STATISTICAL ANALYSIS PLAN (SAP)

A Randomized, Single-Blind Study Assessing the Maximum Maxillary Bite Force When Using Two Novel Denture Adhesives Compared to Using No-Adhesive

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Sponsor: GlaxoSmithKline Consumer Healthcare (GSK)

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This document contains confidentiality statements that are not relevant for this publicly available version

Document History

Document	Version Date	Summary of Changes (New analysis or Change in planned analysis)
Original Analysis Plan	7 July 2022	Not applicable (N/A)

Amendments incorporate all revisions to date.

Table of contents

The purpose of this Statistical Analysis Plan is to describe the planned analyses and outputs to be included in the Clinical Study Report for GSK Protocol 218042.

1 Summary of Key Protocol Information

This will be a single-center, controlled, randomized, single blind (with respect to the examiner performing incisal bite force readings), 4-treatment, 4 treatment-period, cross-over study to evaluate maximum maxillary bite force in a population of full maxillary denture wearers. This research is being done to look at how well three denture adhesives hold the subject's denture in place over a 12-hour study period. Two of the denture adhesives are investigational. The other is a marketed denture adhesive (positive control). The study will also look at how well the subject's denture stays in place over a 12-hour study period when using no adhesive (negative control).

1.1 Study Design

This will be a single-center, controlled, randomized, single-blind (with respect to the examiner performing the incisal bite force (BF) measurements), 4-treatment, 4- period, cross-over study to evaluate the maximum maxillary BF in a population of full maxillary denture wearers. The aims of this study are to investigate the hold properties of two experimental denture adhesives using established maximum incisal BF methodology. A currently marketed denture adhesive will be used as a positive control, whilst use of no adhesive will be employed as a negative control.

1.2 Study Objectives

Objectives	Endpoints
Primary	
To compare the maximum incisal bite force until maxillary denture dislodgement of two experimental denture adhesives to no adhesive over 12 hours	Area over baseline in bite force over 12 hours
Secondary	
To compare the maximum incisal bite force until maxillary denture dislodgement of two experimental denture adhesives to no adhesive for time periods up to 9 hours.	Area over baseline up to 0.5, 1, 3, 6 and 9 hours
Safety	
To assess the local tolerability of two experimental denture adhesives	Treatment emergent adverse events and incidents

1.3 Treatments

The two experimental adhesives being investigated in this study have been formulated to provide denture hold throughout the day. In this study the experimental denture adhesives will be compared to no adhesive for all BF assessments. A marketed denture adhesive with extensive clinical evidence of efficacy, Super Poligrip Free (SPF), will be used as a positive control to assess study validity. All adhesive applications will be applied by clinical site dispensing staff and will be controlled by weight for the maxillary denture only (1.00g ± 0.05grams (g)). If subjects also wear a mandibular denture (either full or partial), then SPF can be used to stabilize the mandibular denture if required.

Treatments	
Test Product 1	Experimental Denture Adhesive 1 CCI
Test Product 2	Experimental Denture Adhesive 2 CCI
Positive Control	Super Poligrip Free Adhesive Cream (CCI
Negative Control	No Adhesive

1.4 Sample Size Calculation

Sample size calculations for this protocol were provided by GSK CH.

Sufficient subjects will be screened to randomize at least 45 subjects to ensure that at least 42 evaluable subjects complete the study. A sample size of 42 subjects completing all treatment periods will provide 90% power to demonstrate study success. Study success is defined as achieving both (a) study validity (Super Poligrip Free superior to no adhesive) and (b) superiority of either or both of experimental denture adhesives compared to no adhesive (two primary objectives). Prior clinical data supports a delta of 2.30 lbs for $AOB_{0\text{-}12}$, using two-sided t-tests with family wise significance level of 5% based on the Dunnett's adjustment with a 5% significance level assuming a residual standard deviation (square root of within mean square error) of 2.83 lbs. The estimate of residual standard deviation was obtained as the higher of the observed variability from two previous bite force studies conducted at OHRI (GSK studies CCI).

2 Planned Analyses

2.1 Interim Analysis

No interim analysis is planned.

2.2 Final Analyses

The final planned primary analyses will be performed after the completion of the following sequential steps:

1. All subjects have completed the study as defined in the protocol.
2. All required database cleaning activities including any external data reconciliation have been completed and database has been locked.
3. All criteria for unblinding the randomization codes have been met and the randomization codes have been distributed.

3 Treatment Assignment

3.1 Randomization

The randomization schedule indicates the treatment order sequence; one of the three adhesives or no adhesive (negative control) to be used for each of the four study periods. The randomization uses a Williams Square layout appropriate for a 4-period / 4-treatment crossover design. The product received by the study site includes actual product information (not coded). Therefore, the randomization schedule uses the same product information. This randomization schedule will be used to dispense study treatments to the subjects. The product names used on the randomization schedule are:

Experimental Denture Adhesive 1 CCI
Experimental Denture Adhesive 2 CCI
Super Poligrip Free Adhesive Cream
No Adhesive

Although the study only plans to enroll approximately 45 subjects to ensure that at least 42 evaluable subjects complete the study, the randomization schedule includes treatment order sequences for 60 subjects.

The randomization schedule was provided to the OHRI study coordinator by the unblinded IU statistician.

