Solvay Dental 360™

DS002 / REFRAME RPD Post-Market Clinical Study

Statistical Analysis Plan
Version 2.0
5 March 2019

Authors:

Title	Name	Signature	Date
Medical Research Biostatistician, Biostatistics NAMSA	Anna Nordell	Anna Nordell Digitally signed by Anna Nordell DN: cn=Anna Nordell, o=NAMSA, ou=C&C, email=anordell@namsa.com, c=US Date: 2019.03.07 13:10:56 -06'00'	

Approval:

Title	Name	Signature	Date
Pr. Medical Research Manager, , NAMSA	Pamela Wolfe	Pamela Wolfe Digitally signed by Pamela Wolfe DN: cn=Pamela Wolfe, o=NAMSA, ou=C&C, email=pwolfe@namsa.com, c=US Date: 2019.03.13 15:07:14 -05'00'	
Compliance and Product Manager, Solvay Dental 360™	Tim Shary		3/21/2019

Table of Contents

1. Purpose

This statistical analysis plan (SAP) describes the statistical methods to be used during the reporting and analysis of data collected under the Solvay Dental 360™, REFRAME RPD Post-Market Clinical Study protocol (CIP #: DS002).

2. Scope

This SAP should be read in conjunction with the study protocol and electronic case report forms (eCRF). This version of the plan has been developed with respect to the U.S. Clinical Study protocol version Rev 05, dated 27July2018 and the U.K protocol version Rev. 05, Dated 02July2018. Any further changes to the protocol or eCRF may necessitate updates to the SAP.

3. Applicable Documents

Document Number	Document Title
DS002	REFRAME RPD Post-Market Clinical Study

4. Software

All tables, listings and figures will be produced using SAS Version 9.4 (SAS Institute, Cary, NC.) or a later version of SAS. All output will be in Microsoft Word or RTF format.

5. Definitions

CoCr - Cobalt Chrome
CRF - Case Report Form
OHIP - Oral Health Impact Profile
OHRQoL - Oral Health-related Quality of Life
RPD - Removable Partial Denture
SOC - Standard of Care

6. Trial Objectives

The primary objective is to evaluate the change in patient Oral Health-related Quality of Life (OHRQoL) while wearing a cobalt chrome (CoCr) removable partial denture (RPD) compared to after wearing the Solvay Dental 360™ polymer Removable Partial Denture (RPD) for 8 weeks.

The secondary objectives are:

1. To investigate the difference in health of the abutment teeth following the use of the polymer Removable Partial Denture (RPD) as compared to the Cobalt Chrome (CoCr) Removable Partial Denture (RPD) as assessed by the plaque score and gingival bleeding index.

2. To investigate the difference in whole plaque score following the use of the polymer Removable Partial Denture (RPD) as compared to the cobalt chrome (CoCr) Removable Partial Denture (RPD).
3. To investigate the health of the mucosal bearing areas of the polymer Removable Partial Denture (RPD) as compared to the cobalt chrome (CoCr) Removable Partial Denture (RPD).
4. To investigate the framework hygiene (disclosing), probing depths, and abutment tooth mobility.
5. To investigate the professional (operator) based outcomes for the fit, fusion, occlusion and aesthetics.
6. To investigate the patient assessment of the comfort, aesthetics and chewing ability after the polymer Removable Partial Denture (RPD) and then Cobalt Chrome (CoCr) Removable Partial Denture (RPD).
7. To determine the denture preference of each patient.

7. Trial Hypotheses

The primary endpoint analysis will be performed on all subjects with an overall score reported on the OHIP questionnaire for both the Cobalt Chrome and Polymer Frame. The primary endpoint in this study is the OHIP overall score after wearing the Cobalt Chrome frame versus the OHIP overall score after wearing the Polymer frame. The hypothesis can be written as follows:

H_0: $OS_{diff} > \Delta$ versus
H_A: $OS_{diff} \leq \Delta$,

where

- OS_{diff} is the overall score for the cobalt chrome frame subtracted from the overall score for the polymer frame
- Δ is the performance goal

No formal hypothesis testing will be done for the secondary endpoints.

8. Trial Success Criteria

Success of the primary endpoints will be based on a significance level of $\alpha = 0.05$. That is, if the hypothesis test results in a p-value that is less than 0.05, the study will be considered a success.

9. Trial Design

This is a multi-center, cohort study conducted in the United States and United Kingdom that will enroll approximately 40 subjects to assess Oral Health Related Quality of Life (OHRQoL) in patients receiving the study polymer Removable Partial Denture (RPD) as compared to their baseline Cobalth Chrome (CoCr) Removable Partial Denture (RPD) Oral Health Related Quality of Life (OHRQoL).

