Analytical Plan for Non-inferiority of pre-hydrated collagenated xenogenic bone mix in periodontal intrabony defects: clinical trial

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Document version

Version	Alterations
01	Initial version

1 ABBREVIATIONS

- CAL: clinical attachment level
- CI: confidence interval
- d: Cohen's D effect size
- PD: probing depth
- REC: gingival recession
- TP: tip of the papillae
- SD: standard deviation

2 CONTEXT

2.1 Objectives

To evaluate the non-inferiority of using pre-hydrated collagenated xenogenic bone mix in periodontal intrabony defects.

2.2 Hypotheses

- The CAL change from baseline in Gel 40 is non-inferior to Gen-Os;
- The PD change from baseline in Gel 40 is non-inferior to Gen-Os;
- The REC change from baseline in Gel 40 is non-inferior to Gen-Os;
- The TP change from baseline in Gel 40 is non-inferior to Gen-Os.

3 DATA

3.1 Raw data

The original data base had 45 variables collected on 20 observations.

3.2 Analytical dataset

CAL will be calculated as the sum of REC and DP. All outcomes will be calculated as the difference between the end-of-study measurements and baseline measurements.

After the cleaning process 17 variables were included in the analysis with 20 observations. The total number of observations excluded due to incompleteness and exclusion criteria will be reported in the analysis. Table 1 shows the structure of the analytical dataset.

Table 1 *Analytical dataset structure after variable selection and cleaning.*

id	exposure	gender	age	tooth	pd0	pd2	tp0	tp2	rec0	rec2	cal0	cal2	outcome	pd	tp	rec
1																
2																
3																
…																
N																

All variables in the analytical set were labeled according to the raw data provided and values were labeled according to the data dictionary for the preparation of production-quality results tables and figures.

4 STUDY PARAMETERS

4.1 Study design

Randomized controlled clinical trial.

4.2 Inclusion and exclusion criteria

N/A

4.3 Exposures

Efficacy of usage of pre-hydrated collagenated xenogenic bone mix (Gel40) will be tested against the gold standard bone graft (Gen-Os).

4.4 Outcomes

Specification of outcome measures (Zarin, 2011):

1. (Domain) Periodontal intrabony defects
2. (Specific measurement) CAL
3. (Specific metric) Change from baseline
4. (Method of aggregation) Mean

Primary outcome

CAL change.

Secondary outcomes

- REC change;
- PD change;
- TP change.

4.5 Covariates

No adjustment for covariates will be performed in this analysis.

5 STATISTICAL METHODS

5.1 Statistical analyses

5.1.1 Descriptive analyses

The epidemiological profile of the study participants will be described. Demographic and clinical variables will be described as mean (SD) or as counts and proportions (%), as appropriate. The distributions of participants' characteristics will be summarized in tables and visualized in exploratory plots.

5.1.2 Inferential analyses

All comparisons between groups will be performed as univariate analyses. The Cohen's d standardized mean difference and its CI will be calculated for all outcomes as the effect size for the efficacy of the main exposure relative to the gold standard.

The non-inferiority of the test intervention will be determined by using the minimum standardized difference detectable by this study d (calculated in section 5.3), where the equivalence interval lies between -d and d. For each outcome non-inferiority will be proven if the CI lies entirely above the lower margin of the equivalence interval -d.

The p-values from the independent t test with Welch correction, will be reported for information purposes.

5.1.3 Statistical modeling

N/A

5.1.4 Missing data

No missing data imputation will be performed. All evaluations will be performed as complete case analyses. Missing data counts and proportions will be reported in tables.

5.2 Significance and Confidence Intervals

All analyses will be performed using the significance level of 5%. All significance hypothesis tests and confidence intervals computed will be two-tailed.

5.3 Study size and Power

Study groups were balanced and the total sample size was 20 including all groups.

With these group sizes a t test can detect an effect size as large as **d = 1.32** with 80% power and 5% significance level (Cohen, 1988).

5.4 Statistical packages

This analysis will be performed using statistical software R version 4.2.1.

6 OBSERVATIONS AND LIMITATIONS

Small sample size

The total sample size of this study is only 20 participants. Cohen considered an effect size of d = 0.8 to be large, which means that this sample size is only able to detect very large clinical effects at the 5% level of significance with 80% power.

Recommended reporting guideline

The adoption of the EQUATOR network (http://www.equator-network.org/) reporting guidelines have seen increasing adoption by scientific journals. All clinical trials are recommended to be reported following the CONSORT guideline (Schulz K F, Altman D G, Moher D., 2010).

7 REFERENCES

- **SAR-2023-010-TK-v01** – Non-inferiority of pre-hydrated collagenated xenogenic bone mix in periodontal intrabony defects: clinical trial
- Cohen, J. (1988). Statistical power analysis for the behavioral sciences (2nd Ed.). New York: Routledge.
- Zarin DA, et al. The ClinicalTrials.gov results database – update and key issues. N Engl J Med 2011;364:852-60 (https://doi.org/10.1056/NEJMsa1012065).
- Gamble C, et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. JAMA. 2017;318(23):2337–2343 (https://doi.org/10.1001/jama.2017.18556).
- Schulz K F, Altman D G, Moher D. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials BMJ 2010; 340 :c332 (https://doi.org/10.1136/bmj.c332).

8 APPENDIX

This document was elaborated following recommendations on the structure for Statistical Analysis Plans (Gamble, 2017) for better transparency and clarity.

8.1 Availability

All documents from this consultation were included in the consultant's Portfolio.

The portfolio is available at:

https://philsf-biostat.github.io/SAR-2023-010-TK/