4 Data Analysis

Data analysis will be performed by PPD The statistical analysis software used will be SAS version 9.4 in a Windows environment.

Prior to database closure a Blind Data Review Meeting (BDRM) will be conducted in which various aspects of the trial will be discussed and agreed between blinded GSK CH team members.

Except as described below, tables and listings will be produced for all randomized subjects.

4.1 Populations for Analysis

Tables and Listings described in this section will be produced for all randomized subjects.

4.1.1 Subject Disposition

Descriptive statistics (frequency and percentage) will be provided for study completion in Table 1. For subjects who discontinue, descriptive statistics (frequency and percentage) will be provided for the reasons for discontinuation in Table 2.

4.1.2 Protocol Deviations

Protocol deviations will be listed in Listing 1. No formal statistical analyses of protocol deviations will be performed.

4.1.3 Analysis Populations

3 analysis populations are defined.

Population	Definition / Criteria	Analyses Evaluated
Safety	• All randomized subjects who receive treatment at least once during the study. • This population will be based on the treatment the subject actually received.	• Study Population • Safety
Intent-To-Treat (Modified) (MITT)	• All randomized subjects with at least one post baseline assessment of efficacy. • This population will be based on the treatment to which the subject was randomized. • Any subject who receives a treatment randomization number will be considered to have been randomized.	• Efficacy
Per-Protocol (PP)	• Subset of the MITT population. • Subjects with a protocol violation that is deemed to affect efficacy assessments in all study periods will be excluded from the PP population. • Subjects with a protocol violation that is deemed to affect efficacy assessments in	• Efficacy

Population	Definition / Criteria	Analyses Evaluated
	some (but not all) study periods will be part of the PP population, but their data will be excluded from the period(s) affected by the protocol violation for a PP analysis. • Performed for the primary efficacy variable if the number of subjects evaluable in any of the treatment groups for the MITT and PP populations differs by 10% or more. The decision on whether a PP analysis will be performed will be made prior to study unblinding.	

The numbers of subjects included in each of the analysis populations, and the number excluded from each population broken down by the reason for exclusion will be presented in Table 3.

4.2 Subject Demographics and Other Baseline Characteristics

Demographic and baseline characteristics summary tables will be produced for the MITT population. Because of the crossover design, demographic and baseline characteristics for the MITT will be tabulated overall only, not by treatment. Demographic and baseline characteristics will be tabulated overall and by treatment for the PP population.

4.2.1 Demographic Characteristics

Descriptive statistics (number of subjects, mean, standard deviation (SD), median, minimum and maximum for continuous variables, and frequency and percentage for categorical variables) will be provided for demographic data in Table 4. Categorical demographic variables include sex, race, and ethnicity. Continuous demographic variables include age.

4.2.2 Baseline Characteristics

Descriptive statistics (frequency and percentage) will be provided for baseline data in Table 5. Baseline variables include denture bearing tissue score, Kapur-Olshan Index, and well-made assessment.

4.2.3 General Medical History

Medical history and conditions, surgical history, denture history, concomitant medications, and non-drug treatment will be collected in the study database but will not be reported in tables or listings.

4.3 Analysis of Efficacy

Efficacy analyses will be performed for the MITT population, and if necessary, the PP population.

4.3.1 Primary Efficacy Endpoint

4.3.1.1 Primary Efficacy Endpoint Definition

Incisal bite force (BF) (lbs) will be recorded at hour 0 (baseline, pre-treatment) and at 0.5, 1, 3, 6, 9, and 12 hours post-treatment.

The primary efficacy endpoint is area over baseline (AOB) over 12 hours for BF (denoted by $AOB_{0\text{-}12}$) for each adhesive.

To calculate $AOB_{0\text{-}12}$, first the AUC is calculated from 0 to 12 hours using the trapezoid method using the nominal bite force times; we denote this by $AUC_{0\text{-}12}$. $AOB_{0\text{-}12}$ is defined as $(AUC_{0\text{-}12})/12$ minus baseline BF. This transformation will return the measurement to the same scale as the original observations whilst also looking at the average amount of improved force over time by subtracting the baseline value. Higher values of AOB demonstrate a stronger BF over time than lower values. Missing readings will be imputed using linear interpolation between pre and post the missing values, if necessary. In the case of more than one missing value or if the 12-hour value is missing, the AOB will be set to missing.

The study validity will first be evaluated by comparing Super Poligrip Free vs no adhesive for $AOB_{0\text{-}12}$. Demonstrating study validity ($p<0.05$ for Super Poligrip Free vs no adhesive) is a prerequisite to making inferences for all other treatment comparisons. If the initial validation step is not achieved, the other treatment comparisons will still be performed and presented but the significance tests will not be formally evaluated. The primary objectives are to compare $AOB_{0\text{-}12}$ of the two test experimental adhesives versus no adhesive. Therefore, study success is defined as achieving both (a) study validity (Super Poligrip Free superior to no adhesive) and (b) superiority of Experimental Denture Adhesive 1 compared to no adhesive, or Experimental Denture Adhesive 2 compared to no adhesive, or both.

4.3.1.2 Statistical Hypothesis, Model, and Method of Analysis

Null Hypothesis 1: No difference between Super Poligrip Free and no adhesive for $AOB_{0\text{-}12}$.

