Short Title:

Statistical Analysis Plan CLY935-C012

Full Title:

Statistical Analysis Plan CLY935-C012 / NCT04422990

Protocol Title:	Clinical Evaluation of a Silicone Hydrogel Daily Wear Monthly Replacement Contact Lens
[redacted]	[redacted]
Protocol TDOC Number:	V-CLN-0000839
[redacted]	[redacted]
	[redacted]
Template Version:	Version 1.0
Approvals:	See last page for electronic approvals
Job Notes:	

This is the first revision (Version 2.0) of the Statistical Analysis Plan for this study. This version of the Statistical Analysis Plan is based on Version 1.0 of the study protocol.

Executive Summary:

Key Objective:

The primary effectiveness objective is to demonstrate noninferiority of [redacted] soft contact lenses ([redacted] compared to BIOFINITY® soft contact lenses (Biofinity), in contact lens corrected distance visual acuity (CLCDVA) at Week 1 Follow-up.

The secondary effectiveness objective is to demonstrate noninferiority of [redacted] compared to Biofinity in the percentage of subjects achieving CLCDVA 20/20 or better, in each eye, at Week 1 Follow-up.

[redacted]:

[redacted]

[redacted]

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[redacted]

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1 STUDY OBJECTIVES AND DESIGN

To address the primary and secondary effectiveness objectives, data from a pre-determined subset of subjects from CLY935-C010 will be combined with data from the current study, and all planned analyses will be performed on the combined set of data.

1.1 Study Objectives

PRIMARY OBJECTIVE

The primary effectiveness objective is to demonstrate noninferiority of [redacted] compared to Biofinity in mean CLCDVA at Week 1 Follow-up.

SECONDARY OBJECTIVE

The secondary effectiveness objective is to demonstrate noninferiority of [redacted] compared to Biofinity in the percentage of subjects achieving CLCDVA 20/20 or better, in each eye, at Week 1 Follow-up.

1.2 Study Description

Key components of the study are summarized in Table 1-1.

Table 1-1 Study Description Summary

Study Design	Prospective, multi-center, randomized, [redacted] controlled, double-masked, parallel-group.
Study Population	Volunteer subjects aged 18 or over who are adapted daily wear frequent replacement soft contact lens wearers, excluding Biofinity habitual wearers, have at least 3 months of soft contact lens wearing experience, and who wear their habitual lenses at least 5 days per week and at least 8 hours per day. [redacted] Target to complete: 120 subjects (80 Test: 40 Control), [redacted]

	[redacted] Planned: ~160 subjects enrolled, ~144 subjects randomized (96 Test: 48 Control)
Number of Sites	~16 (US)
Test Product	[redacted] soft contact lens [redacted]
Control Product	CooperVision® BIOFINITY® (comfilcon A) contact lens (Biofinity)
Planned Duration of Exposure	~ 3 months
Visits	Visit 1: Screening/Baseline/Dispense (Day 1) Visit 2: Week 1 Follow-up [redacted] Visit 3: Month 1 Follow-up [redacted] Visit 4: Month 3 Follow-up/Exit [redacted]

1.3 Randomization

A member of the Randomization Programming group at Alcon who is not part of the study team will generate the randomized allocation schedule(s) for study lens assignment.

[redacted]

Subjects will be randomized in a 2:1 ratio to receive either [redacted] or Biofinity contact lenses, respectively. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

1.4 Masking

This study is double-masked.

[redacted]

2 ANALYSIS SETS

Data from a subset of subjects in the CLY935-C010 study will be combined with data from this study. This combined set will serve as the basis for all planned analyses for the primary and secondary effectiveness objectives[redacted]. Subjects in CLY935-C010 will be included in the combined set only if they satisfy the following criterion:

- Best corrected visual acuity (BCVA) of 20/20 or better in each eye at the Screening/Baseline/Dispense Visit

2.1 Safety Analysis Set

Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. As such, the safety analysis set will include all subjects/eyes exposed to any study lenses evaluated in this study. [redacted]. For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lenses exposed.

