)	0.00 (-1.0, 3.0)	0.00 (-2.0, 3.0)
					Within group p-value	0.3916	1.0000	0.4592
				Visit 5	N	20	36	56
					Mean (SD)	0.20 (0.70)	0.08 (0.94)	0.13 (0.85)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)
					Within group p-value	0.3438	0.5922	0.2779
	Mesio-Lingual	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
					Mean (SD)	0.30 (0.47)	0.64 (0.68)	0.52 (0.63)
					Median (Min, Max)	0.00 (0.0, 1.0)	1.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.40 (0.50)	0.46 (0.56)	0.44 (0.54)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.95 (0.76)	0.72 (0.66)	0.80 (0.70)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.55 (0.69)	0.72 (0.74)	0.66 (0.72)
					Median (Min, Max)	0.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total				
			Absolute change from baseline	Visit 3	N	20	35	55				
					Mean (SD)	0.10 (0.72)	-0.17 (0.89)	-0.07 (0.84)				
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)				
					Within group p-value	0.7539	0.3280	0.5232				
				Visit 4	N	20	36	56				
					Mean (SD)	0.65 (0.88)	0.08 (0.91)	0.29 (0.93)				
					Median (Min, Max)	0.50 (-1.0, 2.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)				
					Within group p-value	0.0078	0.6389	0.0227				
				Visit 5	N	20	36	56				
					Mean (SD)	0.25 (0.97)	0.08 (0.84)	0.14 (0.88)				
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)				
					Within group p-value	0.2830	0.5608	0.2263				
				Total index	Plaque Amount Assessment	Measured value	Screening	N	20	36	56	
								Mean (SD)	0.42 (0.27)	0.64 (0.41)	0.56 (0.38)	
								Median (Min, Max)	0.40 (0.0, 1.0)	0.70 (0.0, 1.5)	0.50 (0.0, 1.5)	
								Visit 3	N	20	35	55
									Mean (SD)	0.57 (0.43)	0.58 (0.36)	0.57 (0.38)
									Median (Min, Max)	0.50 (0.0, 1.8)	0.70 (0.0, 1.5)	0.50 (0.0, 1.8)
								Visit 4	N	20	36	56
									Mean (SD)	0.76 (0.47)	0.64 (0.41)	0.68 (0.43)
Median (Min, Max)	0.75 (0.0, 1.7)	0.60 (0.2, 2.3)	0.70 (0.0, 2.3)									
Visit 5	N	20	36					56				
	Mean (SD)	0.59 (0.54)	0.72 (0.37)					0.67 (0.43)				
	Median (Min, Max)	0.50 (0.0, 2.0)	0.70 (0.0, 1.5)					0.70 (0.0, 2.0)				
Absolute change from baseline	Visit 3	N	20					35	55			
		Mean (SD)	0.15 (0.51)					-0.07 (0.47)	0.01 (0.49)			

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
T41	Buccal	Plaque Amount Assessment	Measured value	Visit 4	Median (Min, Max)	0.20 (-0.8, 1.3)	-0.10 (-1.0, 1.3)	0.00 (-1.0, 1.3)
					Within group p-value	0.2570	0.2256	0.8636
					N	20	36	56
					Mean (SD)	0.34 (0.57)	0.00 (0.57)	0.12 (0.59)
				Visit 5	Median (Min, Max)	0.35 (-0.8, 1.5)	-0.05 (-0.8, 2.1)	0.15 (-0.8, 2.1)
					Within group p-value	0.0222	0.7067	0.2923
					N	20	36	56
					Mean (SD)	0.17 (0.55)	0.08 (0.56)	0.11 (0.55)
				Visit 5	Median (Min, Max)	0.20 (-0.5, 1.5)	0.00 (-1.3, 1.3)	0.00 (-1.3, 1.5)
					Within group p-value	0.4705	0.4855	0.2786
				Screening	N	20	36	56
					Mean (SD)	0.45 (0.51)	0.53 (0.65)	0.50 (0.60)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.30 (0.57)	0.31 (0.53)	0.31 (0.54)
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.35 (0.49)	0.33 (0.53)	0.34 (0.51)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.50 (0.69)	0.25 (0.55)	0.34 (0.61)
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
			Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	-0.15 (0.67)	-0.17 (0.62)	-0.16 (0.63)
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)
					Within group p-value	0.5313	0.1796	0.0931

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total				
				Visit 4	N	20	36	56				
					Mean (SD)	-0.10 (0.64)	-0.19 (0.75)	-0.16 (0.71)				
				Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)					
				Within group p-value	0.7266	0.1566	0.0938					
				Visit 5	N	20	36	56				
					Mean (SD)	0.05 (0.60)	-0.28 (0.74)	-0.16 (0.71)				
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)				
					Within group p-value	1.0000	0.0458	0.0938				
				Disto-Buccal	Plaque Amount Assessment	Measured value		Screening	N	20	36	56
									Mean (SD)	0.40 (0.60)	0.47 (0.65)	0.45 (0.63)
									Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
								Visit 3	N	20	35	55
									Mean (SD)	0.60 (0.50)	0.51 (0.74)	0.55 (0.66)
									Median (Min, Max)	1.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
								Visit 4	N	20	36	56
									Mean (SD)	0.40 (0.60)	0.53 (0.70)	0.48 (0.66)
									Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 3.0)	0.00 (0.0, 3.0)
								Visit 5	N	20	36	56
									Mean (SD)	0.55 (0.69)	0.64 (0.64)	0.61 (0.65)
									Median (Min, Max)	0.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
Absolute change from baseline	Visit 3	N	20					35	55			
		Mean (SD)	0.20 (0.62)					0.06 (0.87)	0.11 (0.79)			
		Median (Min, Max)	0.00 (-1.0, 1.0)					0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)			
		Within group p-value	0.2891					0.7501	0.3137			
	Visit 4	N	20					36	56			
		Mean (SD)	0.00 (0.79)					0.06 (0.75)	0.04 (0.76)			

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
Disto-Lingual	Plaque Amount Assessment	Measured value		Visit 5	Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
					Within group p-value	1.0000	0.7999	0.7246
					N	20	36	56
					Mean (SD)	0.15 (0.67)	0.17 (0.88)	0.16 (0.80)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
					Within group p-value	0.5078	0.2698	0.1431
			Absolute change from baseline	Screening	N	20	36	56
					Mean (SD)	0.25 (0.44)	0.31 (0.52)	0.29 (0.49)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.30 (0.47)	0.23 (0.43)	0.25 (0.44)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.15 (0.37)	0.28 (0.51)	0.23 (0.47)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.20 (0.52)	0.36 (0.54)	0.30 (0.54)
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
		Visit 3		N	20	35	55	
				Mean (SD)	0.05 (0.60)	-0.09 (0.66)	-0.04 (0.64)	
				Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	
				Within group p-value	1.0000	0.6133	0.8331	
				Visit 4	N	20	36	56
					Mean (SD)	-0.10 (0.55)	-0.03 (0.74)	-0.05 (0.67)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
		Within group p-value			0.6875	0.9597	0.6695	

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total	
Lingual	Plaque Amount Assessment	Measured value	Screening	Visit 5	N	20	36	56	
				Mean (SD)	-0.05 (0.60)	0.06 (0.79)	0.02 (0.73)		
				Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)		
				Within group p-value	1.0000	0.8331	0.8569		
				Visit 3	N	20	35	55	
				Mean (SD)	0.30 (0.57)	0.20 (0.41)	0.24 (0.47)		
				Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)		
				Visit 4	N	20	36	56	
				Mean (SD)	0.15 (0.37)	0.19 (0.52)	0.18 (0.47)		
				Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)		
				Visit 5	N	20	36	56	
				Mean (SD)	0.20 (0.52)	0.25 (0.55)	0.23 (0.54)		
				Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)		
				Absolute change from baseline	Visit 3	N	20	35	55
				Mean (SD)	-0.10 (0.64)	-0.11 (0.68)	-0.11 (0.66)		
				Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)		
				Within group p-value	0.7266	0.4602	0.2292		
				Visit 4	N	20	36	56	
				Mean (SD)	-0.25 (0.64)	-0.14 (0.80)	-0.18 (0.74)		
				Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)		
				Within group p-value	0.1797	0.4117	0.0853		
				Visit 5	N	20	36	56	
				Mean (SD)	-0.20 (0.62)	-0.08 (0.69)	-0.13 (0.66)		



Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
Median (Min, Max)						0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)
Within group p-value						0.2891	0.6334	0.1665
Mesio-Buccal	Plaque Amount Assessment	Measured value		Screening	N	20	36	56
					Mean (SD)	0.55 (0.51)	0.56 (0.73)	0.55 (0.66)
					Median (Min, Max)	1.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.65 (0.59)	0.54 (0.66)	0.58 (0.63)
					Median (Min, Max)	1.00 (0.0, 2.0)	0.00 (0.0, 2.0)	1.00 (0.0, 2.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.50 (0.51)	0.69 (0.79)	0.63 (0.70)
					Median (Min, Max)	0.50 (0.0, 1.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.85 (0.75)	0.69 (0.62)	0.75 (0.67)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
		Absolute change from baseline		Visit 3	N	20	35	55
					Mean (SD)	0.10 (0.79)	0.03 (0.75)	0.05 (0.76)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
				Visit 4	Within group p-value	0.7744	0.9597	0.6023
					N	20	36	56
					Mean (SD)	-0.05 (0.69)	0.14 (0.83)	0.07 (0.78)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
				Visit 5	Within group p-value	1.0000	0.4037	0.5013
					N	20	36	56
					Mean (SD)	0.30 (0.80)	0.14 (0.76)	0.20 (0.77)
					Median (Min, Max)	0.50 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)
					Within group p-value	0.1796	0.3863	0.0618

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
Mesio-Lingual	Plaque Amount Assessment	Measured value		Screening	N	20	36	56
					Mean (SD)	0.15 (0.37)	0.31 (0.52)	0.25 (0.48)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.25 (0.44)	0.11 (0.32)	0.16 (0.37)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.05 (0.22)	0.25 (0.44)	0.18 (0.39)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.25 (0.55)	0.42 (0.65)	0.36 (0.62)
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
		Absolute change from baseline	Visit 3	N	20	35	55	
				Mean (SD)	0.10 (0.55)	-0.20 (0.58)	-0.09 (0.59)	
				Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	
				Within group p-value	0.6875	0.0918	0.3629	
				Visit 4	N	20	36	56
					Mean (SD)	-0.10 (0.45)	-0.06 (0.71)	-0.07 (0.63)
			Median (Min, Max)		0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)	
				Within group p-value	0.6250	0.8167	0.5262	
				Visit 5	N	20	36	56
					Mean (SD)	0.10 (0.55)	0.11 (0.82)	0.11 (0.73)
			Median (Min, Max)		0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)	
				Within group p-value	0.6875	0.4095	0.2784	
Total index	Plaque Amount Assessment	Measured value		Screening	N	20	36	56
					Mean (SD)	0.38 (0.35)	0.42 (0.39)	0.41 (0.37)

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total	
				Visit 3	Median (Min, Max)	0.20 (0.0, 1.2)	0.30 (0.0, 1.5)	0.30 (0.0, 1.5)	
					N	20	35	55	
					Mean (SD)	0.41 (0.34)	0.32 (0.35)	0.35 (0.35)	
				Visit 4	Median (Min, Max)	0.30 (0.0, 1.2)	0.30 (0.0, 1.5)	0.30 (0.0, 1.5)	
					N	20	36	56	
					Mean (SD)	0.27 (0.28)	0.38 (0.39)	0.34 (0.36)	
				Visit 5	Median (Min, Max)	0.20 (0.0, 0.8)	0.30 (0.0, 1.5)	0.25 (0.0, 1.5)	
					N	20	36	56	
					Mean (SD)	0.43 (0.48)	0.42 (0.40)	0.42 (0.43)	
				Absolute change from baseline	Median (Min, Max)	0.30 (0.0, 2.0)	0.30 (0.0, 1.8)	0.30 (0.0, 2.0)	
					Visit 3	N	20	35	55
					Mean (SD)	0.03 (0.35)	-0.09 (0.43)	-0.05 (0.40)	
					Median (Min, Max)	0.00 (-0.7, 0.5)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)	
					Within group p-value	0.6746	0.3564	0.5270	
					Visit 4	N	20	36	56
					Mean (SD)	-0.11 (0.38)	-0.04 (0.51)	-0.06 (0.46)	
					Median (Min, Max)	-0.05 (-0.6, 0.8)	0.00 (-1.2, 1.0)	0.00 (-1.2, 1.0)	
					Within group p-value	0.2162	0.9680	0.3619	
				Visit 5	N	20	36	56	
					Mean (SD)	0.05 (0.39)	0.00 (0.52)	0.02 (0.47)	
					Median (Min, Max)	0.05 (-0.7, 0.8)	0.05 (-1.2, 1.1)	0.05 (-1.2, 1.1)	
					Within group p-value	0.5679	0.8190	0.6683	
T44	Buccal	Plaque Amount Assessment	Measured value	Screening	N	20	36	56	
					Mean (SD)	0.30 (0.47)	0.31 (0.47)	0.30 (0.46)	
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	0.00 (0.0, 1.0)	
				Visit 3	N	20	35	55	