Alternative Hypothesis 1: Difference (superiority) for Super Poligrip Free compared to no adhesive for $AOB_{0\text{-}12}$.

Null Hypothesis 2: No difference between Experimental Denture Adhesive 1 and no adhesive for $AOB_{0\text{-}12}$.

Alternative Hypothesis 2: Difference (superiority) for Experimental Denture Adhesive 1 compared to no adhesive for $AOB_{0\text{-}12}$.

Null Hypothesis 3: No difference between Experimental Denture Adhesive 2 and no adhesive for $AOB_{0\text{-}12}$.

Alternative Hypothesis 3: Difference (superiority) for Experimental Denture Adhesive 2 compared to no adhesive for $AOB_{0\text{-}12}$.

An analysis of covariance (ANCOVA) model will be used to analyze $AOB_{0\text{-}12}$, with treatment and period as fixed effects; the covariates in this model are the subject level baseline and period level baseline minus subject level baseline. Subject will be included as a random effect. Pairwise treatment comparisons will be obtained as a difference in adjusted means and presented with 95% confidence intervals (CI) and associated p-values. Violations of normality and homogeneity of variance assumptions may be evaluated and if found will be overcome using transformations (e.g. natural logarithm) or performing a non-parametric analysis (Friedman's test). The study validity will first be evaluated by comparing Super Poligrip Free vs no adhesive for $AOB_{0\text{-}12}$. The primary objectives are to compare incisal bite forces of Experimental Denture Adhesive 1 and Experimental Denture Adhesive 2 versus no adhesive over 12 hours, $AOB_{0\text{-}12}$.

A two-sided 5% significance level will be used for all tests. The comparison of Super Poligrip Free against no adhesive will be performed with no multiple-testing adjustment. The comparisons of the two test products against no adhesive will use a Dunnett adjustment for multiple comparisons against a control.

The ANOVA table from the $AOB_{0\text{-}12}$ ANCOVA will be tabulated in Table 6. Adjusted means, standard errors, and 95% confidence intervals for $AOB_{0\text{-}12}$ will be tabulated by treatment in Table 7. For differences in $AOB_{0\text{-}12}$ between Super Poligrip Free and no adhesive, Experimental Denture Adhesive 1 and no adhesive, and Experimental Denture Adhesive 2 and no adhesive, adjusted differences, standard errors, p-values and 95% confidence intervals will be tabulated in Table 8; 95% CI and p-value for Super Poligrip Free against no adhesive will use with no multiple-testing adjustment; 95% CIs and p-values for the two test products against no adhesive will use a Dunnett adjustment for multiple comparisons against a control. The adjusted differences with 95% confidence intervals for $AOB_{0\text{-}12}$ between pairs of treatments from Table 8 will be plotted in Figure 2.

4.3.2 Secondary Efficacy Variables

$AOB_{0\text{-}0.5}$, $AOB_{0\text{-}1}$, $AOB_{0\text{-}3}$, $AOB_{0\text{-}6}$, $AOB_{0\text{-}9}$: AOB for 0.5, 1, 3, 6 and 9 hours will be defined and analyzed in a similar manner as $AOB_{0\text{-}12}$ in section 4.3.1. However, no adjustments for multiple testing will be carried out. The ANOVA tables for $AOB_{0\text{-}0.5}$, $AOB_{0\text{-}1}$, $AOB_{0\text{-}3}$, $AOB_{0\text{-}6}$, and $AOB_{0\text{-}9}$ will be tabulated in Table 9. Adjusted means, standard errors, and 95% confidence intervals for $AOB_{0\text{-}0.5}$, $AOB_{0\text{-}1}$, $AOB_{0\text{-}3}$, $AOB_{0\text{-}6}$, $AOB_{0\text{-}9}$ will be tabulated by treatment in Table 10. For differences in $AOB_{0\text{-}12}$ between Super Poligrip Free and no adhesive, Experimental Denture Adhesive 1 and no adhesive, and Experimental Denture Adhesive 2 and no adhesive, adjusted differences, standard errors, and 95% confidence intervals will be tabulated in Table 8.

Subject-level profile plots (connected scatter plots, spa) of $AOB_{0\text{-}0.5}$, $AOB_{0\text{-}1}$, $AOB_{0\text{-}3}$, $AOB_{0\text{-}6}$, $AOB_{0\text{-}9}$, and $AOB_{0\text{-}12}$, with all treatments overlayed on the same figure will be plotted by subject in Figure 3.

Adjusted bite force means over time at 0, 0.5, 1, 3, 6, 9, and 12 hours by treatment will be tabulated in Table 12 and plotted in Figure 1. The adjusted means will come from a repeated measures ANCOVA model. Bite force at each time will be the outcome. Fixed effects will be study period, treatment, time, period-by-time interaction, and treatment-by-time interaction. The covariate is the subject level baseline. Subject will be included as a random effect. Time within study period will be included as a repeated factor, with an unstructured variance/covariance matrix. If the repeated measures ANCOVA model is unable to converge, the analysis will be split into separate analyses for each time point: time 0 will use analysis of variance with treatment and period as fixed effects and subject as a random effect; subsequent time points will use ANCOVA with treatment and period as fixed effects, subject as a random effect, and subject-level baseline as the covariate. No statistical comparisons will be taken from this analysis; the purpose of the model is only to generate the adjusted means and standard errors.