2.2 Full Analysis Set

The full analysis set (FAS) is the set of all randomized subjects who are exposed to any study lenses evaluated in this study, [redacted] and who have at least one post-baseline (post-Dispense) CLCDVA.

2.3 Per Protocol Analysis Set

The per protocol (PP) analysis set is a subset of FAS and excludes all data/subjects that have met any of the critical deviation or evaluability criteria identified in the Deviations and Evaluability Plan (DEP).

3 SUBJECT CHARACTERISTICS AND STUDY CONDUCT SUMMARIES

Demographic information (age, sex, ethnicity, and race), recent lens-wearing experience (wear modality, wear success), and habitual lens information will be presented by lens group and overall for the safety, full, and per protocol analysis sets.

Baseline data will also be summarized by lens group and overall on the safety, full and per protocol analysis sets.

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

4 EFFECTIVENESS ANALYSIS STRATEGY

This study defines 1 primary, 1 secondary [redacted] effectiveness endpoints. [redacted]. Primary inference will be done on the PP analysis set. [redacted]

[redacted]

[redacted]

[redacted]

All data obtained in evaluable subjects/eyes will be included in the analysis. No imputation for missing values will be carried out for the effectiveness analyses.

[redacted]

4.1 Effectiveness Endpoints

Primary Endpoint

The primary endpoint is the mean CLCDVA at Week 1 Follow-up. The corresponding assessment is collected with study lenses, in Snellen, for each eye. Conversion will be made to the logMAR scale.

Secondary Endpoints

The secondary endpoint is the percentage (proportion) of subjects with CLCDVA of 20/20 or better, measured monocularly, in both OD and OS at Week 1 Follow-up.

[redacted]

[redacted]

4.2 Effectiveness Hypotheses

Primary Effectiveness

The null and alternative hypotheses are formulated in terms of the predefined margin of 0.10 (in logMAR scale) for noninferiority:

H_0: $\mu_{(T)} - \mu_{(C)} \geq 0.10$

H_a: $\mu_{(T)} - \mu_{(C)} < 0.10$

where $\mu_{(T)}$ and $\mu_{(C)}$ denote the Week 1 Follow-up mean CLCDVA for [redacted] and Biofinity, contact lenses, respectively, on the logMAR scale.

Secondary Effectiveness

The null and alternative hypotheses are formulated in terms of the predefined margin of 0.10 (10%) for noninferiority.

H_0: $P_{(T)} - P_{(C)} \leq -0.10$

H_a: $P_{(T)} - P_{(C)} > -0.10$

where $P_{(T)}$ and $P_{(C)}$ denote the proportion of subjects attaining at least 20/20 in CLCDVA at Week 1 Follow-up in each eye (OD and OS) for [redacted] and Biofinity contact lenses, respectively.

[redacted]

4.3 Statistical Methods for Effectiveness Analyses

4.3.1 Primary Effectiveness Analyses

A mixed effects repeated measures model will be utilized to test these hypotheses. [redacted]. Lens difference ([redacted] minus Biofinity) and the corresponding two-sided 95% CI will be computed for Week 1 Follow-up. Noninferiority in CLCDVA will be declared if the upper confidence limit is less than 0.10.

[redacted]

4.3.2 Secondary Effectiveness Analyses

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] From the two-sided 95% CI on the lens difference ([redacted] minus Biofinity), noninferiority in proportion of subjects achieving 20/20 or better in CLCDVA in both eyes will be declared if the lower confidence limit is greater than -0.10.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

5.1 Safety Endpoints

The safety endpoints are:

- Adverse events (AE)
- Biomicroscopy Findings/Slit Lamp Examinations
  - [redacted]
- Device deficiencies

5.2 Safety Hypotheses

There are no formal safety hypotheses in this study. The focus of the safety analysis will be a comprehensive descriptive assessment of safety endpoints listed in Section 5.1.