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
				Visit 4	Mean (SD)	0.40 (0.50)	0.37 (0.60)	0.38 (0.56)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
					N	20	36	56
				Visit 5	Mean (SD)	0.55 (0.60)	0.33 (0.48)	0.41 (0.53)
					Median (Min, Max)	0.50 (0.0, 2.0)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)
					N	20	36	56
				Visit 3	Mean (SD)	0.65 (0.59)	0.42 (0.50)	0.50 (0.54)
					Median (Min, Max)	1.00 (0.0, 2.0)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)
					N	20	35	55
				Visit 4	Mean (SD)	0.10 (0.45)	0.06 (0.73)	0.07 (0.63)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)
					Within group p-value	0.6250	0.8167	0.5262
				Visit 5	N	20	36	56
					Mean (SD)	0.25 (0.64)	0.03 (0.61)	0.11 (0.62)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)
					Within group p-value	0.1797	1.0000	0.2080
					N	20	36	56
					Mean (SD)	0.35 (0.67)	0.11 (0.67)	0.20 (0.67)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)
					Within group p-value	0.0654	0.4545	0.0314
Disto-Buccal	Plaque Amount Assessment	Measured value		Screening	N	20	36	56
					Mean (SD)	0.70 (0.66)	0.53 (0.65)	0.59 (0.65)
					Median (Min, Max)	1.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.50 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.65 (0.49)	0.57 (0.61)	0.60 (0.56)
					Median (Min, Max)	1.00 (0.0, 1.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total			
			Absolute change from baseline	Visit 4	N	20	36	56			
					Mean (SD)	0.85 (0.67)	0.58 (0.65)	0.68 (0.66)			
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)			
				Visit 5	N	20	36	56			
					Mean (SD)	0.80 (0.41)	0.72 (0.61)	0.75 (0.55)			
					Median (Min, Max)	1.00 (0.0, 1.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)			
				Visit 3	N	20	35	55			
					Mean (SD)	-0.05 (0.69)	0.03 (0.79)	0.00 (0.75)			
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)			
					Within group p-value	1.0000	0.9564	1.0000			
				Visit 4	N	20	36	56			
					Mean (SD)	0.15 (0.88)	0.06 (0.79)	0.09 (0.82)			
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)			
					Within group p-value	0.6133	0.8331	0.4155			
				Visit 5	N	20	36	56			
					Mean (SD)	0.10 (0.64)	0.19 (0.71)	0.16 (0.68)			
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 3.0)	0.00 (-1.0, 3.0)			
					Within group p-value	0.7266	0.1826	0.1344			
				Disto-Lingual	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
								Mean (SD)	0.40 (0.68)	0.61 (0.55)	0.54 (0.60)
				Median (Min, Max)	0.00 (0.0, 2.0)	1.00 (0.0, 2.0)	0.00 (0.0, 2.0)				
			Visit 3	N	20	35	55				
				Mean (SD)	0.30 (0.47)	0.43 (0.56)	0.38 (0.53)				
				Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)				
			Visit 4	N	20	36	56				
				Mean (SD)	0.75 (0.55)	0.50 (0.56)	0.59 (0.56)				

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
					Median (Min, Max)	1.00 (0.0, 2.0)	0.00 (0.0, 2.0)	1.00 (0.0, 2.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.25 (0.55)	0.72 (0.66)	0.55 (0.66)
					Median (Min, Max)	0.00 (0.0, 2.0)	1.00 (0.0, 3.0)	0.00 (0.0, 3.0)
		Absolute change from baseline		Visit 3	N	20	35	55
					Mean (SD)	-0.10 (0.72)	-0.20 (0.83)	-0.16 (0.79)
					Median (Min, Max)	0.00 (-2.0, 1.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
					Within group p-value	0.7656	0.2296	0.1327
				Visit 4	N	20	36	56
					Mean (SD)	0.35 (0.75)	-0.11 (0.82)	0.05 (0.82)
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
					Within group p-value	0.0918	0.5317	0.6262
				Visit 5	N	20	36	56
					Mean (SD)	-0.15 (0.88)	0.11 (0.85)	0.02 (0.86)
					Median (Min, Max)	0.00 (-2.0, 2.0)	0.00 (-1.0, 3.0)	0.00 (-2.0, 3.0)
					Within group p-value	0.6250	0.5723	0.9436
Lingual	Plaque Amount Assessment	Measured value		Screening	N	20	36	56
					Mean (SD)	0.40 (0.60)	0.50 (0.61)	0.46 (0.60)
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.45 (0.51)	0.26 (0.51)	0.33 (0.51)
					Median (Min, Max)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.55 (0.69)	0.31 (0.58)	0.39 (0.62)
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 5	N	20	36	56

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Absolute change from baseline	Visit 3	Mean (SD)	0.30 (0.57)	0.31 (0.47)	0.30 (0.50)
					Median (Min, Max)	0.00 (0.0, 2.0)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)
					N	20	35	55
					Mean (SD)	0.05 (0.76)	-0.23 (0.81)	-0.13 (0.79)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 1.0)
				Visit 4	Within group p-value	1.0000	0.1244	0.2404
					N	20	36	56
					Mean (SD)	0.15 (0.75)	-0.19 (0.89)	-0.07 (0.85)
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)
					Within group p-value	0.5625	0.2680	0.5712
				Visit 5	N	20	36	56
					Mean (SD)	-0.10 (0.72)	-0.19 (0.62)	-0.16 (0.65)
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)
					Within group p-value	0.7656	0.1185	0.0706
				Screening	N	20	36	56
					Mean (SD)	0.70 (0.66)	0.67 (0.59)	0.68 (0.61)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
					N	20	35	55
					Mean (SD)	0.85 (0.67)	0.74 (0.56)	0.78 (0.60)
Mesio-Buccal	Plaque Amount Assessment	Measured value		Visit 3	Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
					N	20	35	55
					Mean (SD)	0.85 (0.67)	0.74 (0.56)	0.78 (0.60)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)
				Visit 4	N	20	36	56
					Mean (SD)	1.10 (0.72)	0.86 (0.68)	0.95 (0.70)
					Median (Min, Max)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.90 (0.64)	0.94 (0.58)	0.93 (0.60)
					Median (Min, Max)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)	1.00 (0.0, 2.0)

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	0.15 (0.59)	0.09 (0.66)	0.11 (0.63)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)
					Within group p-value	0.4531	0.6072	0.2080
				Visit 4	N	20	36	56
					Mean (SD)	0.40 (0.88)	0.19 (0.67)	0.27 (0.75)
					Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)
					Within group p-value	0.0859	0.1447	0.0076
				Visit 5	N	20	36	56
					Mean (SD)	0.20 (0.62)	0.28 (0.78)	0.25 (0.72)
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 2.0)	0.00 (-1.0, 2.0)
					Within group p-value	0.2891	0.0378	0.0106
	Mesio-Lingual	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
					Mean (SD)	0.30 (0.47)	0.67 (0.68)	0.54 (0.63)
					Median (Min, Max)	0.00 (0.0, 1.0)	1.00 (0.0, 2.0)	0.00 (0.0, 2.0)
				Visit 3	N	20	35	55
					Mean (SD)	0.55 (0.60)	0.37 (0.49)	0.44 (0.54)
					Median (Min, Max)	0.50 (0.0, 2.0)	0.00 (0.0, 1.0)	0.00 (0.0, 2.0)
				Visit 4	N	20	36	56
					Mean (SD)	0.60 (0.68)	0.64 (0.72)	0.63 (0.70)
					Median (Min, Max)	0.50 (0.0, 2.0)	0.50 (0.0, 2.0)	0.50 (0.0, 2.0)
				Visit 5	N	20	36	56
					Mean (SD)	0.40 (0.60)	0.58 (0.55)	0.52 (0.57)
					Median (Min, Max)	0.00 (0.0, 2.0)	1.00 (0.0, 2.0)	0.00 (0.0, 2.0)
			Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	0.25 (0.79)	-0.29 (0.86)	-0.09 (0.87)



Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Female	Male	Total					
				Visit 4	Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-2.0, 1.0)	0.00 (-2.0, 2.0)				
					Within group p-value	0.2734	0.0650	0.4342				
					N	20	36	56				
					Mean (SD)	0.30 (0.73)	-0.03 (0.94)	0.09 (0.88)				
				Visit 5	Median (Min, Max)	0.00 (-1.0, 2.0)	0.00 (-2.0, 2.0)	0.00 (-2.0, 2.0)				
					Within group p-value	0.1484	0.8783	0.4448				
					N	20	36	56				
					Mean (SD)	0.10 (0.64)	-0.08 (0.77)	-0.02 (0.73)				
					Median (Min, Max)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)	0.00 (-1.0, 1.0)				
					Within group p-value	0.7266	0.5259	0.8564				
					Total index	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
									Mean (SD)	0.47 (0.42)	0.55 (0.34)	0.52 (0.37)
								Median (Min, Max)	0.30 (0.0, 1.2)	0.50 (0.0, 1.2)	0.50 (0.0, 1.2)	
				Visit 3	N	20	35	55				
					Mean (SD)	0.54 (0.33)	0.45 (0.35)	0.48 (0.34)				
					Median (Min, Max)	0.50 (0.0, 1.2)	0.30 (0.0, 1.3)	0.50 (0.0, 1.3)				
					Visit 4	N	20	36	56			
				Mean (SD)		0.73 (0.43)	0.53 (0.31)	0.60 (0.36)				
				Median (Min, Max)		0.70 (0.2, 2.0)	0.50 (0.0, 1.2)	0.50 (0.0, 2.0)				
				Visit 5		N	20	36	56			
					Mean (SD)	0.55 (0.43)	0.62 (0.36)	0.60 (0.38)				
					Median (Min, Max)	0.50 (0.0, 1.7)	0.70 (0.0, 1.8)	0.70 (0.0, 1.8)				
					Absolute change from baseline	Visit 3	N	20	35	55		
	Mean (SD)	0.07 (0.45)	-0.10 (0.42)	-0.04 (0.43)								
	Median (Min, Max)	0.20 (-1.0, 0.7)	-0.10 (-0.8, 0.8)	0.00 (-1.0, 0.8)								
	Within group p-value	0.3618	0.1813	0.5947								

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
TOT	Buccal	Plaque Amount Assessment	Measured value	Visit 4	N	20	36	56
					Mean (SD)	0.26 (0.45)	-0.02 (0.40)	0.08 (0.44)
				Visit 5	N	20	36	56
					Mean (SD)	0.09 (0.44)	0.07 (0.40)	0.08 (0.41)
				Visit 3	N	20	35	55
					Mean (SD)	0.43 (0.32)	0.43 (0.39)	0.43 (0.36)
				Visit 4	N	20	36	56
					Mean (SD)	0.48 (0.26)	0.39 (0.33)	0.42 (0.31)
				Visit 5	N	20	36	56
					Mean (SD)	0.51 (0.46)	0.42 (0.37)	0.45 (0.40)
				Visit 3	N	20	35	55
					Mean (SD)	-0.03 (0.35)	-0.05 (0.33)	-0.04 (0.33)
				Visit 4	N	20	36	56
					Mean (SD)	0.02 (0.40)	-0.10 (0.40)	-0.06 (0.40)

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
Disto-Buccal	Plaque Amount Assessment	Measured value		Visit 5	Median (Min, Max)	0.05 (-0.8, 0.7)	-0.05 (-1.4, 0.6)	0.00 (-1.4, 0.7)
					Within group p-value	0.6237	0.1731	0.3566
					N	20	36	56
					Mean (SD)	0.06 (0.42)	-0.08 (0.43)	-0.03 (0.42)
					Median (Min, Max)	0.05 (-1.0, 1.0)	-0.10 (-1.0, 0.8)	0.00 (-1.0, 1.0)
					Within group p-value	0.4731	0.3666	0.6992
				Screening	N	20	36	56
					Mean (SD)	0.51 (0.37)	0.67 (0.48)	0.61 (0.45)
					Median (Min, Max)	0.40 (0.0, 1.5)	0.70 (0.0, 2.2)	0.60 (0.0, 2.2)
				Visit 3	N	20	35	55
					Mean (SD)	0.69 (0.34)	0.59 (0.41)	0.62 (0.38)
					Median (Min, Max)	0.70 (0.2, 1.5)	0.50 (0.0, 1.5)	0.70 (0.0, 1.5)
				Visit 4	N	20	36	56
					Mean (SD)	0.64 (0.33)	0.64 (0.33)	0.64 (0.33)
					Median (Min, Max)	0.60 (0.0, 1.3)	0.60 (0.2, 1.5)	0.60 (0.0, 1.5)
				Visit 5	N	20	36	56
					Mean (SD)	0.67 (0.40)	0.72 (0.37)	0.70 (0.38)
					Median (Min, Max)	0.70 (0.0, 1.5)	0.70 (0.0, 2.2)	0.70 (0.0, 2.2)
			Absolute change from baseline	Visit 3	N	20	35	55
					Mean (SD)	0.18 (0.41)	-0.08 (0.40)	0.01 (0.42)
					Median (Min, Max)	0.20 (-0.7, 1.0)	0.00 (-0.8, 0.5)	0.00 (-0.8, 1.0)
					Within group p-value	0.0368	0.2818	0.7501
				Visit 4	N	20	36	56
					Mean (SD)	0.13 (0.46)	-0.03 (0.44)	0.02 (0.45)
					Median (Min, Max)	0.20 (-0.6, 0.9)	0.00 (-1.2, 0.7)	0.10 (-1.2, 0.9)
					Within group p-value	0.2524	0.8782	0.5543