4.3.3 Handling of Missing Values/Censoring/Discontinuations

As described above for the calculation of $AOB_{0\text{-}12}$, missing readings will be imputed using linear interpolation between pre and post the missing values, if necessary. In the case of more than one missing value or if the 12-hour value is missing, $AOB_{0\text{-}12}$ will be set to missing. Similar rules will apply for the AOB calculations for 0.5, 1, 3, 6 and 9 hours. No other imputation of missing data will be considered.

The following will be considered violations that may lead to the exclusion of data from the PP population and hence PP analyses:

- Violation of inclusion or exclusion criteria at screening that may affect efficacy
- Violation of pre-treatment baseline bite force continuance criteria

• Treatment administration errors
• Use of prohibited treatment or medication before or during the study, which it is felt will affect the assessment of efficacy.

The above list is not exhaustive and all protocol violations will be assessed by the blinded GSK CH team members as to whether any subjects and /or data will be excluded from PP analysis as part of a Blind Data Review (BDR) Meeting prior to database lock. Any reasons for exclusion from an analysis population will be listed, if applicable.

Subjects with a protocol violation that is deemed to affect efficacy assessments in some, but not all, study periods will be part of the PP population, but their data will be excluded from the period(s) affected by the protocol violation for a PP analysis.

4.4 Analysis of Safety

All safety results will be produced from the Safety population.

4.4.1 Adverse Events and Serious Adverse Events

Adverse events (AEs) will be categorized as oral or non-oral by the examiner prior to database lock. AEs will be deemed to be treatment emergent if they occur after the first supervised use of the randomized treatment. No specific risks or anticipated adverse device effects are expected to be observed within this study, however all AEs and medical device incidents will be assessed to evaluate the tolerability and safety of the treatments. No formal statistical analyses of AEs will be performed. AEs will be listed in Listing 2. Serious Adverse Events (SAEs) will be listed in Listing 3.

4.4.2 Medical device events

The medical devices in this study are the supplied denture adhesive creams, the denture cleansing paste and the denture cleaning brushes. Medical device incidents involving an AE will be included in the AE listing. No formal statistical analyses of medical device events will be performed.

4.4.3 Oral Soft Tissue Examination

Oral soft tissue exam (OSTE) will be collected in the study database but will not be reported in tables or listings. Any treatment emergent abnormal findings will be included in the AE listing. No formal statistical analyses of OSTE will be performed.

4.4.4 Oral Hard Tissue Examination

Oral hard tissue exam (OHTE) will be collected in the study database but will not be reported in tables or listings. Any treatment emergent abnormal findings will be included in the AE listing. No formal statistical analyses of OHTE will be performed.

5 Changes to the Protocol Defined Statistical Analysis Plan

The repeated measures analysis of covariance described in section 4.3.2 to generate the bite force adjusted means and standard errors at each time point was added to create the figure requested by GSK.

List of Tables, Figures, and Listings

Tables

1. Premature discontinuation
2. Reason for Discontinuation (for subjects with premature discontinuation)
3. Analysis populations
4. Demographic characteristics
5. Baseline characteristics
6. ANOVA table for AOB_{0-12}
7. Adjusted means, standard errors, and 95% confidence intervals for AOB_{0-12} by treatment.
8. Adjusted differences, standard errors, and 95% confidence intervals for AOB_{0-12} between pairs of treatments.
9. ANOVA tables for $AOB_{0-0.5}$, AOB_{0-1}, AOB_{0-3}, AOB_{0-6}, and AOB_{0-9}
10. Adjusted means, standard errors, and 95% confidence intervals for $AOB_{0-0.5}$, AOB_{0-1}, AOB_{0-3}, AOB_{0-6}, and AOB_{0-9} by treatment.
11. Adjusted differences, standard errors, and 95% confidence intervals for $AOB_{0-0.5}$, AOB_{0-1}, AOB_{0-3}, AOB_{0-6}, and AOB_{0-9} between pairs of treatments.
12. Bite force adjusted means and standard errors over time by treatment.
13. Bite force, AUC, and AOB summary statistics by treatment and time
14. Number and percent of subjects with AE, Oral AE, TEAE, Product-related AE, Device Incidents, SAE

{note, tables 4-13 will be repeated as 4b-13b if the PP analysis is performed}

Listings

1. Protocol deviations.
2. Adverse events.
3. Medical device events.
4. Serious adverse events.

Figures

1. Line plot of bite force adjusted means over time with SE error bars by treatment.
2. Subject-level profile plots (connected scatter plots) of $AOB_{0-0.5}$, AOB_{0-1}, AOB_{0-3}, AOB_{0-6}, AOB_{0-9}, and AOB_{0-12}, with all treatments overlayed on the same figure. Plotted by subject.
3. Plot of adjusted differences with 95% confidence intervals for AOB_{0-12} between pairs of treatments.