Subjects who are current wearers of a Cobalt Chrome (CoCr) Removable Partial Denture (RPD) will complete an Oral Health Related Quality of Life (OHRQoL) instrument, the Oral Health Impact Profile (OHIP) questionnaire, at baseline and again after wearing their prescribed polymer Removable Partial Denture (RPD) for 8 weeks.

9.1 Randomization

Randomization will not be used in this study as it is a single-arm cohort study.

9.2 Blinding

Blinding will not be used in this study.

10. Sample Size Considerations

Power calculations of the non-inferiority of the overall score on the OHIP questionnaire for subjects wearing a polymer frame versus the overall score on the OHIP questionnaire for subjects wearing a cobalt chrome denture were based on a non-inferiority test for one mean where higher means are worse and α=0.05.

In a previous study (S. Shaghaghian, 2014), the average overall score on the OHIP questionnaire for subjects wearing a cobalt chrome denture was 13.8 (standard deviation = 10.1). Based on the anticipated improved performance of the polymer frame, 36 subjects provides approximately 80% power to detect a difference of -3 (standard deviation = 11) between the 2 overall scores with a non-inferiority margin of 1.5. The total number of subjects enrolled will be 40, given the anticipated attrition rate of 10%.

11. Data Structure and Handling

11.1 Data Handling and Transfer

Data management will be undertaken by NAMSA. NAMSA Biostatistics will be provided access to download SAS datasets or will be provided them upon request.

Programming of analysis datasets, tables, figures and listings will be conducted during the data management phase of the study. Tables, figures, and listings may be reviewed prior to final data lock for data review. Any data values requiring investigation or correction will be identified, and protocol deviations will be reviewed. The final run of outputs will take place after the data is deemed final.

11.2 Missing Data

Endpoint data may be missing because patients have died, refused follow-up, or have withdrawn from the study. The missing data does not bias the results as long as the data is missing at random. The primary analysis will be done on all patients who have an overall score from the baseline and 8 week OHIP questionnaire.

All efforts will be made to obtain information regarding subject's overall score on the OHIP questionnaire. The sponsor will report the reason for censoring for all subjects with missing endpoint data.

11.3 Visit Windows

There are 8 scheduled visits throughout the duration of the study. There are no windows specific to timing of each visit. The 8 visits are defined as follows:

Pre-Treatment Evaluations:

Visit 1: Eligibility, consent, initial impressions taken)

Treatment Evaluations:

Visit 2: Patient Identification number assigned, 2nd impression taken

Visit 3: Standard of Care (SOC) visit for prescribing Removable Partial Dentures (RPDs). Assess cast.

Visit 4: Trial Insertion.

Visit 5: Denture Fit.

Visit 6: Recall 1 week

Visit 7: Recall 4 week

Visit 8: Recall 8 week

11.4 Pooling of Data Across Trial Sites

Data from all study sites will be pooled. Poolability analyses will be performed on the primary endpoint to assess whether results are poolable across the participating centers.

A linear regression model with change in the overall score of the OHIP questionnaire as the dependent variable will be reported using a categorical variable for site. If there is evidence that the data is not poolable across centers, examination of the data will be performed to determine the underlying cause(s).

12. Statistical Analyses

12.1 General Considerations

Continuous measures will be summarized with sample size, mean, median, standard deviation, minimum and maximum; categorical measures will be presented with the counts and percentages of subjects in each category.

The date of enrollment will be considered study day 1.

12.2 Analysis Populations

The primary endpoint will be analyzed among all subjects with an overall score reported on the OHIP questionnaire for both the Cobalt Chrome and Polymer Frame.

12.3 Subject Disposition

Subject disposition will be presented by:

- Summary of completed subjects per follow up.
- Summary of discontinuation in the study and reason for discontinuation.

12.4 Demographics and Baseline Characteristics

Demographics and baseline characteristics of enrolled subjects will be summarized. These factors will include (but not be limited to):

- Age
- Gender
- Race and Ethnicity

12.5 Primary Analysis

12.5.1 Primary Objective

The purpose of the study is to evaluate the change in patient Oral Health-related Quality of Life (OHRQoL) from wearing a cobalt chrome (CoCr) removable partial denture (RPD) to wearing the Solvay Dental 360™ polymer Removable Partial Denture (RPD) for 8 weeks.

12.5.1.1 *Endpoint Definition*

The primary endpoint in this study is the change in patient oral health related quality of life (OHRQoL) after wearing the polymer removable partial denture (RPD) and cobalt chrome (CoCr) removable partial denture (RPD).