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
Disto-Lingual	Plaque Amount Assessment	Measured value		Visit 5	N	20	36	56
				Mean (SD)	0.16 (0.37)	0.05 (0.51)	0.09 (0.46)	
				Median (Min, Max)	0.15 (-0.5, 0.8)	0.05 (-0.9, 1.5)	0.10 (-0.9, 1.5)	
				Within group p-value	0.0914	0.7446	0.2459	
				Screening	N	20	36	56
				Mean (SD)	0.26 (0.23)	0.39 (0.30)	0.34 (0.28)	
				Median (Min, Max)	0.20 (0.0, 0.7)	0.40 (0.0, 1.0)	0.30 (0.0, 1.0)	
				Visit 3	N	20	35	55
			Mean (SD)		0.27 (0.25)	0.32 (0.23)	0.30 (0.24)	
			Median (Min, Max)		0.20 (0.0, 0.8)	0.30 (0.0, 1.0)	0.30 (0.0, 1.0)	
			Visit 4	N	20	36	56	
				Mean (SD)	0.42 (0.22)	0.37 (0.24)	0.39 (0.23)	
				Median (Min, Max)	0.50 (0.0, 0.7)	0.30 (0.0, 1.2)	0.30 (0.0, 1.2)	
			Visit 5	N	20	36	56	
				Mean (SD)	0.26 (0.27)	0.43 (0.24)	0.37 (0.26)	
				Median (Min, Max)	0.20 (0.0, 1.0)	0.50 (0.0, 1.0)	0.30 (0.0, 1.0)	
			Absolute change from baseline	Visit 3	N	20	35	55
				Mean (SD)	0.01 (0.27)	-0.07 (0.31)	-0.04 (0.30)	
				Median (Min, Max)	0.00 (-0.7, 0.6)	0.00 (-0.8, 0.5)	0.00 (-0.8, 0.6)	
				Within group p-value	0.9462	0.1316	0.2360	
				Visit 4	N	20	36	56
				Mean (SD)	0.16 (0.23)	-0.02 (0.37)	0.04 (0.34)	
				Median (Min, Max)	0.20 (-0.3, 0.5)	-0.10 (-0.6, 1.2)	0.00 (-0.6, 1.2)	
				Within group p-value	0.0126	0.5140	0.5155	
			Visit 5	N	20	36	56	
				Mean (SD)	-0.01 (0.33)	0.04 (0.37)	0.02 (0.35)	

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name	Female	Male	Total
Median (Min, Max)					0.00 (-0.5, 0.5)	0.00 (-0.6, 0.8)	0.00 (-0.6, 0.8)
Within group p-value					1.0000	0.6506	0.8512
Lingual	Plaque Amount Assessment	Measured value	Screening	N	20	36	56
				Mean (SD)	0.25 (0.21)	0.31 (0.30)	0.29 (0.27)
				Median (Min, Max)	0.25 (0.0, 0.7)	0.20 (0.0, 1.2)	0.20 (0.0, 1.2)
			Visit 3	N	20	35	55
				Mean (SD)	0.24 (0.27)	0.22 (0.21)	0.23 (0.23)
				Median (Min, Max)	0.20 (0.0, 1.0)	0.20 (0.0, 0.7)	0.20 (0.0, 1.0)
			Visit 4	N	20	36	56
				Mean (SD)	0.31 (0.25)	0.21 (0.27)	0.25 (0.26)
				Median (Min, Max)	0.30 (0.0, 0.8)	0.20 (0.0, 1.2)	0.20 (0.0, 1.2)
			Visit 5	N	20	36	56
				Mean (SD)	0.21 (0.28)	0.26 (0.22)	0.24 (0.24)
				Median (Min, Max)	0.10 (0.0, 1.0)	0.20 (0.0, 1.0)	0.20 (0.0, 1.0)
		Absolute change from baseline	Visit 3	N	20	35	55
				Mean (SD)	-0.01 (0.32)	-0.08 (0.39)	-0.05 (0.37)
				Median (Min, Max)	-0.05 (-0.5, 0.7)	0.00 (-1.0, 0.7)	0.00 (-1.0, 0.7)
			Visit 4	Within group p-value	0.7841	0.2697	0.3219
				N	20	36	56
				Mean (SD)	0.06 (0.32)	-0.10 (0.43)	-0.04 (0.40)
				Median (Min, Max)	0.15 (-0.4, 0.5)	0.00 (-1.2, 0.8)	0.00 (-1.2, 0.8)
			Visit 5	Within group p-value	0.3847	0.2303	0.6723
				N	20	36	56
				Mean (SD)	-0.05 (0.28)	-0.06 (0.30)	-0.05 (0.29)
				Median (Min, Max)	0.00 (-0.5, 0.3)	0.00 (-0.9, 0.5)	0.00 (-0.9, 0.5)
				Within group p-value	0.6239	0.5677	0.4277

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
Mesio-Buccal	Plaque Amount Assessment	Measured value		Screening	N	20	36	56
					Mean (SD)	0.55 (0.33)	0.66 (0.42)	0.62 (0.39)
					Median (Min, Max)	0.50 (0.0, 1.3)	0.70 (0.0, 1.7)	0.70 (0.0, 1.7)
				Visit 3	N	20	35	55
					Mean (SD)	0.76 (0.28)	0.69 (0.37)	0.71 (0.34)
					Median (Min, Max)	0.80 (0.2, 1.3)	0.70 (0.0, 1.3)	0.70 (0.0, 1.3)
				Visit 4	N	20	36	56
					Mean (SD)	0.74 (0.33)	0.69 (0.35)	0.71 (0.34)
					Median (Min, Max)	0.80 (0.0, 1.2)	0.70 (0.0, 1.5)	0.70 (0.0, 1.5)
				Visit 5	N	20	36	56
					Mean (SD)	0.77 (0.33)	0.80 (0.34)	0.79 (0.33)
					Median (Min, Max)	0.80 (0.2, 1.7)	0.80 (0.2, 2.0)	0.80 (0.2, 2.0)
		Absolute change from baseline	Visit 3	N	20	35	55	
				Mean (SD)	0.21 (0.41)	0.05 (0.32)	0.10 (0.36)	
				Median (Min, Max)	0.15 (-0.5, 0.9)	0.00 (-0.5, 0.9)	0.10 (-0.5, 0.9)	
			Visit 4	Within group p-value	0.0466	0.4777	0.0558	
				N	20	36	56	
				Mean (SD)	0.19 (0.45)	0.03 (0.42)	0.09 (0.44)	
				Median (Min, Max)	0.20 (-0.7, 1.0)	0.00 (-0.9, 0.9)	0.10 (-0.9, 1.0)	
			Visit 5	Within group p-value	0.1204	0.5584	0.1422	
				N	20	36	56	
				Mean (SD)	0.22 (0.31)	0.15 (0.49)	0.17 (0.43)	
				Median (Min, Max)	0.15 (-0.3, 1.0)	0.10 (-0.8, 1.2)	0.10 (-0.8, 1.2)	
				Within group p-value	0.0035	0.0919	0.0038	
Mesio-Lingual	Plaque Amount Assessment	Measured value		Screening	N	20	36	56
					Mean (SD)	0.28 (0.28)	0.39 (0.33)	0.35 (0.31)

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Absolute change from baseline	Visit 3	Median (Min, Max)	0.20 (0.0, 1.0)	0.30 (0.0, 1.3)	0.20 (0.0, 1.3)
					N	20	35	55
					Mean (SD)	0.27 (0.18)	0.27 (0.23)	0.27 (0.21)
				Visit 4	Median (Min, Max)	0.20 (0.0, 0.7)	0.20 (0.0, 0.8)	0.20 (0.0, 0.8)
					N	20	36	56
					Mean (SD)	0.37 (0.26)	0.37 (0.28)	0.37 (0.27)
				Visit 5	Median (Min, Max)	0.30 (0.0, 1.0)	0.30 (0.0, 1.2)	0.30 (0.0, 1.2)
					N	20	36	56
					Mean (SD)	0.27 (0.26)	0.38 (0.27)	0.34 (0.27)
				Visit 3	Median (Min, Max)	0.20 (0.0, 1.0)	0.30 (0.0, 1.2)	0.30 (0.0, 1.2)
					N	20	35	55
					Mean (SD)	-0.01 (0.34)	-0.12 (0.33)	-0.08 (0.34)
				Visit 4	Median (Min, Max)	0.00 (-0.8, 0.7)	0.00 (-0.8, 0.5)	0.00 (-0.8, 0.7)
					Within group p-value	0.8507	0.0535	0.0879
					N	20	36	56
				Visit 5	Mean (SD)	0.10 (0.26)	-0.02 (0.40)	0.02 (0.35)
					Median (Min, Max)	0.10 (-0.4, 0.5)	0.00 (-1.0, 0.6)	0.05 (-1.0, 0.6)
					Within group p-value	0.1652	0.9911	0.4602
			Visit 5	N	20	36	56	
				Mean (SD)	-0.01 (0.39)	-0.01 (0.38)	-0.01 (0.38)	
				Median (Min, Max)	0.10 (-1.0, 0.7)	0.00 (-1.0, 0.7)	0.05 (-1.0, 0.7)	
				Within group p-value	0.8276	0.9923	0.8792	
Total index	Plaque Amount Assessment	Measured value		Screening	N	20	36	56
					Mean (SD)	0.39 (0.22)	0.49 (0.26)	0.46 (0.25)
					Median (Min, Max)	0.35 (0.0, 0.9)	0.50 (0.1, 1.2)	0.40 (0.0, 1.2)
				Visit 3	N	20	35	55

Category of Measurement	Subcategory of Measurement	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Absolute change from baseline	Visit 4	Mean (SD)	0.46 (0.18)	0.42 (0.23)	0.43 (0.21)
					Median (Min, Max)	0.40 (0.2, 1.0)	0.40 (0.1, 1.0)	0.40 (0.1, 1.0)
					N	20	36	56
				Visit 5	Mean (SD)	0.49 (0.19)	0.46 (0.19)	0.47 (0.18)
					Median (Min, Max)	0.50 (0.1, 0.8)	0.40 (0.2, 0.9)	0.40 (0.1, 0.9)
					N	20	36	56
				Visit 3	Mean (SD)	0.46 (0.29)	0.52 (0.21)	0.49 (0.24)
					Median (Min, Max)	0.40 (0.1, 1.3)	0.50 (0.2, 1.2)	0.40 (0.1, 1.3)
					N	20	35	55
				Visit 4	Mean (SD)	0.07 (0.23)	-0.07 (0.22)	-0.02 (0.23)
					Median (Min, Max)	0.05 (-0.4, 0.5)	-0.10 (-0.5, 0.4)	0.00 (-0.5, 0.5)
					Within group p-value	0.2378	0.1323	0.6468
					N	20	36	56
				Visit 5	Mean (SD)	0.10 (0.26)	-0.03 (0.26)	0.01 (0.27)
					Median (Min, Max)	0.05 (-0.3, 0.6)	0.00 (-0.6, 0.4)	0.00 (-0.6, 0.6)
					Within group p-value	0.1138	0.5271	0.8405
					N	20	36	56
					Mean (SD)	0.07 (0.25)	0.03 (0.30)	0.04 (0.28)
					Median (Min, Max)	0.00 (-0.4, 0.5)	0.00 (-0.6, 0.7)	0.00 (-0.6, 0.7)
					Within group p-value	0.3051	0.7589	0.4463

Data based on Per Protocol Set population.