5.3 Statistical Methods for Safety Analyses

5.3.1 Adverse Events

The applicable definition of an AE is in the study protocol. All AEs occurring from when a subject signs informed consent to when a subject exits the study will be accounted for in the reporting. Analysis and presentation of pre-treatment AEs will be separated from treatment-emergent AEs occurring during the study period. A pre-treatment AE is an event that occurs after signing informed consent but prior to exposure to study lenses (not including trial fitting lenses). The period for treatment-emergent AE analysis starts from exposure to study lenses until the subject completes or is discontinued from the study.

Descriptive summaries (counts and percentages) for ocular and nonocular AEs will be presented by Medical Dictionary for Regulatory Activities (MedDRA) Preferred Terms (PT). Serious AEs and significant non-serious ocular AEs will be noted. Additionally, relationship to lens will be identified in all AE tables. Unit of presentation for ocular AEs will be eye and nonocular AEs will be subject.

Individual subject listings will be provided for both pre-treatment and treatment-emergent AEs, where any AE leading to study discontinuation will be indicated.

5.3.2 Biomicroscopy Findings/Slit Lamp Examination

Biomicroscopy assessment will be performed at all study visits, including Screening/Baseline/Dispense, Week 1 Follow-up, Month 1 Follow-up, Month 3 Follow-up and unscheduled visits. The reporting unit for each biomicroscopy finding will be eye.

[redacted]

5.3.3 Device Deficiencies

A frequency table showing counts for each treatment-emergent Device Deficiency category will be presented. In addition, listings for treatment-emergent and pre-treatment device deficiencies will be provided.

[redacted]

[redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]

[redacted]

[redacted] [redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]
  - [redacted]

[redacted]

11 APPENDIX

Table 11-1 Schedule of Study Procedures and Assessments

Procedure/ Assessment	**Visit 1** Screening/ Baseline/ Dispense	**Visit 2** Week 1 Follow-up[5]	**Visit 3** Month 1 Follow-up[5]	**Visit 4** Month 3 Follow-up/Exit[5]	**Early Exit**	**USV**
	Day 1	Day 8 [redacted]	Day 30 [redacted]	Day 95 [redacted]		
Informed Consent	X					
Demographics	X					
Medical History	X	X	X	X	X	(X)
Pregnancy	X	X	X	X	X	(X)
Concomitant Medications	X	X	X	X	X	(X)
Inclusion/Exclusion	X					
Habitual lens information (brand/manufacturer, power, modality/wear success, habitual lens care brand)	X					
[redacted]	[redacted]			[redacted]	[redacted]	[redacted]
[redacted]	[redacted]			[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	X			[redacted]	[redacted]	[redacted]
Biomicroscopy [redacted]	X	X	X	X	X	(X)
[redacted]	[redacted]			[redacted]	[redacted]	[redacted]
[redacted]	[redacted]			[redacted]	[redacted]	[redacted]

Procedure/ Assessment	**Visit 1** Screening/ Baseline/ Dispense Day 1	**Visit 2** Week 1 Follow-up[5] Day 8	**Visit 3** Month 1 Follow-up[5]	**Visit 4** Month 3 Follow-up/Exit[5]	**Early Exit**	**USV**
[redacted]	[redacted]					
Randomize and record lens power	X					
[redacted]	[redacted]					
[redacted]	[redacted]	[redacted]	[redacted]			[redacted])
IP Dispense*	X	(X)	X			(X)
VA w/ study lenses (OD, OS Snellen distance)	X	X	X	X	X	(X)
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Procedure/ Assessment	**Visit 1** Screening/ Baseline/ Dispense Day 1	**Visit 2** Week 1 Follow-up[5] Day 8	**Visit 3** Month 1 Follow-up[5] Day 30	**Visit 4** Month 3 Follow-up/Exit[5] Day 95	**Early Exit**	**USV**
[redacted]						
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]			[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]				[redacted]	[redacted]	[redacted]
Adverse Events	X	X	X	X	X	(X)
Device deficiencies	X	X	X	X	X	(X)
Exit Form	(X)	(X)	(X)	X	X	(X)

[redacted]

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