Rough draft of table shells

Table 1. Premature discontinuation

	N (%)
No	
Yes	
Total	

Table 2. Reason for Discontinuation (for subjects who did not complete study), check all that apply

	N
Subject Discontinued/Withdrew from the study due to COVID-19 pandemic	
Subject withdrew from the study at his or her own request	
Subject did not meet study criteria; specify the criterion or assessment not met	
Adverse event(s)	
The discretion of the investigator or sponsor for safety,	
Behavioral reasons	
Inability of the subject to comply with the protocol required schedule of study visits or procedures.	
Protocol violation that may impact the subject's safety	
Withdrawal of informed consent	
Subject lost to follow-up	
Pregnancy	
Death	

Table 3. Analysis populations

	Total	Experimental Denture Adhesive 1	Experimental Denture Adhesive 2	Super Poligrip Free Adhesive Cream	No Adhesive
	N	N	N	N	N
Safety					
MITT					
Reason for MITT exclusion					
PP					
Reason for PP exclusion					

Table 4. Demographic characteristics. MITT population.

	Total	Experimental Denture Adhesive 1	Experimental Denture Adhesive 2	Super Poligrip Free Adhesive Cream	No Adhesive
Age; N, Mean (SD), Median, Minimum-Maximum					
Sex					
Male; N (%)					
Female; N (%)					
Race (check all that apply)					
American Indian or Alaska Native; N (%)					
Asian; N (%)					
Black or African American; N (%)					
Native Hawaiian or Other Pacific Islander; N (%)					
White; N (%)					
Other; N (%)					
Ethnicity					
Hispanic or Latino; N (%)					
Not Hispanic or Latino; N (%)					

Table 4b. Demographic characteristics. PP population.

	Total	Experimental Denture Adhesive 1	Experimental Denture Adhesive 2	Super Poligrip Free Adhesive Cream	No Adhesive
Age; N, Mean (SD), Median, Minimum-Maximum					
Sex					
Male; N (%)					
Female; N (%)					
Race (check all that apply)					
American Indian or Alaska Native; N (%)					
Asian; N (%)					
Black or African American; N (%)					
Native Hawaiian or Other Pacific Islander; N (%)					
White; N (%)					
Other; N (%)					
Ethnicity					
Hispanic or Latino; N (%)					
Not Hispanic or Latino; N (%)					

Table 5. Baseline characteristics. MITT population.

	Total	Experimental Denture Adhesive 1	Experimental Denture Adhesive 2	Super Poligrip Free Adhesive Cream	No Adhesive
	N (%)	N (%)	N (%)	N (%)	N (%)
Denture bearing tissue evaluation					
Ridge shape					
Flat					
V-shaped					
U-shaped					
Tissue Resiliency					
Flabby					
Resilient					
Firm					
Border Tissue Attachment					
Low					
Medium					
High					
Well-made Assessment					
Has this denture clinically acceptable vertical dimension, freeway space, horizontal occlusal relationships and border extensions?					
Acceptable					
Unacceptable					
Has this denture clinically acceptable contour and finish?					
Acceptable					
Unacceptable					
Has this denture clinically acceptable porosity, tissue surfaces, polished surfaces, color and thickness?					
Acceptable					
Unacceptable					

Table 5b. Baseline characteristics. PP population.

	Total	Experimental Denture Adhesive 1	Experimental Denture Adhesive 2	Super Poligrip Free Adhesive Cream	No Adhesive
	N (%)	N (%)	N (%)	N (%)	N (%)
Denture bearing tissue evaluation					
Ridge shape					
Flat					
V-shaped					
Shaped between U & V					
U-shaped					
Tissue Resiliency					
Flabby					
Resilient					
Firm					
Border Tissue Attachment					
Low					
Medium					
High					
Well-made Assessment					
Has this denture clinically acceptable vertical dimension, freeway space, horizontal occlusal relationships and border extensions?					
Acceptable					
Unacceptable					
Has this denture clinically acceptable contour and finish?					
Acceptable					
Unacceptable					
Has this denture clinically acceptable porosity, tissue surfaces, polished surfaces, color and thickness?					
Acceptable					
Unacceptable					

Table 6. ANOVA table for $AOB_{0\text{-}12}$. MITT population.

	Num DF	Den DF	F-value	p-value
Treatment				
Period				
Subject-level baseline				
Period level baseline minus subject level baseline				

Table 6b. ANOVA table for $AOB_{0\text{-}12}$. PP population.

	Num DF	Den DF	F-value	p-value
Treatment				
Period				
Subject-level baseline				
Period level baseline minus subject level baseline				

Table 7. Adjusted means, standard errors, and 95% confidence intervals for $AOB_{0\text{-}12}$ (lbs) by treatment. MITT population.

		$AOB_{0\text{-}12}$ (lbs)			
	N	LS Mean	SE	95% LCL	95% UCL
Experimental Denture Adhesive 1					
Experimental Denture Adhesive 2					
Super Poligrip Free Adhesive Cream					
No Adhesive					

Table 7b. Adjusted means, standard errors, and 95% confidence intervals for $AOB_{0\text{-}12}$ (lbs) by treatment. PP population.