SM17\_02\_B Biofilm acidogenicity (Silness-Löe Index), SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:54:59



Table 14.3-12 Oral microflora (PPS) (Part 2)

Category for Lab Test					Female	Male	Total
	Assessment (unit)	Result Category	Visit Name				
LOGARITHMIC	Lactobacilli (Bacterial Count) (log(CFU/mL))	Measured value	Screening	N	11	27	38
				Mean (SD)	3.23 (0.6561)	3.657 (1.239)	3.533 (1.11)
				Median (Min, Max)	3.26 (2.3, 4.04)	3.3 (2.3, 6.85)	3.28 (2.3, 6.85)
			Visit 3	N	10	23	33
				Mean (SD)	3.419 (0.7823)	3.731 (0.9997)	3.636 (0.9383)
				Median (Min, Max)	3.43 (2.3, 5.08)	3.64 (2.3, 6.66)	3.56 (2.3, 6.66)
			Visit 4	N	10	23	33
				Mean (SD)	3.551 (0.7584)	3.5 (1.081)	3.516 (0.9828)
				Median (Min, Max)	3.34 (2.6, 4.98)	3.3 (2.3, 5.93)	3.3 (2.3, 5.93)
			Visit 5	N	12	28	40
				Mean (SD)	3.414 (1.135)	3.547 (1.166)	3.507 (1.144)
				Median (Min, Max)	3.28 (2.3, 5.2)	3.2 (2.3, 6.2)	3.23 (2.3, 6.2)
		Absolute change from baseline	Visit 3	N	7	18	25
				Mean (SD)	0.2157 (0.8728)	0.1839 (0.8795)	0.1928 (0.8594)
				Median (Min, Max)	0.07 (-1.18, 1.26)	0.145 (-1.72, 1.34)	0.11 (-1.72, 1.34)
				Within group p-value	0.6875	0.3550	0.2565
			Visit 4	N	9	20	29
				Mean (SD)	0.3511 (0.7843)	-0.2835 (0.8967)	-0.08655 (0.9003)
				Median (Min, Max)	0.3 (-0.93, 1.36)	-0.245 (-2.58, 1.04)	-0.18 (-2.58, 1.36)
				Within group p-value	0.2656	0.2158	0.8249
			Visit 5	N	8	23	31
				Mean (SD)	0.7163 (0.9223)	-0.08478 (1.107)	0.1219 (1.106)
				Median (Min, Max)	1.135 (-0.7, 1.9)	-0.01 (-3.18, 1.9)	0 (-3.18, 1.9)
				Within group p-value	0.0781	0.6747	0.4902
S. Mutans (Bacterial Count)		Measured value	Screening	N	18	28	46

			Female		Male		Total		
Category for Lab Test	Assessment (unit)	Result Category	Visit Name						
(log(CFU/mL))			Visit 3	Mean (SD)	5.217 (0.9861)	5.409 (0.9702)	5.334 (0.9701)		
				Median (Min, Max)	5.405 (2.3, 6.98)	5.505 (3.6, 7.41)	5.495 (2.3, 7.41)		
				N	18	25	43		
			Visit 4	Mean (SD)	5.423 (0.7735)	5.336 (1.115)	5.372 (0.9767)		
				Median (Min, Max)	5.51 (3.9, 6.62)	5.26 (3.51, 7.15)	5.38 (3.51, 7.15)		
				N	18	29	47		
			Visit 5	Mean (SD)	5.696 (0.9155)	5.556 (1.15)	5.61 (1.058)		
				Median (Min, Max)	5.63 (4.15, 7.32)	5.82 (3.3, 7.32)	5.82 (3.3, 7.32)		
				N	18	29	47		
			Absolute change from baseline	Visit 3	Mean (SD)	5.753 (0.9045)	5.643 (0.9932)	5.685 (0.9517)	
					Median (Min, Max)	5.565 (4.15, 7.46)	5.72 (3, 7.48)	5.7 (3, 7.48)	
					N	18	24	42	
			Visit 4	Mean (SD)	0.2056 (0.6058)	-0.09458 (0.6976)	0.03405 (0.6691)		
				Median (Min, Max)	0.115 (-0.61, 1.96)	0.065 (-1.74, 1.07)	0.065 (-1.74, 1.96)		
				Within group p-value	0.2573	0.6775	0.6726		
			Visit 5	N	18	24	42		
				Mean (SD)	0.4783 (0.7051)	0.1104 (0.6658)	0.2681 (0.6991)		
				Median (Min, Max)	0.4 (-0.92, 2.26)	0.19 (-2.22, 1.11)	0.34 (-2.22, 2.26)		
			Visit 5	Within group p-value	0.0143	0.1179	0.0027		
				N	18	25	43		
				Mean (SD)	0.5361 (0.8585)	0.164 (0.8007)	0.3198 (0.8362)		
Visit 5	Median (Min, Max)	0.505 (-0.83, 3.23)	0.11 (-1.72, 1.15)	0.33 (-1.72, 3.23)					
	Within group p-value	0.0104	0.1867	0.0054					
	OBSERVED	Lactobacilli (Bacterial Count) (CFU/mL)	Measured value	Screening	N	20	36	56	
				Mean (SD)	2090 (3518)	277200 (1210000)	179000 (974400)		
				Median (Min, Max)	200 (0, 11000)	800 (0, 7000000)	700 (0, 7000000)		

Category for Lab Test	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
			Visit 3	N	20	31	51
				Mean (SD)	7440 (26660)	160700 (824500)	100600 (643300)
				Median (Min, Max)	100 (0, 120000)	1800 (0, 4600000)	1000 (0, 4600000)
			Visit 4	N	20	36	56
				Mean (SD)	7990 (22900)	39970 (152500)	28550 (123400)
				Median (Min, Max)	200 (0, 96000)	400 (0, 860000)	400 (0, 860000)
			Visit 5	N	20	36	56
				Mean (SD)	16290 (41000)	80950 (291500)	57860 (235900)
				Median (Min, Max)	200 (0, 160000)	500 (0, 1600000)	400 (0, 1600000)
		Absolute change from baseline	Visit 3	N	20	31	51
				Mean (SD)	5350 (25050)	65390 (439400)	41850 (342000)
				Median (Min, Max)	0 (-8600, 111000)	0 (-294000, 2400000)	0 (-294000, 2400000)
				Within group p-value	0.6583	0.4268	0.3325
			Visit 4	N	20	36	56
				Mean (SD)	5900 (21460)	-237300 (1125000)	-150400 (905200)
				Median (Min, Max)	0 (-7600, 90000)	-200 (-6660000, 102000)	0 (-6660000, 102000)
				Within group p-value	0.5566	0.1095	0.3017
			Visit 5	N	20	36	56
				Mean (SD)	14200 (39310)	-196300 (1117000)	-121100 (897500)
				Median (Min, Max)	0 (-11000, 151000)	0 (-6260000, 1460000)	0 (-6260000, 1460000)
				Within group p-value	0.2162	0.8174	0.5809
S. Mutans (Bacterial Count) (CFU/mL)	Measured value		Screening	N	20	36	56
				Mean (SD)	774700 (2107000)	1463000 (4464000)	1217000 (3785000)
				Median (Min, Max)	150000 (0, 9600000)	89000 (0, 26000000)	100000 (0, 26000000)
			Visit 3	N	20	31	51
				Mean (SD)	765100 (1208000)	1624000 (3278000)	1287000 (2680000)

Category for Lab Test	Assessment (unit)	Result Category	Visit Name		Female	Male	Total
		Absolute change from baseline	Visit 4	Median (Min, Max)	280000 (0, 4200000)	100000 (0, 1400000)	120000 (0, 1400000)
				N	20	36	56
				Mean (SD)	2477000 (5121000)	2131000 (4403000)	2255000 (4628000)
			Visit 5	Median (Min, Max)	240000 (0, 2100000)	250000 (0, 2100000)	240000 (0, 2100000)
				N	20	36	56
				Mean (SD)	3011000 (6796000)	2475000 (6239000)	2666000 (6387000)
			Visit 3	Median (Min, Max)	340000 (0, 2900000)	340000 (0, 3000000)	340000 (0, 3000000)
				N	20	31	51
				Mean (SD)	-9610 (1429000)	47850 (4793000)	25310 (3816000)
			Visit 4	Median (Min, Max)	0 (-5400000, 2540000)	0 (-22400000, 11400000)	0 (-22400000, 11400000)
				Within group p-value	0.2979	0.3776	0.1758
				N	20	36	56
			Visit 5	Mean (SD)	1702000 (3401000)	667700 (5197000)	1037000 (4629000)
				Median (Min, Max)	150000 (-176000, 1140000)	4000 (-1760000, 2100000)	59000 (-1760000, 2100000)
				Within group p-value	0.0005	0.1667	0.0010
			Visit 5	N	20	36	56
				Mean (SD)	2236000 (4920000)	1011000 (7146000)	1449000 (6419000)
				Median (Min, Max)	173000 (-260000, 1940000)	500 (-2060000, 2740000)	81000 (-2060000, 2740000)
				Within group p-value	0.0047	0.2037	0.0065

Data based on Per Protocol Set population.

SM17\_02\_B Oral Microflora, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:54:59

*Table 14.3-13 Gingival retraction and lesions in the mucosa at the placement of the pouch (PPS) (Part 2)*

Assessment	Visit Name	Result	Female	Male	Total
Gingival Retraction	Screening	N	10(50%)/20	15(42%)/36	25(45%)/56
		Y	10(50%)/20	21(58%)/36	31(55%)/56

Assessment	Visit Name	Result	Female	Male	Total
	Visit 3	N	10(50%)/20	15(43%)/35	25(45%)/55
		Y	10(50%)/20	20(57%)/35	30(55%)/55
	Visit 4	N	10(50%)/20	14(39%)/36	24(43%)/56
		Y	10(50%)/20	22(61%)/36	32(57%)/56
	Visit 5	N	10(50%)/20	16(44%)/36	26(46%)/56
		Y	10(50%)/20	20(56%)/36	30(54%)/56
Degree of Lesion	Screening	Degree 1	4(20%)/20	5(14%)/36	9(16%)/56
		Degree 2	6(30%)/20	14(39%)/36	20(36%)/56
		Degree 3	5(25%)/20	10(28%)/36	15(27%)/56
		Degree 4	3(15%)/20	4(11%)/36	7(13%)/56
		No lesions	2(10%)/20	3(8.3%)/36	5(8.9%)/56
	Visit 3	Degree 1	5(25%)/20	17(49%)/35	22(40%)/55
		Degree 2	6(30%)/20	10(29%)/35	16(29%)/55
		Degree 3	5(25%)/20	4(11%)/35	9(16%)/55
		No lesions	4(20%)/20	4(11%)/35	8(15%)/55
	Visit 4	Degree 1	9(45%)/20	10(28%)/36	19(34%)/56
		Degree 2	3(15%)/20	10(28%)/36	13(23%)/56
		Degree 3	2(10%)/20	6(17%)/36	8(14%)/56
		Degree 4	1(5%)/20	3(8.3%)/36	4(7.1%)/56
		No lesions	5(25%)/20	7(19%)/36	12(21%)/56
	Visit 5	Degree 1	7(35%)/20	13(36%)/36	20(36%)/56
		Degree 2	3(15%)/20	6(17%)/36	9(16%)/56
		Degree 3	2(10%)/20	8(22%)/36	10(18%)/56
		No lesions	8(40%)/20	9(25%)/36	17(30%)/56
Lesions in the mucosa at the placement of the pouch	Screening	N	2(10%)/20	3(8.3%)/36	5(8.9%)/56
		Y	18(90%)/20	33(92%)/36	51(91%)/56

Assessment	Visit Name	Result	Female	Male	Total
	Visit 3	N	4(20%)/20	4(11%)/35	8(15%)/55
		Y	16(80%)/20	31(89%)/35	47(85%)/55
	Visit 4	N	5(25%)/20	7(19%)/36	12(21%)/56
		Y	15(75%)/20	29(81%)/36	44(79%)/56
	Visit 5	N	8(40%)/20	9(25%)/36	17(30%)/56
		Y	12(60%)/20	27(75%)/36	39(70%)/56

Data based on Per Protocol Set population. Results are presented as n(%) / N, where N is the total number of observations at that specific timepoint.

