Short Title:

Statistical Analysis Plan CLY935-C004

Full Title:

Statistical Analysis Plan CLY935-C004 / NCT03586167

Protocol Title:	Clinical Performance of a Monthly Replacement Silicone Hydrogel Lens
Project Number:	A02491
Protocol TDOC Number:	TDOC-0055118
Author:	[redacted]
	[redacted]
Template Version:	Version 4.0
Approvals:	See last page for electronic approvals
Job Notes:	

This is the original (Version 1.0) 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 objective of this study is to describe the clinical performance of an investigational, coated silicone hydrogel contact lens over 30 days of wear.

Decision Criteria for Study Success:

Decision criteria for study success are not applicable for this study.

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1 Study Objectives and Design

1.1 Study Objectives

PRIMARY OBJECTIVE

The primary objective of this study is to describe the clinical performance of an investigational, coated silicone hydrogel contact lens over 30 days of daily wear.

1.2 Study Description

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

Table 1-1 Study Description Summary

Study Design	Prospective, randomized, bilateral, parallel group, single-masked (trial subject) Lens care solution also randomized: OPTI-FREE® REPLENISH® multi-purpose disinfection solution (OFR) and CLEAR CARE® Cleaning & Disinfecting Solution (CC)
Study Population	Volunteer subjects aged 18 or over who are habitual monthly replacement soft contact lens wearers, have at least 3 months of contact lens wearing experience, and who wear their habitual lenses at least 5 days per week and at least 8 hours per day. Pregnant or breast-feeding women are not excluded from this study. Target to complete: 78; Planned to enroll: ~86
Number of Sites	~4 (US)
Test Product	LID014341
Control Product	CooperVision® Biofinity® contact lenses (BIOFINITY)
Duration of Treatment	Test Product: 30 days (-4/+2 days) Control Product: 30 days (-4/+2 days)
Visits	Visit 1, Day 1: Screen/Baseline/Dispense* Visit 2, Day 8 (-1/+2 Days): 1-Week Follow-up Visit 3, Day 15 (±2 Days): 2-Week Follow-up Visit 4, Day 30 (-4/+2 Days): 1-Month Follow-up/Exit *Randomization will occur at Visit 1

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 and lens care solution assignment. Randomization will be implemented in iMedidata Balance.

Qualifying subjects will be randomized in a 2:2:1:1 manner to one of 4 parallel regimen groups consisting of test or control lens and a lens care solution as described below.

1. LID014341 + OFR
2. LID014341 + CC
3. BIOFINITY + OFR
4. BIOFINITY + CC

1.4 Masking

This study is single-masked (trial subject).

1.5 Interim Analysis

There are no plans to conduct an interim analysis and no criteria by which the study would be terminated early based upon statistical determination

2 Analysis Sets

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. For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lens exposed.

Adverse events occurring from the time of informed consent but prior to first exposure to study lenses will be summarized in subject listings.

3 Subject Characteristics and Study Conduct Summaries

The following tables will be presented:

- Subject Disposition
- Analysis Set by Lens
- Analysis Set by Regimen

- Subject Accounting by Lens
- Demographics Characteristics
- Baseline Characteristics [lens brand, power, lens care brand, [redacted]]
- [redacted]

In addition, the following subject listings will be provided:

- Listing of Subjects Excluded from Protocol Defined Analysis Set
- Listing of Regimen Assignment by Investigator
- Listing of Subjects Discontinued from Study

4 Effectiveness Analysis Strategy

This study defines one primary endpoint [redacted]. The Safety Analysis Set will serve as the primary set for all effectiveness analyses.

Continuous variables will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum, as well as confidence intervals where applicable. Categorical variables will be summarized with counts and percentages from each category. Line graphs may also be generated for selected endpoints.