12.5.1.2 *Hypothesis and/or parameters to be estimated*

The primary endpoint analysis will be performed on all subjects with an overall score reported on the OHIP questionnaire for both the Cobalt Chrome and Polymer Frame. The objective of the primary analysis is to show non-inferiority of the difference in the overall score of the OHIP questionnaire after using the CoCr removable partial denture and after using the polymer RPD to a performance goal of 1.5. The hypothesis will be tested, and can be written as follows:

H_0: $OS_{diff} > \Delta$ versus
H_A: $OS_{diff} \leq \Delta$,

where

- OSdiff is the overall score for the cobalt chrome frame subtracted from the overall score for the polymer frame
- Δ is the performance goal

The statistical analysis of the non-inferiority of the difference in the overall score from the OHIP for each frame to a performance goal of 1.5 will be done using the PROC TTEST procedure in SAS.

12.5.1.3 *Data Collection and Analysis Methods*

Results of the OHIP questionnaire for the metal and polymer frame are collected on the OHIP CRF at the corresponding visit (Visit 2 and Visit 8). The overall score for each frame is calculated by a summation of the score from each of the 14 questions; each having the following scoring:

Response	Score
Never	0 Points
Hardly Ever	1 Point
Occasionally	2 Points
Fairly Often	3 Points
Very Often	4 Points

Thus the range of possible scores for the overall score is 0 to 56. Questions that are left blank or responded to with a 'Don't Know' response will be recoded as the average score of all available responses for the subject at the corresponding time point.

The overall score from the questionnaire provided at baseline to assess the cobalt chrome frame will be subtracted from the overall score obtained at 8 weeks follow-up when assessing the polymer frame.

12.6 Secondary Analysis

All secondary endpoints will be assessed for all subjects with available data. No formal statistical hypothesis testing will be performed. All objectives will be summarized descriptively as described in section 12.1.

12.6.1 Secondary Objective #1

The first secondary objective of the study is to investigate the difference in health of the abutment teeth following the use of the polymer RPD as compared to the CoCr RPD as assessed by the plaque score and gingival bleeding index.

12.6.1.1 *Endpoint Definition*

The first secondary endpoint is the health of the abutment teeth during/following the use of the polymer RPD as compared to the CoCr RPD.

12.6.1.2 *Hypothesis and/or parameters to be estimated*

No formal statistical hypothesis testing will be performed for the secondary endpoint, however, the arch plaque score and bleeding on probing will be summarized as a continuous variable at Visit 2 (corresponding to the metal frame) and Visit 8 (corresponding to the polymer frame). The gingival bleeding index of abutment teeth as compared to baseline will only be summarized at Visit 8, with frequencies of improved, worsened, or no change.

12.6.1.3 *Data Collection and Analysis Methods*

Arch plaque and bleeding on probing collected on the Visit 2 Oral Exam and Final Impression CRF in relation to the metal frame. Arch plaque, bleeding on probing, and bleeding index are collected on the Visit 8 CRF in relation to the polymer frame.

12.6.2 Secondary Objective #2

The second secondary objective of the study is to investigate the difference in whole plaque score following the use of the polymer RPD as compared to the CoCr RPD.

12.6.2.1 *Endpoint Definition*

The second secondary endpoint is the health of the abutment teeth during/following the use of the polymer RPD as compared to the CoCr RPD.

12.6.2.2 *Hypothesis and/or parameters to be estimated*

No formal statistical hypothesis testing will be performed for the secondary endpoint, however, the whole plaque score will be summarized as continuous variable at Visit 2 (corresponding to the metal frame) and Visit 8 (corresponding to the polymer frame).

12.6.2.3 *Data Collection and Analysis Methods*

Whole plaque is collected on the Visit 2 Oral Exam and Final Impression CRF in relation to the metal frame and collected on the Visit 8 CRF in relation to the polymer frame.

12.6.3 Secondary Objective #3

The third secondary objective of the study is to investigate the health of the mucosal bearing areas of the polymer RPD as compared to the CoCr RPD.

12.6.3.1 *Endpoint Definition*

The third secondary endpoint is the operator assessment of the adaptation of the polymer frame, adaptation of the tissue base areas and their relationship to the frame adaptation, functional evaluation, aesthetic assessment and oral health assessment of abutment teeth and the periodontium.

12.6.3.2 *Hypothesis and/or parameters to be estimated*

No formal statistical hypothesis testing will be performed for the secondary endpoint, however, the health of the mucosal bearing area will be reported at Visits 2 and 8.

12.6.3.3 *Data Collection and Analysis Methods*

Health of the mucosal bearing area is collected on the Visit 2 and Visit 8 CRFs.