SM17\_02\_B Gingival Retraction and Lesions in the mucosa at the placement of the pod, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:54:59

*Table 14.3-14 Degree of lesions in the mucosa at the placement of the pouch (PPS) (Part 2)*

Assessment	Result Category	Visit Name		Female	Male	Total
Degree of Lesion	Measured value	Screening	N	20	36	56
			Mean (SD)	2.15 (1.23)	2.19 (1.09)	2.18 (1.13)
			Median (Min, Max)	2.00 (0.0, 4.0)	2.00 (0.0, 4.0)	2.00 (0.0, 4.0)
		Visit 3	N	20	35	55
			Mean (SD)	1.60 (1.10)	1.40 (0.85)	1.47 (0.94)
			Median (Min, Max)	2.00 (0.0, 3.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)
		Visit 4	N	20	36	56
			Mean (SD)	1.25 (1.12)	1.67 (1.22)	1.52 (1.19)
			Median (Min, Max)	1.00 (0.0, 4.0)	2.00 (0.0, 4.0)	1.00 (0.0, 4.0)
		Visit 5	N	20	36	56
			Mean (SD)	0.95 (1.00)	1.36 (1.10)	1.21 (1.07)
			Median (Min, Max)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)	1.00 (0.0, 3.0)
	Absolute change from baseline	Visit 3	N	20	35	55
			Mean (SD)	-0.55 (0.76)	-0.74 (0.85)	-0.67 (0.82)

Assessment	Result Category	Visit Name	Female	Male	Total
Relative change from baseline (%)		Median (Min, Max)	-0.50 (-2.0, 1.0)	-1.00 (-3.0, 1.0)	-1.00 (-3.0, 1.0)
		Within group p-value	0.0098	0.0000	0.0000
		Visit 4 N	20	36	56
		Mean (SD)	-0.90 (0.91)	-0.53 (1.21)	-0.66 (1.12)
		Median (Min, Max)	-1.00 (-3.0, 0.0)	-1.00 (-4.0, 1.0)	-1.00 (-4.0, 1.0)
		Within group p-value	0.0005	0.0097	0.0000
		Visit 5 N	20	36	56
		Mean (SD)	-1.20 (0.95)	-0.83 (1.25)	-0.96 (1.16)
		Median (Min, Max)	-1.00 (-3.0, 0.0)	-1.00 (-4.0, 2.0)	-1.00 (-4.0, 2.0)
		Within group p-value	0.0001	0.0002	0.0000
		Visit 3 N	18	32	50
		Mean (SD)	-27.3 (37.9)	-32.5 (30.8)	-30.6 (33.2)
		Median (Min, Max)	-29.0 (-100, 50)	-33.0 (-100, 0)	-33.0 (-100, 50)
		Within group p-value	0.0137	0.0000	0.0000
		Visit 4 N	18	33	51
		Mean (SD)	-44.0 (37.1)	-18.9 (55.1)	-27.8 (50.5)
		Median (Min, Max)	-50.0 (-100, 0)	-33.0 (-100, 100)	-33.0 (-100, 100)
		Within group p-value	0.0005	0.0798	0.0004
		Visit 5 N	18	33	51
		Mean (SD)	-59.3 (36.8)	-30.1 (65.3)	-40.4 (58.2)
		Median (Min, Max)	-58.5 (-100, 0)	-33.0 (-100, 200)	-50.0 (-100, 200)
		Within group p-value	0.0001	0.0044	0.0000

Data based on Per Protocol Set population.

SM17\_02\_B Degree of Lesions in the mucosa at the placement of the pod, SAS program: descriptive\_stat\_tables.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:54:59

**Table 14.3-15** *Correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used (PPS) (Part 2)*

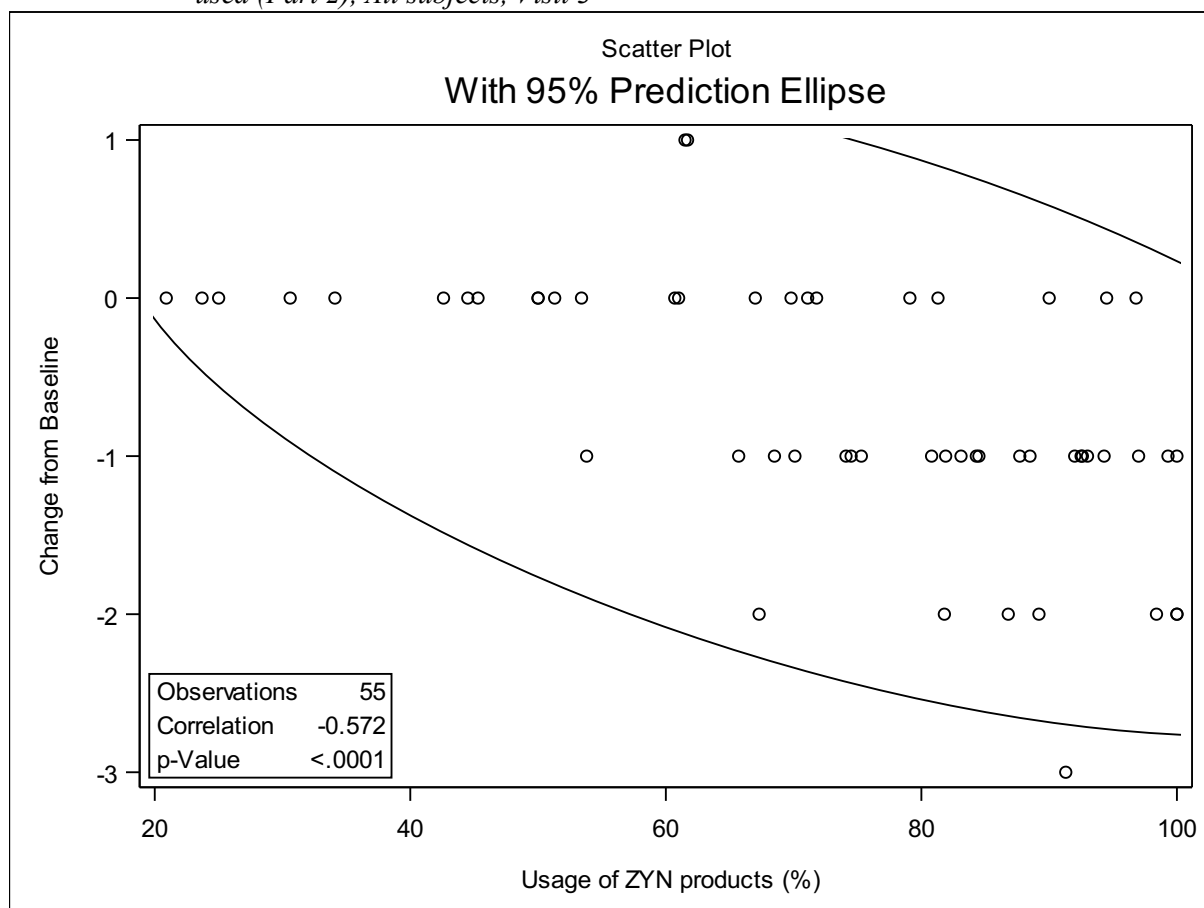
Gender	Visit Name	N	Correlation
Female	Visit 3	20	-0.634
	Visit 4	20	-0.361
	Visit 5	20	-0.521
Male	Visit 3	35	-0.534
	Visit 4	36	-0.546
	Visit 5	36	-0.480
Total	Visit 3	55	-0.572
	Visit 4	56	-0.494
	Visit 5	56	-0.502

ZYN usage is based on self-reported usage in the study period prior to the visit.

Data based on per protocol analysis set population.

SM17\_02\_B Correlation between change in oral mucosal lesions and percent of ZYN products used, SAS program: lesion\_zyn\_corr.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:52:38

**Figure 14.3-1** *Correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used (Part 2), All subjects, Visit 3*



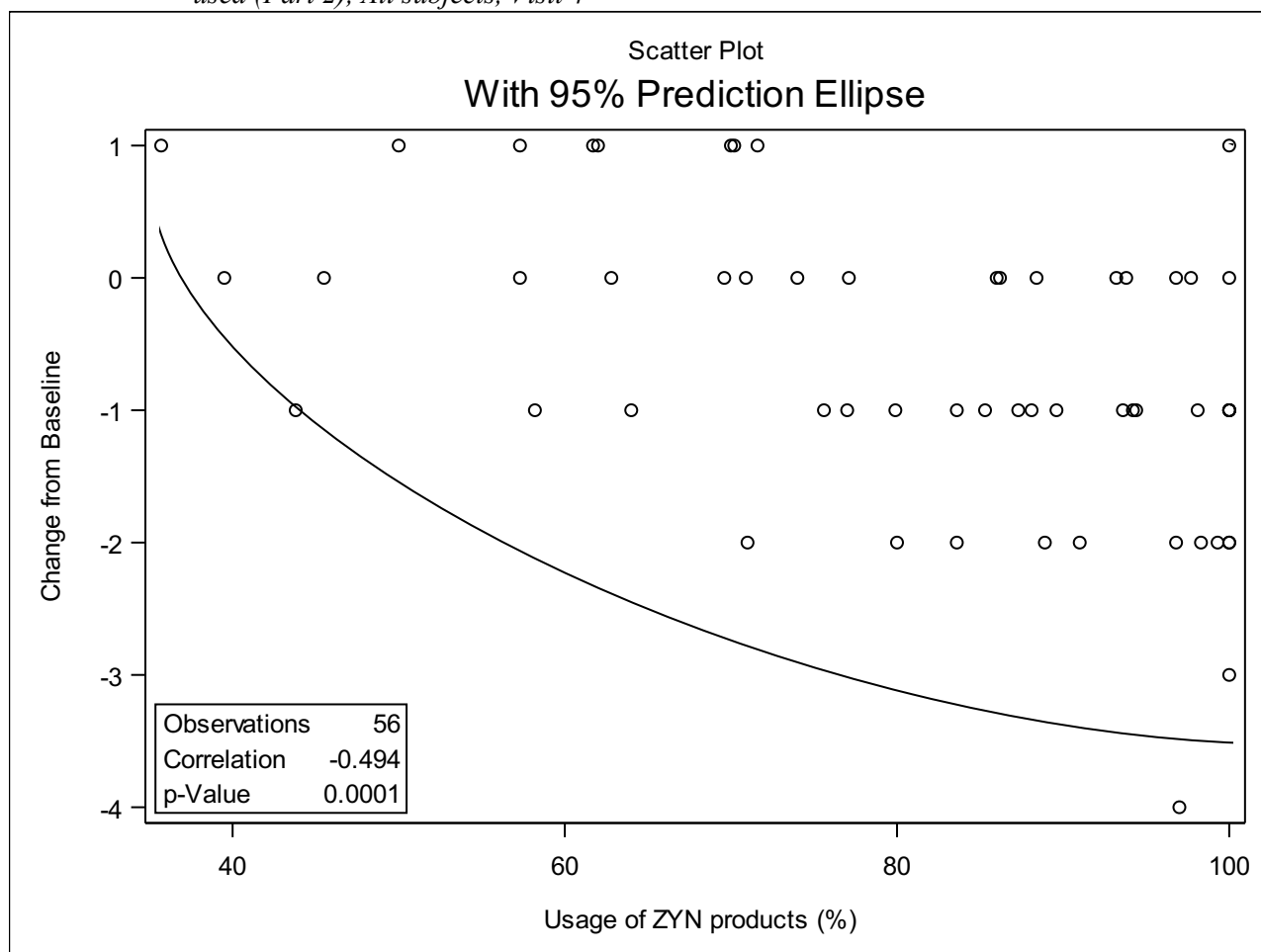
ZYN usage is based on self-reported usage in the study period prior to the visit.

Data based on per protocol analysis set population.

SM17\_02\_B Correlation between change in oral mucosal lesions and percent of ZYN products used, SAS program: lesion\_zyn\_corr.sas. Run by: Fredrik Hansson, fredrik.hansson@ctc-ab.se 2019-01-09T12:05:18



Figure 14.3-2 Correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used (Part 2), All subjects, Visit 4

