Statistical Analysis Plan Summary

Study Title:
Streamlined Facial Rejuvenation: A Randomized Split-Face Trial of Premixed Intradermal Botulinum Toxin Type A and Hyaluronic Acid Biorevitalization

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1. Study Objectives

Primary Objective:
To compare changes in wrinkle severity between BoNT-A monotherapy and BoNT-A + NCTF®135HA combination at Day 60 using the Wrinkle Severity Rating Scale (WSRS).

Secondary Objectives:

- To evaluate improvements in skin quality parameters (hydration, firmness, radiance, and tone homogeneity).
- To compare patient and evaluator Global Aesthetic Improvement Scale (GAIS) scores between treatment sides.
- To assess safety and patient satisfaction following both treatments.

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2. Statistical Design

Study Design:
A prospective, randomized, double-blind, split-face clinical trial. Each participant received both interventions on opposite facial sides, serving as their own control.

Sample Size:
52 participants completed the study. The sample size was determined pragmatically to ensure feasibility and adequate power for within-subject comparison.

Randomization:
Treatment sides were assigned via a computer-generated random sequence (1:1 ratio). Allocation was concealed using sealed opaque envelopes opened only at injection time by a study coordinator not involved in assessments.

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3. Statistical Analysis

Software:
IBM SPSS Statistics Version 27 (Armonk, NY, USA).

Primary Endpoint Analysis:

- WSRS scores at baseline and Day 60 were compared using paired t-tests for normally distributed data or Wilcoxon signed-rank tests for non-parametric data.
- Effect sizes were calculated as Cohen's *d* (t-tests) or *r* (non-parametric tests).

Secondary Endpoint Analysis:

- Skin biophysical parameters (hydration, firmness, radiance, tone homogeneity) were analyzed using the same approach.
- GAIS scores (from patients and evaluators) were compared using Wilcoxon signed-rank tests.
- Categorical outcomes (patient satisfaction, willingness to repeat/recommend, and adverse event frequencies) were expressed as percentages and compared using McNemar's test when applicable.

Missing Data Handling:
No missing data were reported, as all participants completed both baseline and follow-up assessments.

Significance Threshold:
All tests were two-tailed with a significance level set at $p < 0.05$.

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4. Safety Analysis

Adverse events were coded and analyzed descriptively, comparing frequency and type between treatment sides. All AEs were assessed for severity and causality. No serious AEs were expected or reported.

5. Data Integrity and Quality Control

Data entry and analysis were double-checked by independent investigators. Study outcomes were reviewed for consistency and accuracy. All raw data are stored in encrypted institutional servers under restricted access.

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6. Transparency and Data Sharing

Summary-level results will be made publicly available through the ISRCTN registry and corresponding journal publication. Individual participant data will not be shared to protect privacy.