		$AOB_{0\text{-}12}$ (lbs)			
	N	LS Mean	SE	95% LCL	95% UCL
Experimental Denture Adhesive 1					
Experimental Denture Adhesive 2					
Super Poligrip Free Adhesive Cream					
No Adhesive					

Table 8. Adjusted differences, standard errors, and 95% confidence intervals for AOB_{0-12} (lbs) between pairs of treatments. MITT population

		AOB_{0-12} (lbs)				
	N/N	Difference	SE	p-value	95% LCL	95% UCL
Super Poligrip Free Adhesive Cream vs. No Adhesive						
Experimental Denture Adhesive 1 vs. No Adhesive						
Experimental Denture Adhesive 2 vs. No Adhesive						

Table 8b. Adjusted differences, standard errors, and 95% confidence intervals for AOB_{0-12} (lbs) between pairs of treatments. PP population

		AOB_{0-12} (lbs)				
	N/N	Difference	SE	p-value	95% LCL	95% UCL
Super Poligrip Free Adhesive Cream vs. No Adhesive						
Experimental Denture Adhesive 1 vs. No Adhesive						
Experimental Denture Adhesive 2 vs. No Adhesive						

Table 9. ANOVA table for $AOB_{0\text{-}0.5}$, $AOB_{0\text{-}1}$, $AOB_{0\text{-}3}$, $AOB_{0\text{-}6}$, and $AOB_{0\text{-}9}$. MITT population.

		Num DF	Den DF	F-value	p-value
$AOB_{0\text{-}0.5}$	Treatment				
	Period				
	Subject-level baseline				
	Period level baseline minus subject level baseline				
$AOB_{0\text{-}1}$	Treatment				
	Period				
	Subject-level baseline				
	Period level baseline minus subject level baseline				
$AOB_{0\text{-}3}$	Treatment				
	Period				
	Subject-level baseline				
	Period level baseline minus subject level baseline				
$AOB_{0\text{-}6}$	Treatment				
	Period				
	Subject-level baseline				
	Period level baseline minus subject level baseline				
$AOB_{0\text{-}9}$	Treatment				
	Period				
	Subject-level baseline				
	Period level baseline minus subject level baseline				

Table 9b. ANOVA table for $AOB_{0-0.5}$, AOB_{0-1}, AOB_{0-3}, AOB_{0-6}, and AOB_{0-9}. PP population.

		Num DF	Den DF	F-value	p-value
$AOB_{0-0.5}$	Treatment				
	Period				
	Subject-level baseline				
	Period level baseline minus subject level baseline				
AOB_{0-1}	Treatment				
	Period				
	Subject-level baseline				
	Period level baseline minus subject level baseline				
AOB_{0-3}	Treatment				
	Period				
	Subject-level baseline				
	Period level baseline minus subject level baseline				
AOB_{0-6}	Treatment				
	Period				
	Subject-level baseline				
	Period level baseline minus subject level baseline				
AOB_{0-9}	Treatment				
	Period				
	Subject-level baseline				
	Period level baseline minus subject level baseline				

Table 10. Adjusted means, standard errors, and 95% confidence intervals for $AOB_{0-0.5}$, AOB_{0-1}, AOB_{0-3}, AOB_{0-6}, and AOB_{0-9} by treatment. MITT population.

		N	LS Mean	SE	95% LCL	95% UCL
$AOB_{0-0.5}$ (lbs)	Experimental Denture Adhesive 1					
	Experimental Denture Adhesive 2					
	Super Poligrip Free Adhesive Cream					
	No Adhesive					
AOB_{0-1} (lbs)	Experimental Denture Adhesive 1					
	Experimental Denture Adhesive 2					
	Super Poligrip Free Adhesive Cream					
	No Adhesive					
AOB_{0-3} (lbs)	Experimental Denture Adhesive 1					
	Experimental Denture Adhesive 2					
	Super Poligrip Free Adhesive Cream					
	No Adhesive					
AOB_{0-6} (lbs)	Experimental Denture Adhesive 1					
	Experimental Denture Adhesive 2					
	Super Poligrip Free Adhesive Cream					
	No Adhesive					

AOB_{0-9} (lbs)	Experimental Denture Adhesive 1					
	Experimental Denture Adhesive 2					
	Super Poligrip Free Adhesive Cream					
	No Adhesive					

Table 10b. Adjusted means, standard errors, and 95% confidence intervals for $AOB_{0-0.5}$, AOB_{0-1}, AOB_{0-3}, AOB_{0-6}, and AOB_{0-9} by treatment. PP population.

		N	LS Mean	SE	95% LCL	95% UCL
$AOB_{0-0.5}$ (lbs)	Experimental Denture Adhesive 1					
	Experimental Denture Adhesive 2					
	Super Poligrip Free Adhesive Cream					
	No Adhesive					
AOB_{0-1} (lbs)	Experimental Denture Adhesive 1					
	Experimental Denture Adhesive 2					
	Super Poligrip Free Adhesive Cream					
	No Adhesive					
AOB_{0-3} (lbs)	Experimental Denture Adhesive 1					
	Experimental Denture Adhesive 2					
	Super Poligrip Free Adhesive Cream					
	No Adhesive					
AOB_{0-6} (lbs)	Experimental Denture Adhesive 1					
	Experimental Denture Adhesive 2					
	Super Poligrip Free Adhesive Cream					
	No Adhesive					

AOB_{0-9} (lbs)	Experimental Denture Adhesive 1					
	Experimental Denture Adhesive 2					
	Super Poligrip Free Adhesive Cream					
	No Adhesive					