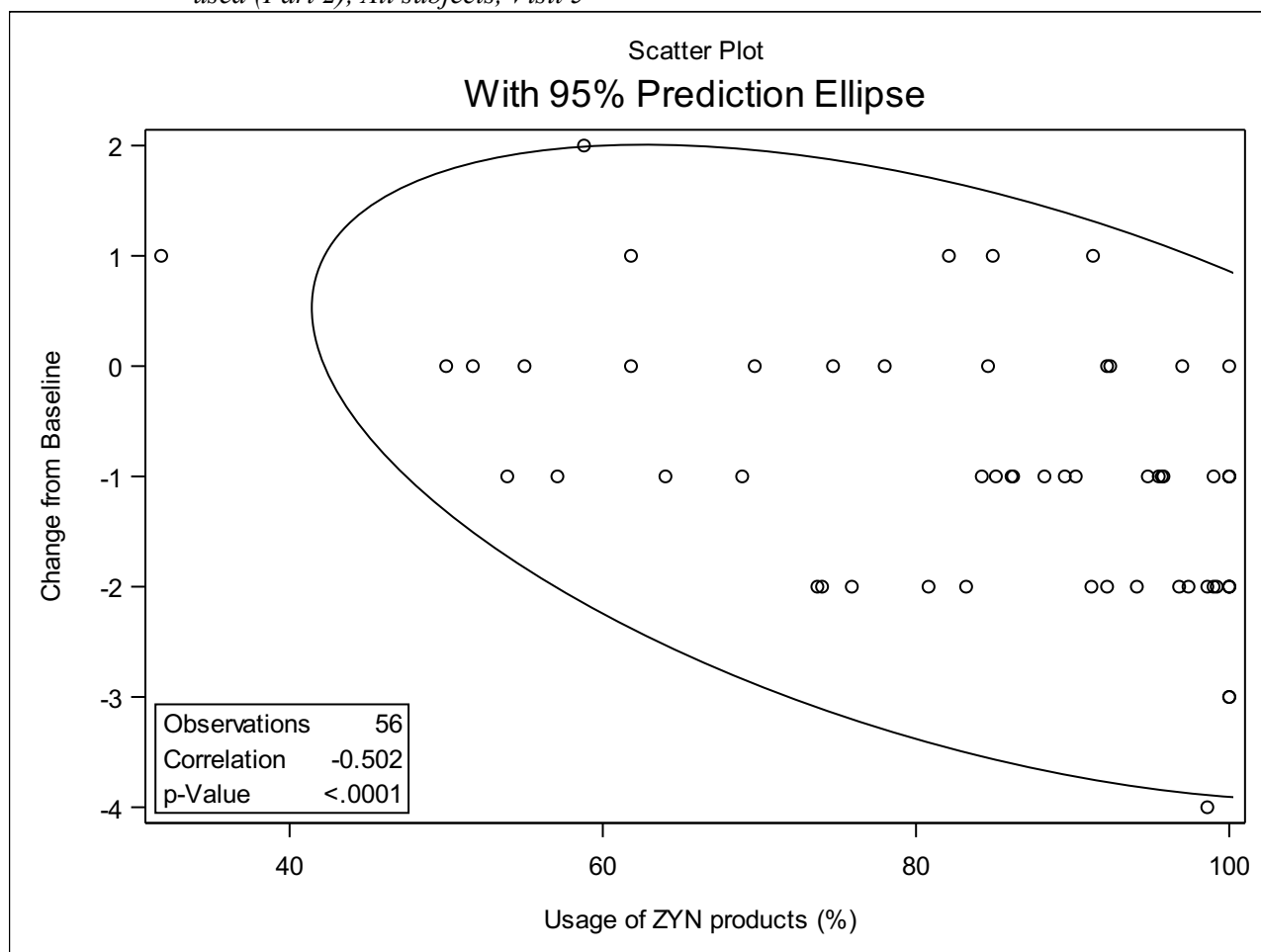


ZYN usage is based on self-reported usage in the study period prior to the visit.

Data based on per protocol analysis set population.

SM17\_02\_B Correlation between change in oral mucosal lesions and percent of ZYN products used,  
SAS program: lesion\_zyn\_corr.sas. Run by: Fredrik Hansson, fredrik.hansson@ctc-ab.se 2019-01-09T12:05:18

Figure 14.3-3 Correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used (Part 2), All subjects, Visit 5

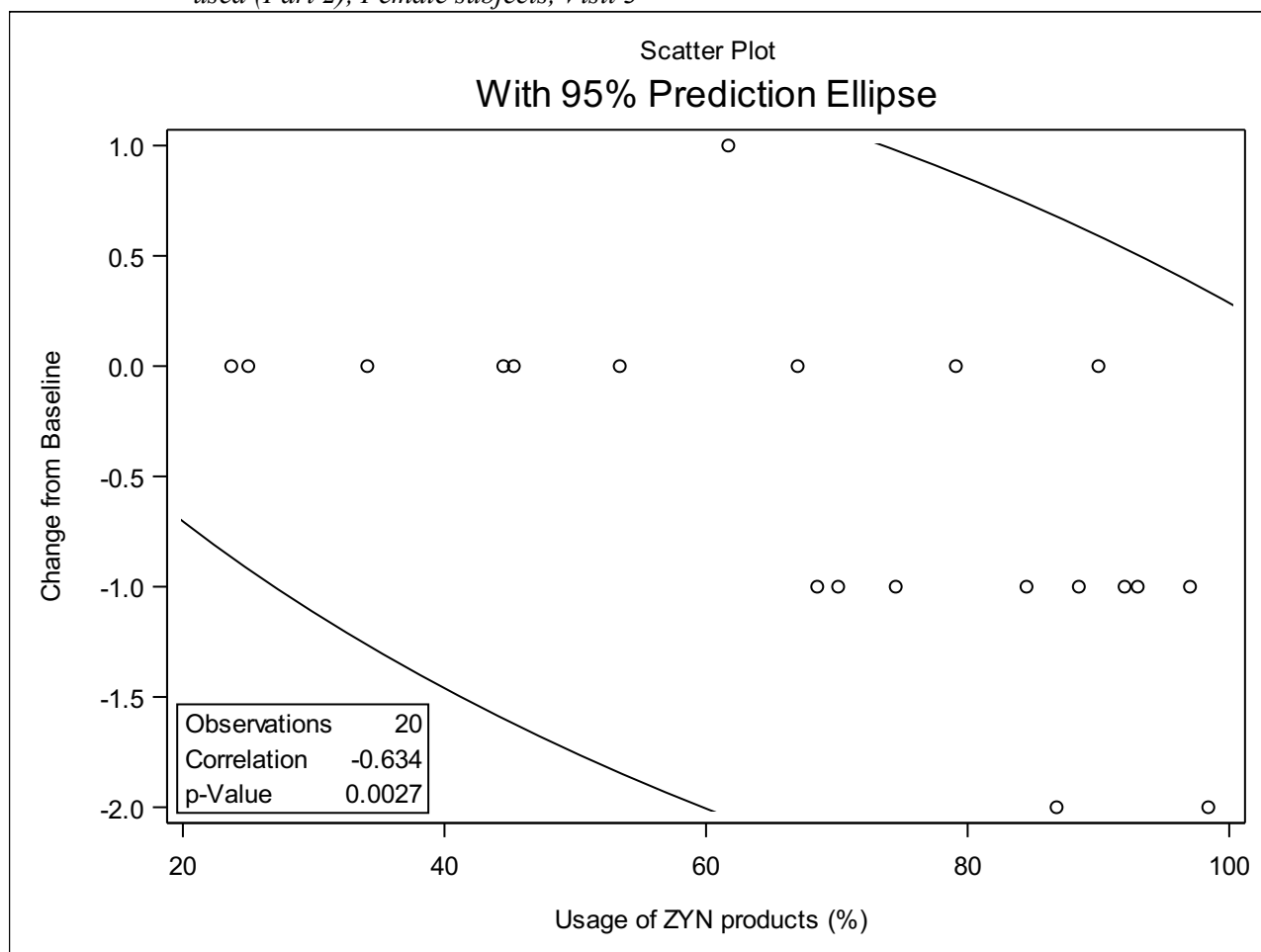


ZYN usage is based on self-reported usage in the study period prior to the visit.

Data based on per protocol analysis set population.

SM17\_02\_B Correlation between change in oral mucosal lesions and percent of ZYN products used,  
SAS program: lesion\_zyn\_corr.sas. Run by: Fredrik Hansson, fredrik.hansson@ctc-ab.se 2019-01-09T12:05:18

Figure 14.3-4 Correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used (Part 2), Female subjects, Visit 3

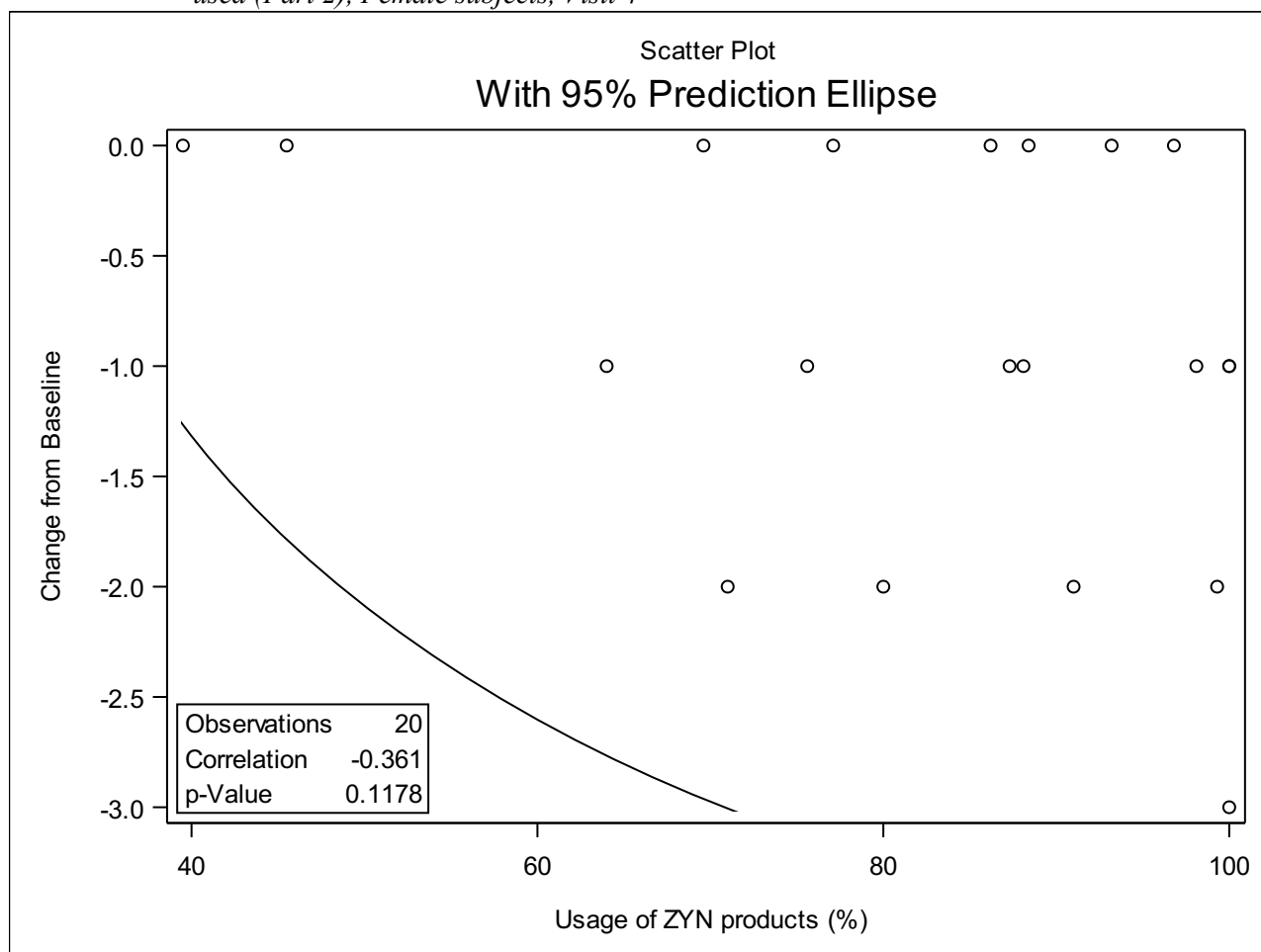


ZYN usage is based on self-reported usage in the study period prior to the visit.

Data based on per protocol analysis set population.

SM17\_02\_B Correlation between change in oral mucosal lesions and percent of ZYN products used,  
SAS program: lesion\_zyn\_corr.sas. Run by: Fredrik Hansson, fredrik.hansson@ctc-ab.se 2019-01-09T12:05:18

Figure 14.3-5 Correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used (Part 2), Female subjects, Visit 4