12.6.4 Secondary Objective #4

The fourth secondary objective of the study is to investigate framework hygiene (disclosing), probing depths, and abutment tooth mobility.

12.6.4.1 *Endpoint Definition*

The fourth secondary endpoint is the oral health parameters associated with RPD abutment teeth (probing depths and mobility) and RPD mucosal areas.

12.6.4.2 *Hypothesis and/or parameters to be estimated*

No formal statistical hypothesis testing will be performed for the secondary endpoint, however, the bleeding on probing, pocket depths and mobility of abutment teeth will be reported at Visit 2 (baseline) and Visit 8 (recall week 8).

12.6.4.3 *Data Collection and Analysis Methods*

Bleeding on probing, pocket depths, and mobility of abutment teeth are all collected on the both on the Visit 2 and Visit 8 CRF.

12.6.5 Secondary Objective #5

The fifth secondary objective of the study is to investigate the professional (operator) based outcomes for the fit, function, occlusion and aesthetics.

12.6.5.1 *Endpoint Definition*

The fifth secondary endpoint is the operator assessment of the adaptation of the polymer frame, adaptation of the tissue base areas and their relationship to the frame adaptation, functional evaluation, aesthetic assessment and oral health assessment of abutment teeth and the periodontium.

12.6.5.2 *Hypothesis and/or parameters to be estimated*

No formal statistical hypothesis testing will be performed for the secondary endpoint, however, the operator aesthetics assessment of the frame will be reported at Visit 2, 5, 6, 7, and 8.

12.6.5.3 *Data Collection and Analysis Methods*

Operator aesthetics assessment of existing metal RPD will be assessed at Visit 2 on the Oral exam and final impression CRF. Operator aesthetics assessment of polymer RPD will be assessed at visit 5 on the Final Fitting CRF. Operator aesthetics assessment of the polymer RPD is also collected on the Visit 6, Visit 7 and Visit 8 CRF.

12.6.6 Secondary Objective #6

The sixth secondary objective of the study is to investigate the patient assessment of the comfort, aesthetics, and chewing ability after the polymer RPD and CoCr PRD.

12.6.6.1 *Endpoint Definition*

The sixth secondary endpoint is the patient-centered assessment of comfort, aesthetics and chewing ability before and after construction of the new denture by a 5 point Likert scale.

12.6.6.2 *Hypothesis and/or parameters to be estimated*

No formal statistical hypothesis testing will be performed for the secondary endpoint, however, the patient satisfaction questionnaire for the metal frame will be collected at Visit 5, and the questionnaire for the polymer frame will be collected at Visit 6, Visit 7 and Visit 8 (recall week 8) CRF.

12.6.6.3 *Data Collection and Analysis Methods*

Patient satisfaction with the comfort of the metal frame, the aesthetics of the metal frame, and their chewing ability with the metal frame are collected at visit 5 on the patient satisfaction – metal CRF. Patient satisfaction with the comfort of the polymer frame, the aesthetics of the polymer frame, and their chewing ability with the polymer frame are collected at Visit 6, 7, and 8 on the patient satisfaction – polymer CRF.

12.6.7 Secondary Objective #7

The seventh secondary objective of the study is to determine the denture preference of each patient.

12.6.7.1 *Endpoint Definition*

The seventh secondary endpoint is the patient-centered assessment of the new polymer partial denture.

12.6.7.2 *Hypothesis and/or parameters to be estimated*

No formal statistical hypothesis testing will be performed for the secondary endpoint, however, the patient preference between the metal partial denture or the polymer partial denture will be reported at Visit 8.

12.6.7.3 *Data Collection and Analysis Methods*

Patient preference between the metal and polymer frame will be collected at visit 8 on the patient satisfaction – polymer CRF.

12.7 Exploratory Analyses

Additional analyses may be performed but are not currently planned or part of the primary and secondary endpoints of the study.

12.8 Subset Analysis

No subset analysis are planned for this study.

12.9 Safety Analysis

There are no expected adverse events for this study. However, any adverse events reported will be listed and summarized.

12.10 Other Data

Protocol deviations will be listed and summarized.

13. Version History

Version	Date	Changes
1.0	27JAN2017	Initial version.
2.0	05MAR2019	Updates to data collection and reporting of endpoint data.

14. References

S. Shaghaghian, e. a. (2014). Oral health-related quality of life of removable partial denture wearers and related factors. *Journal of Oral Rehabilitation*. Retrieved July 23, 2016, from https://www.researchgate.net/profile/Rafat_Bagheri/publication/264984808_Oral_health-related_quality_of_life_of_removable_partial_denture_wearers_and_related_factors/links/540d51d00cf2df04e7548a42.pdf