Table 11. Adjusted differences, standard errors, and 95% confidence intervals for $AOB_{0-0.5}$, AOB_{0-1}, AOB_{0-3}, AOB_{0-6}, and AOB_{0-9} between pairs of treatments. MITT population

		N/N	Difference	SE	p-value	95% LCL	95% UCL
$AOB_{0-0.5}$ (lbs)	Super Poligrip Free Adhesive Cream vs. No Adhesive						
	Experimental Denture Adhesive 1 vs. No Adhesive						
	Experimental Denture Adhesive 2 vs. No Adhesive						
AOB_{0-1} (lbs)	Super Poligrip Free Adhesive Cream vs. No Adhesive						
	Experimental Denture Adhesive 1 vs. No Adhesive						
	Experimental Denture Adhesive 2 vs. No Adhesive						
AOB_{0-3} (lbs)	Super Poligrip Free Adhesive Cream vs. No Adhesive						
	Experimental Denture Adhesive 1 vs. No Adhesive						
	Experimental Denture Adhesive 2 vs. No Adhesive						
AOB_{0-6} (lbs)	Super Poligrip Free Adhesive Cream vs. No Adhesive						
	Experimental Denture Adhesive 1 vs. No Adhesive						
	Experimental Denture Adhesive 2 vs. No Adhesive						
AOB_{0-9} (lbs)	Super Poligrip Free Adhesive Cream vs. No Adhesive						

	Experimental Denture Adhesive 1 vs. No Adhesive						
	Experimental Denture Adhesive 2 vs. No Adhesive						

Table 11b. Adjusted differences, standard errors, and 95% confidence intervals for $AOB_{0-0.5}$, AOB_{0-1}, AOB_{0-3}, AOB_{0-6}, and AOB_{0-9} between pairs of treatments. PP population

		N/N	Difference	SE	p-value	95% LCL	95% UCL
$AOB_{0-0.5}$ (lbs)	Super Poligrip Free Adhesive Cream vs. No Adhesive						
	Experimental Denture Adhesive 1 vs. No Adhesive						
	Experimental Denture Adhesive 2 vs. No Adhesive						
AOB_{0-1} (lbs)	Super Poligrip Free Adhesive Cream vs. No Adhesive						
	Experimental Denture Adhesive 1 vs. No Adhesive						
	Experimental Denture Adhesive 2 vs. No Adhesive						
AOB_{0-3} (lbs)	Super Poligrip Free Adhesive Cream vs. No Adhesive						
	Experimental Denture Adhesive 1 vs. No Adhesive						
	Experimental Denture Adhesive 2 vs. No Adhesive						
AOB_{0-6} (lbs)	Super Poligrip Free Adhesive Cream vs. No Adhesive						
	Experimental Denture Adhesive 1 vs. No Adhesive						
	Experimental Denture Adhesive 2 vs. No Adhesive						
AOB_{0-9} (lbs)	Super Poligrip Free Adhesive Cream vs. No Adhesive						

	Experimental Denture Adhesive 1 vs. No Adhesive						
	Experimental Denture Adhesive 2 vs. No Adhesive						

Table 12. Bite force (lbs) adjusted means and standard errors over time by treatment. MITT population.

		Bite Force (lbs)										
		Experimental Denture Adhesive 1			Experimental Denture Adhesive 2			Super Poligrip Free Adhesive Cream			No Adhesive	
Time	N	Mean	SE	N	Mean	SE	N	Mean	SE	N	Mean	SE
0												
0.5												
1												
3												
6												
9												
12												

Table 12b. Bite force (lbs) adjusted means and standard errors over time by treatment. PP population.

		Bite Force (lbs)										
		Experimental Denture Adhesive 1			Experimental Denture Adhesive 2			Super Poligrip Free Adhesive Cream			No Adhesive	
Time	N	Mean	SE	N	Mean	SE	N	Mean	SE	N	Mean	SE
0												
0.5												
1												
3												
6												
9												
12												

Table 13a. Bite force (lbs), AUC (lbs), and AOB (lbs) summary statistics by treatment and time. MITT population.

		N	Mean	SD	SE	Median	Min	Max
Bite Force (lbs)								
Experimental Denture Adhesive 1	BF_0							
	$BF_{0.5}$							
	BF_1							
	BF_3							
	BF_6							
	BF_9							
	BF_{12}							
Experimental Denture Adhesive 2	BF_0							
	$BF_{0.5}$							
	BF_1							
	BF_3							
	BF_6							
	BF_9							
	BF_{12}							
Super Poligrip Free Adhesive Cream	BF_0							
	$BF_{0.5}$							
	BF_1							
	BF_3							
	BF_6							
	BF_9							
	BF_{12}							
No Adhesive	BF_0							
	$BF_{0.5}$							
	BF_1							
	BF_3							
	BF_6							
	BF_9							
	BF_{12}							
AUC (lbs)								