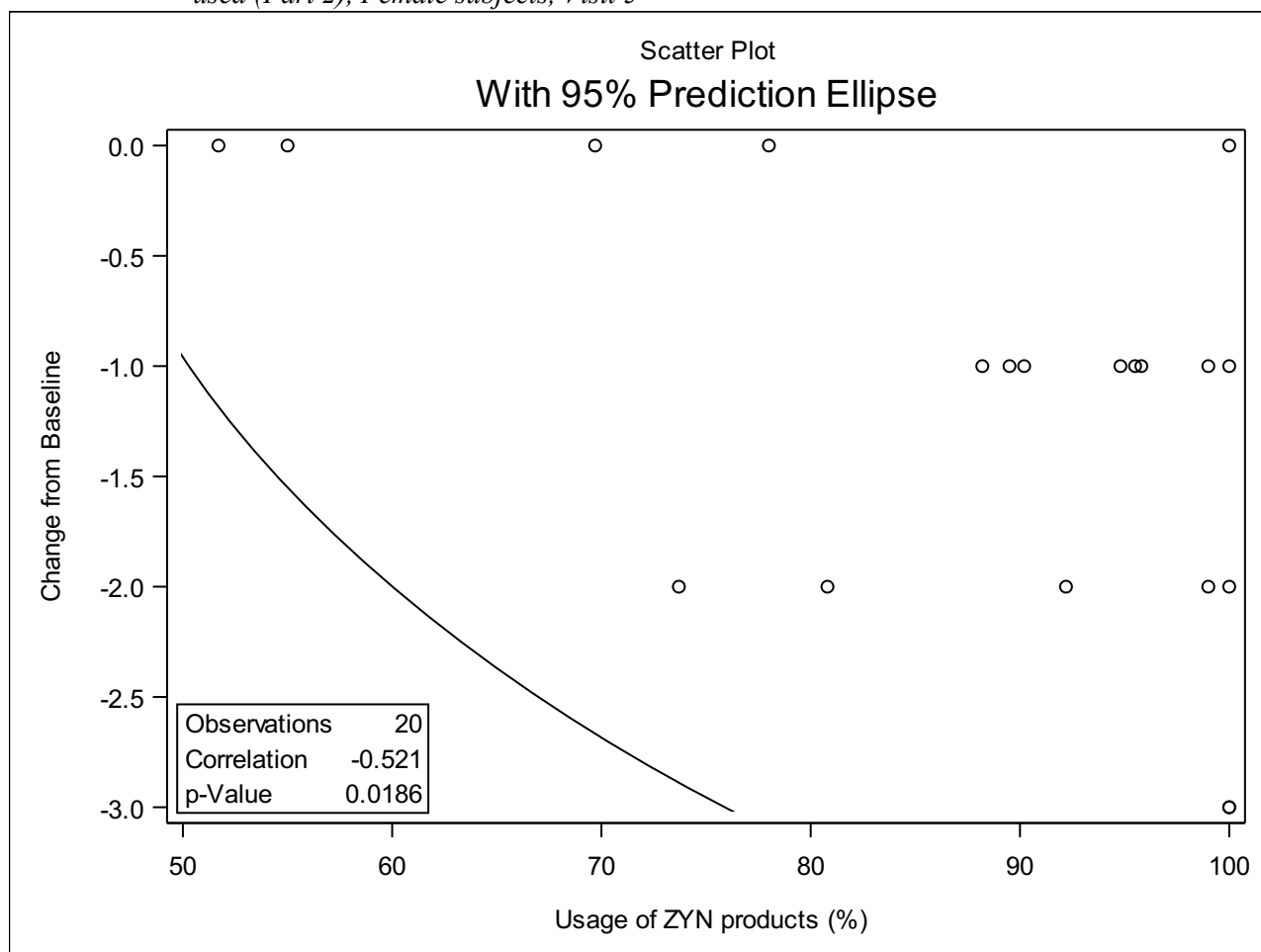


ZYN usage is based on self-reported usage in the study period prior to the visit.

Data based on per protocol analysis set population.

SM17\_02\_B Correlation between change in oral mucosal lesions and percent of ZYN products used,  
SAS program: lesion\_zyn\_corr.sas. Run by: Fredrik Hansson, fredrik.hansson@ctc-ab.se 2019-01-09T12:05:18

Figure 14.3-6 Correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used (Part 2), Female subjects, Visit 5

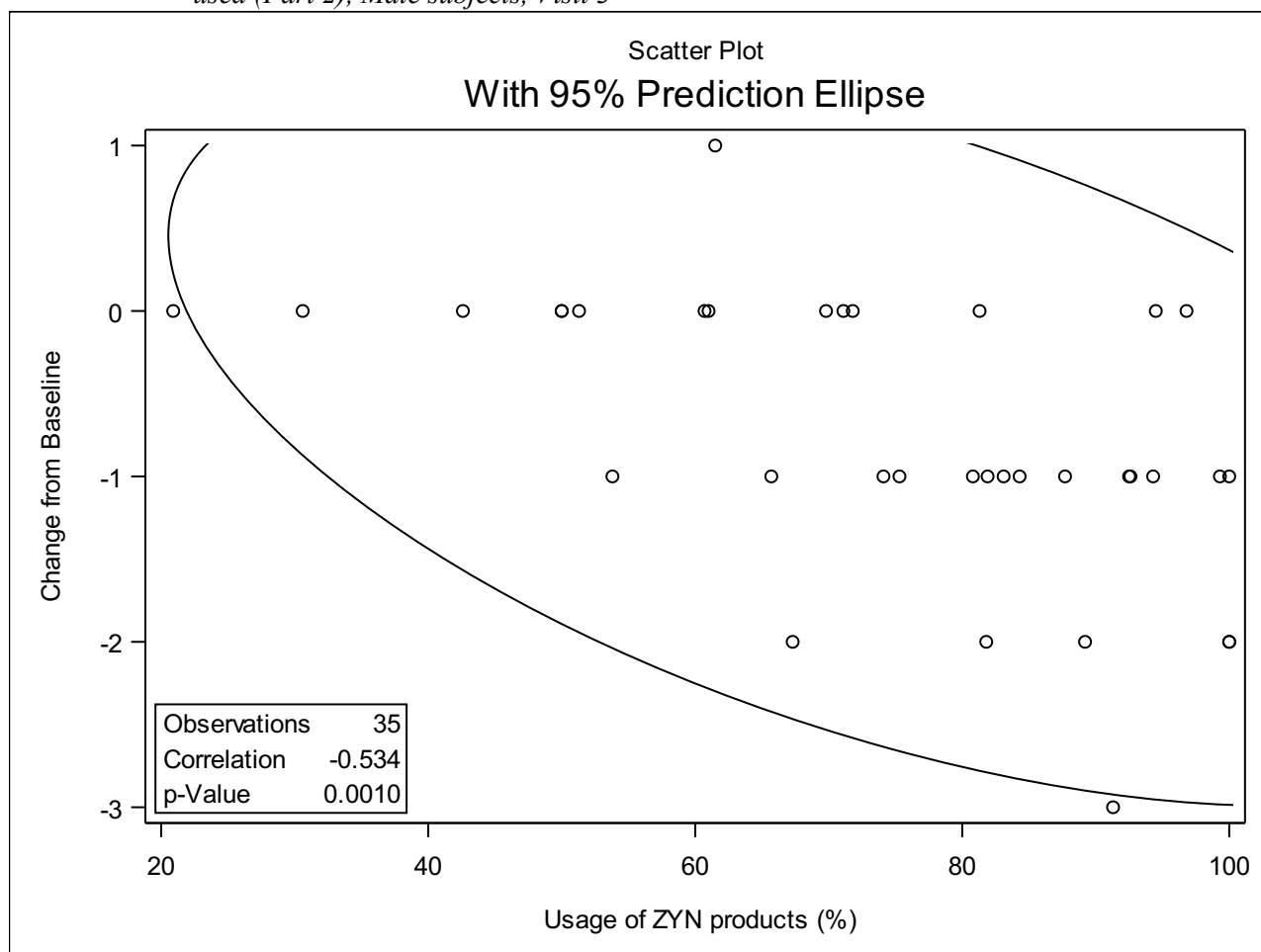


ZYN usage is based on self-reported usage in the study period prior to the visit.

Data based on per protocol analysis set population.

SM17\_02\_B Correlation between change in oral mucosal lesions and percent of ZYN products used,  
SAS program: lesion\_zyn\_corr.sas. Run by: Fredrik Hansson, fredrik.hansson@ctc-ab.se 2019-01-09T12:05:18

Figure 14.3-7 Correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used (Part 2), Male subjects, Visit 3

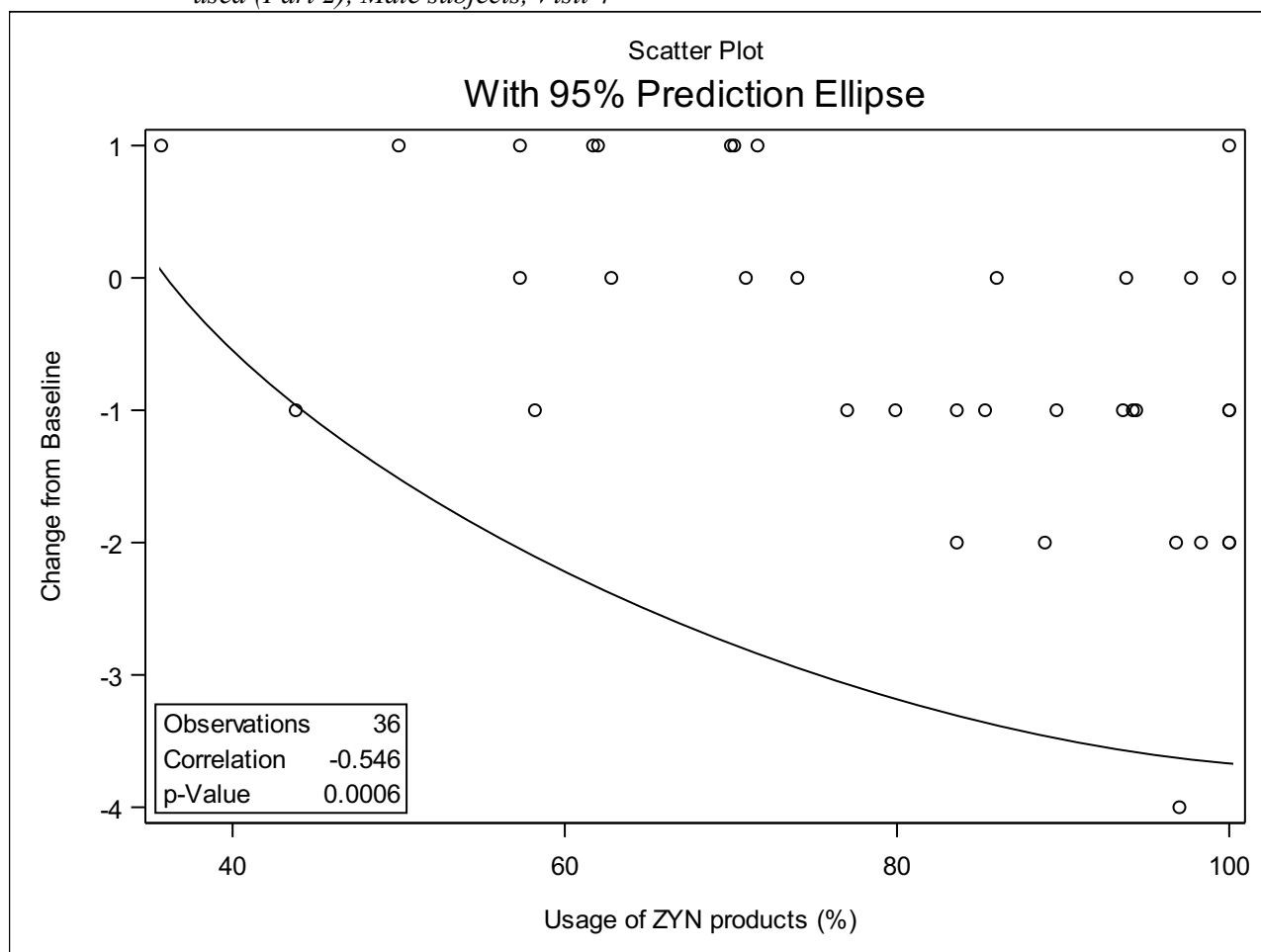


ZYN usage is based on self-reported usage in the study period prior to the visit.

Data based on per protocol analysis set population.

SM17\_02\_B Correlation between change in oral mucosal lesions and percent of ZYN products used,  
SAS program: lesion\_zyn\_corr.sas. Run by: Fredrik Hansson, fredrik.hansson@ctc-ab.se 2019-01-09T12:05:18

Figure 14.3-8 Correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used (Part 2), Male subjects, Visit 4

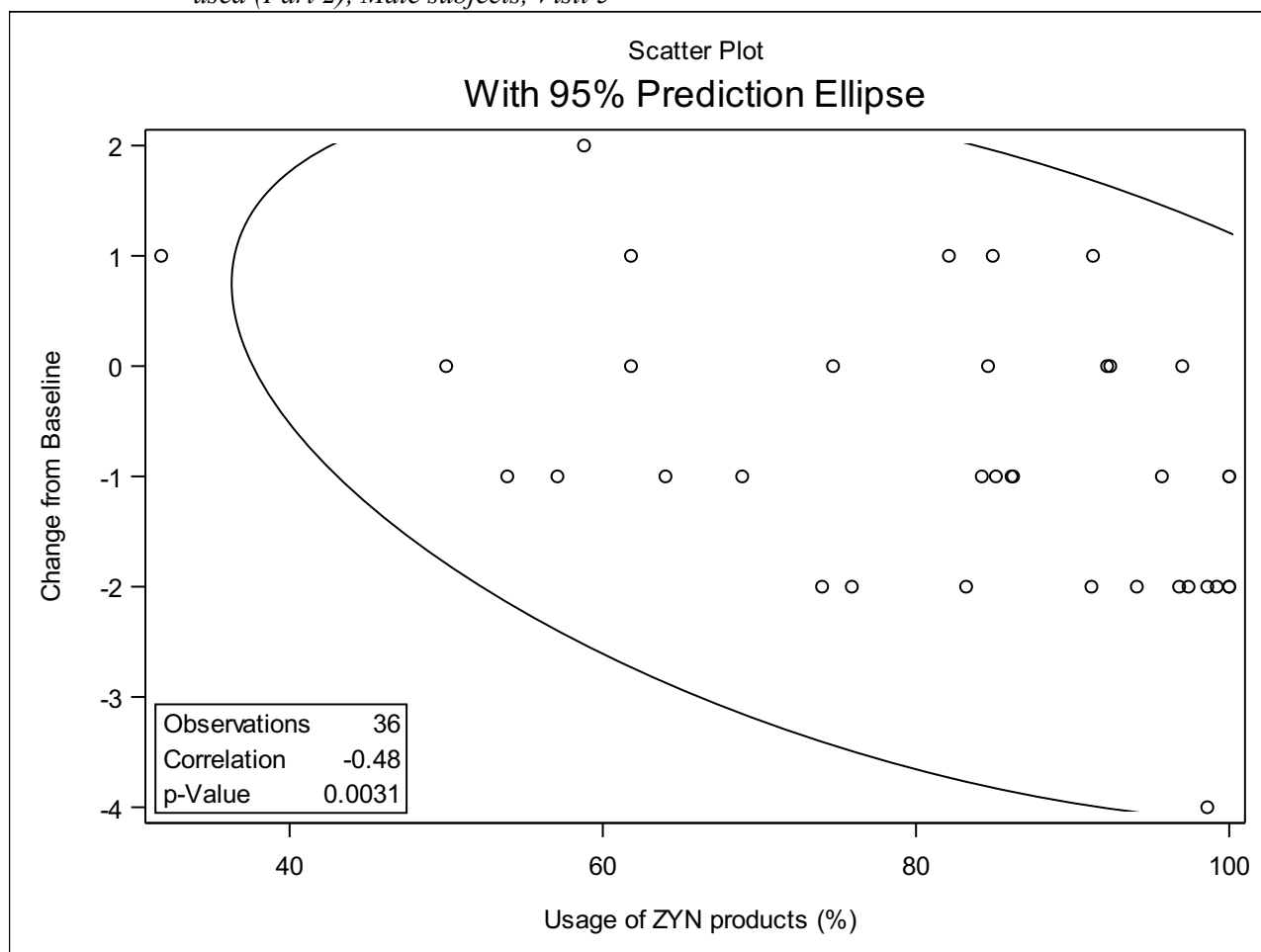


ZYN usage is based on self-reported usage in the study period prior to the visit.

Data based on per protocol analysis set population.

SM17\_02\_B Correlation between change in oral mucosal lesions and percent of ZYN products used,  
SAS program: lesion\_zyn\_corr.sas. Run by: Fredrik Hansson, fredrik.hansson@ctc-ab.se 2019-01-09T12:05:18

Figure 14.3-9 Correlation between change in oral mucosal lesions and percent of ZYN<sup>®</sup> products used (Part 2), Male subjects, Visit 5



ZYN usage is based on self-reported usage in the study period prior to the visit.

Data based on per protocol analysis set population.

SM17\_02\_B Correlation between change in oral mucosal lesions and percent of ZYN products used,  
SAS program: lesion\_zyn\_corr.sas. Run by: Fredrik Hansson, fredrik.hansson@ctc-ab.se 2019-01-09T12:05:18



## 14.4 Adverse events

### 14.4.1 Displays of adverse events

Table 14.4-1 Adverse events by SOC and PT (FAS) (Part 1)

	10% sucrose (pos control) N=19		10% xylitol (neg control) N=18		ZYN® Peppermint 3 mg N=19		ZYN® Smooth 3 mg N=18		WASH-OUT N=20		Total N=20	
System organ class Preferred term	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m
<b>Infections and infestations</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>1(5%)</b>	<b>2</b>	<b>1(5%)</b>	<b>2</b>
Nasopharyngitis	0	0	0	0	0	0	0	0	1(5%)	2	1(5%)	2

n, number of subjects; m, number of events

Percentages are based on the number of subjects in the treatment period included in the full analysis set.

Wash-out defined as the period between treatments starting 24 hours after dosing.

Adverse events that occurred during follow-up are omitted from summary.

SM17\_02\_A\_14\_03\_01\_02.rtf Adverse events by system organ class and preferred term, SAS program: ae\_summary\_by\_soc\_and\_pt.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:42:24

Table 14.4-2 Adverse events by SOC and PT (FAS) (Part 2)

	Female N=20		Male N=39		Total N=59	
System organ class Preferred term	n(%)	m	n(%)	m	n(%)	m
<b>Gastrointestinal disorders</b>	<b>2(10%)</b>	<b>2</b>	<b>3(8%)</b>	<b>3</b>	<b>5(8%)</b>	<b>5</b>
Dry mouth	0	0	1(3%)	1	1(2%)	1
Gingival blister	0	0	1(3%)	1	1(2%)	1
Lip pain	0	0	1(3%)	1	1(2%)	1
Nausea	2(10%)	2	0	0	2(3%)	2
<b>Infections and infestations</b>	<b>2(10%)</b>	<b>2</b>	<b>2(5%)</b>	<b>2</b>	<b>4(7%)</b>	<b>4</b>
Diarrhoea infectious	0	0	1(3%)	1	1(2%)	1
Gastroenteritis viral	1(5%)	1	0	0	1(2%)	1
Influenza	0	0	1(3%)	1	1(2%)	1
Nasopharyngitis	1(5%)	1	0	0	1(2%)	1
<b>Nervous system disorders</b>	<b>1(5%)</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>1(2%)</b>	<b>1</b>
Dizziness	1(5%)	1	0	0	1(2%)	1

n, number of subjects; m, number of events

Percentages are based on the number of subjects in the treatment period included in the full analysis set.

Adverse events that occurred during follow-up are omitted from summary.

SM17\_02\_B\_14\_03\_01\_02.rtf Adverse events by system organ class and preferred term, SAS program: ae\_summary\_by\_soc\_and\_pt.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:53:32

**Table 14.4-3 Adverse events: severity and relation, with subject identifications (FAS) (Part 1)**

			Mild --- NR	Total --- NR	Total --- R+NR
WASH-OUT (N=20)	Infections and infestations	Nasopharyngitis	1 (5%)	1 (5%)	1 (5%)

113 \*\*

\*\*: Subject randomization number

R: Related. NR: Not related. AEs judged as 'Possibly Related' or 'Probably Related' are grouped as 'Related'.

Wash-out defined as the period between treatments starting 24 hours after dosing.

Adverse events that occurred during follow-up are omitted from summary.

SM17\_02\_A\_14\_03\_01\_03.rtf AE: Adverse events: Severity and relation, with patient identifications, FAS, SAS program: ae\_tabulations.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:43:00

**Table 14.4-4 Adverse events: severity and relation, with subject identifications (FAS) (Part 2)**

			Mild --- NR	Mild --- Related	Moderate --- NR	Moderate --- Related	Total --- NR	Total --- Related	Total --- R+NR
Female (N=20)	Gastrointestinal disorders	Nausea		2 (10%)				2 (10%)	2 (10%)
				223 **					
				234					
	Infections and infestations	Gastroenteritis viral			1 (5%)		1 (5%)		1 (5%)
					229				
		Nasopharyngitis	1 (5%)				1 (5%)		1 (5%)
				228					
	Nervous system disorders	Dizziness		1 (5%)				1 (5%)	1 (5%)
				223					
Male (N=39)	Gastrointestinal disorders	Dry mouth		1 (3%)				1 (3%)	1 (3%)
				205					
		Gingival blister				1 (3%)		1 (3%)	1 (3%)
						227			
		Lip pain	1 (3%)				1 (3%)		1 (3%)
				253					
	Infections and infestations	Diarrhoea infectious			1 (3%)		1 (3%)		1 (3%)
					208				
		Influenza	1 (3%)				1 (3%)		1 (3%)
				231					

\*\*: Subject randomisation number

R: Related. NR: Not related. AEs judged as 'Possibly Related' or 'Probably Related' are grouped as 'Related'.

Adverse events that occurred during follow-up are omitted from summary.

SM17\_02\_B\_14\_03\_01\_03.rtf AE: Adverse events: Severity and relation, with patient identifications, FAS, SAS program: ae\_tabulations.sas. Run by: Calle Joachimsson, calle.joachimsson@ctc-ab.se 2018-10-24T13:53:02

**14.4.2 Listings of deaths, other serious adverse events and significant adverse events**

Not applicable.

**14.4.3 Narratives of deaths, other serious adverse events and significant adverse events**

Not applicable.

**14.4.4 Abnormal laboratory value listing (each subject)**

Not applicable.

## 15 REFERENCE LIST

1. Axéll T, Mörnstad H, Sundström B. The relation of the clinical picture to the histopathology of snuff dipper's lesions in a Swedish population. *J Oral Pathol* 1976;5:229-36.
2. Andersson G, Axéll T. Clinical appearance of lesions associated with the use of loose and portion-bag packed Swedish moist snuff: a comparative study. *J Oral Pathol Med* 1989;18:2-7.
3. Wallström M, Sand L, Nilsson F, Hirsch JM. The long-term effect of nicotine on the oral mucosa. *Addiction* 1999;94(3):417-23.
4. Silness J, Loe H. Periodontal disease in pregnancy. II. Correlation between oral hygiene and periodontal condition. *Acta Odontol Scand* 1964;22:121-135.
5. Kristoffersson K, Bratthall D. Transient reduction of *Streptococcus mutans* interdentally by chlorhexidine gel. *Scand J Dent Res* 1982;90:417-422.

## 16 APPENDICES

### 16.1 Study information

- 16.1.1 Protocol and protocol amendments
- 16.1.2 Sample CRF (unique pages only)
- 16.1.3 IEC approval including list of IEC members. Representative written subject information and sample consent form.
- 16.1.4 List and description of Investigators and other important participants in the study, including brief (1 page) CVs (*or equivalent summaries of training and experience relevant to the performance of the clinical study*).
- 16.1.5 Signatures of the Sponsor, Statistician and Principal Investigator
- 16.1.6 Listing of subjects receiving IP from specific batches, where more than one batch was used
- 16.1.7 Randomization scheme and codes (subject identification and treatment assigned)
- 16.1.8 Audit certificates (*if available*)
- 16.1.9 Documentation of statistical methods (*Statistical Analysis Plan*)
- 16.1.10 Documentation of inter-laboratory standardization methods and quality assurance procedures if used
- 16.1.11 Publications based on the study (*if applicable*)
- 16.1.12 Important publications referenced in the report

### 16.2 Subject data listings

- 16.2.1 Discontinued subjects
  - Discontinued subjects (Part 1 and Part 2)
- 16.2.2 Protocol deviations
  - Protocol deviations (Part 1 and Part 2)

- 16.2.3 Subjects excluded from the (efficacy) analysis
  - Subjects excluded from PPS (Part 1 and Part 2)
  - Subjects populations (Part 1 and Part 2)
  - Inclusion/exclusion exceptions (Part 1 and Part 2)
- 16.2.4 Demographic data and other baseline characteristics
  - Demographic data (Part 1 and Part 2)
  - Pregnancy test results (Part 1 and Part 2)
  - Medical history (Part 1 and Part 2)
  - Medications prior to first dose, indications (Part 1 and Part 2)
  - Medications prior to first dose, durations (Part 1 and Part 2)
  - Baseline symptoms, duration (Part 1 and Part 2)
  - Baseline symptoms, coding and severity (Part 1 and Part 2)
- 16.2.5 Compliance and/or drug concentration data
  - Exposure to study product (Part 1 and Part 2)
  - Concomitant medications, indications (Part 1 and Part 2)
  - Concomitant medications, durations (Part 1 and Part 2)
- 16.2.6 Individual clinical data (primary endpoints)
  - Saliva status at screening (Part 1)
  - Saliva and oral mucosa status (Part 2)
  - Physical examination (Part 1 and Part 2)
  - Dental plaque acidogenicity (Part 1)
  - Dental plaque acidogenicity (pH) site 1 (Part 2)
  - Dental plaque acidogenicity (pH) site 2 (Part 2)
  - Dental plaque acidogenicity (pH) mean of site 1 and site 2 (Part 2)
  - Plaque amount (Silness-Löe) T16 (Part 2)
  - Plaque amount (Silness-Löe) T21 (Part 2)
  - Plaque amount (Silness-Löe) T24 (Part 2)
  - Plaque amount (Silness-Löe) T36 (Part 2)
  - Plaque amount (Silness-Löe) T41 (Part 2)
  - Plaque amount (Silness-Löe) T44 (Part 2)
  - Plaque amount (Silness-Löe) mean of all sites (Part 2)
  - Oral microflora (Part 2)
- 16.2.7 AE listings
  - Adverse events, duration (Part 1 and Part 2)
  - Adverse events, coding and severity (Part 1 and Part 2)
- 16.2.8 Listing of individual laboratory measurements by subject
- 16.2.9 Subject disposition
  - Disposition events (Part 1 and Part 2)
  - Subjects visits (Part 1 and Part 2)
  - Subjects elements (Part 1 and Part 2)

### 16.3 Case report forms

- 16.3.1 CRFs for deaths, other SAEs and withdrawals for AE
- 16.3.2 Other CRFs submitted

Appendix 16 is provided as a separate document to the Clinical Study Report (CSR).