Experimental Denture Adhesive 1	$AUC_{0-0.5}$							
	AUC_{0-1}							
	AUC_{0-3}							
	AUC_{0-6}							
	AUC_{0-9}							
	AUC_{0-12}							
Experimental Denture Adhesive 2	$AUC_{0-0.5}$							
	AUC_{0-1}							
	AUC_{0-3}							
	AUC_{0-6}							
	AUC_{0-9}							
	AUC_{0-12}							
Super Poligrip Free Adhesive Cream	$AUC_{0-0.5}$							
	AUC_{0-1}							
	AUC_{0-3}							
	AUC_{0-6}							
	AUC_{0-9}							
	AUC_{0-12}							
No Adhesive	$AUC_{0-0.5}$							
	AUC_{0-1}							
	AUC_{0-3}							
	AUC_{0-6}							
	AUC_{0-9}							
	AUC_{0-12}							
AOB (lbs)								
Experimental Denture Adhesive 1	$AOB_{0-0.5}$							
	AOB_{0-1}							
	AOB_{0-3}							

	AOB_{0-6}							
	AOB_{0-9}							
	AOB_{0-12}							
Experimental Denture Adhesive 2	$AOB_{0-0.5}$							
	AOB_{0-1}							
	AOB_{0-3}							
	AOB_{0-6}							
	AOB_{0-9}							
	AOB_{0-12}							
Super Poligrip Free Adhesive Cream	$AOB_{0-0.5}$							
	AOB_{0-1}							
	AOB_{0-3}							
	AOB_{0-6}							
	AOB_{0-9}							
	AOB_{0-12}							
No Adhesive	$AOB_{0-0.5}$							
	AOB_{0-1}							
	AOB_{0-3}							
	AOB_{0-6}							
	AOB_{0-9}							
	AOB_{0-12}							

Table 13b. Bite force (lbs), AUC (lbs), and AOB (lbs) summary statistics by treatment and time. PP population.

		N	Mean	SD	SE	Median	Min	Max
Bite Force (lbs)								
Experimental Denture Adhesive 1	BF_0							
	$BF_{0.5}$							
	BF_1							
	BF_3							
	BF_6							
	BF_9							
	BF_{12}							
Experimental Denture Adhesive 2	BF_0							
	$BF_{0.5}$							
	BF_1							
	BF_3							
	BF_6							
	BF_9							
	BF_{12}							
Super Poligrip Free Adhesive Cream	BF_0							
	$BF_{0.5}$							
	BF_1							
	BF_3							
	BF_6							
	BF_9							
	BF_{12}							
No Adhesive	BF_0							
	$BF_{0.5}$							
	BF_1							
	BF_3							
	BF_6							
	BF_9							
	BF_{12}							
AUC (lbs)								

Experimental Denture Adhesive 1	$AUC_{0-0.5}$							
	AUC_{0-1}							
	AUC_{0-3}							
	AUC_{0-6}							
	AUC_{0-9}							
	AUC_{0-12}							
Experimental Denture Adhesive 2	$AUC_{0-0.5}$							
	AUC_{0-1}							
	AUC_{0-3}							
	AUC_{0-6}							
	AUC_{0-9}							
	AUC_{0-12}							
Super Poligrip Free Adhesive Cream	$AUC_{0-0.5}$							
	AUC_{0-1}							
	AUC_{0-3}							
	AUC_{0-6}							
	AUC_{0-9}							
	AUC_{0-12}							
No Adhesive	$AUC_{0-0.5}$							
	AUC_{0-1}							
	AUC_{0-3}							
	AUC_{0-6}							
	AUC_{0-9}							
	AUC_{0-12}							
AOB (lbs)								
Experimental Denture Adhesive 1	$AOB_{0-0.5}$							
	AOB_{0-1}							
	AOB_{0-3}							

	AOB_{0-6}							
	AOB_{0-9}							
	AOB_{0-12}							
Experimental Denture Adhesive 2	$AOB_{0-0.5}$							
	AOB_{0-1}							
	AOB_{0-3}							
	AOB_{0-6}							
	AOB_{0-9}							
	AOB_{0-12}							
Super Poligrip Free Adhesive Cream	$AOB_{0-0.5}$							
	AOB_{0-1}							
	AOB_{0-3}							
	AOB_{0-6}							
	AOB_{0-9}							
	AOB_{0-12}							
No Adhesive	$AOB_{0-0.5}$							
	AOB_{0-1}							
	AOB_{0-3}							
	AOB_{0-6}							
	AOB_{0-9}							
	AOB_{0-12}							

Table 14. AE, TEAE, Product-related AE, Medical device related AE, SAE, Medical device event

	Total
AE; N (%)	
Oral AE; N (%)	
TEAE; N (%)	
Product-related AE; N (%)	
Medical Device related AE; N (%)	
SAE; N (%)	
Medical Device Event; N (%)	

Listing 1. Protocol deviations

ID	Deviation date	Visit(s) affected	Nature of deviation	Missed applications	Additional applications	Other	Description	Comments	Exclusion from PP

Listing 2. Adverse events.

ID	Age	Sex	Race	AE	Start date	Stop date	COVID-related	Severity	Product-related	Oral	TEAE	Product Action	Outcome	SAE	Ongoing	Expected	Frequency	Discontinue	Comment

Listing 3. Medical device events.

ID	Device type	Incident type	Incident type other	Start date	Stop date	Outcome	Treatment given	Corrective action	AE	Device cause AE	Subject Withdrawn	Device available	Device details

Listing 4. Serious adverse events.

{same as Listing 2, subset to SAEs}