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

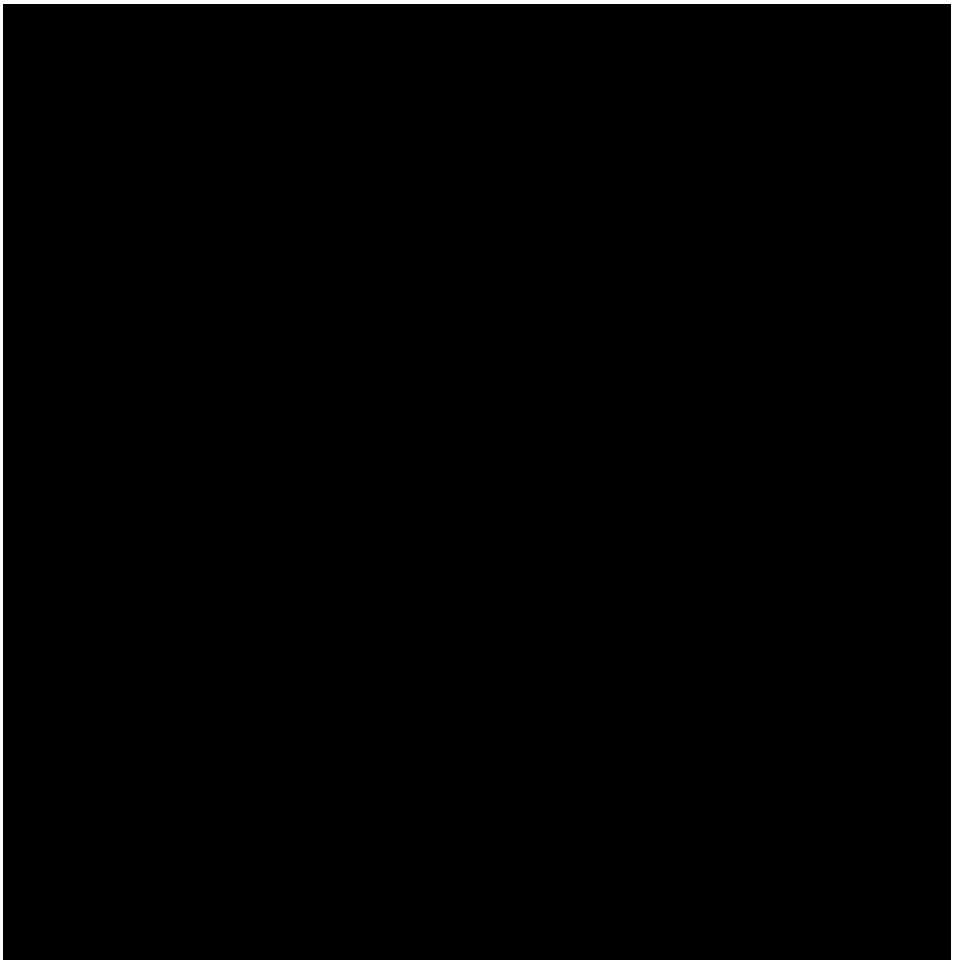
A listing of selected effectiveness data will also be provided.

4.1 Effectiveness Endpoints

Primary Endpoint

The primary endpoint is distance VA with study lenses, collected in logMAR scale, for each eye.

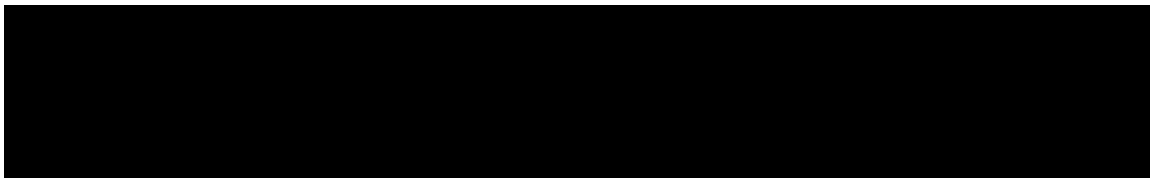
[redacted]



4.2 Effectiveness Hypotheses

Primary Effectiveness

No inferences are to be made on the primary effectiveness endpoint; therefore, no hypotheses are formulated.



4.3 Statistical Methods for Effectiveness Analyses

4.3.1 Primary Effectiveness Analyses

Descriptive statistics as well as a two-sided 95% confidence interval for the mean of each study lens will be provided.

[redacted]

4.4 Multiplicity Strategy

No multiplicity adjustment needs to be considered for the effectiveness endpoints since no formal hypothesis testing will be conducted.

[redacted]

4.6 Interim Analysis for Effectiveness

No interim analysis is planned for effectiveness endpoints.

5 Safety Analysis Strategy

5.1 Safety Endpoints

The safety endpoints are

- Adverse events (AE)
- Biomicroscopy findings
    - Limbal hyperemia
    - Bulbar hyperemia
    - Corneal staining
    - Conjunctival staining
    - Palpebral conjunctival observations
    - Corneal epithelial edema
    - Corneal stromal edema
    - Corneal vascularization
    - Conjunctival compression/indention
    - Chemosis
    - Corneal infiltrates
    - Other findings
- 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

The analysis set for all safety analyses is defined in Section 2.1. Baseline will be defined as the last measurement prior to exposure to study lenses on Visit 1. Safety variables will be summarized descriptively.

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. The period for treatment-emergent AE analysis starts from exposure to study lenses until the subject completes or is discontinued from the study.

The following tables and supportive listings will be provided:

- Incidence of All Ocular Treatment-Emergent Adverse Events
- Incidence of All Nonocular Treatment-Emergent Adverse Events
- Listing of All Ocular Treatment-Emergent Adverse Events
- Listing of All Nonocular Treatment-Emergent Adverse Events
- Listing of All Ocular Pre-Treatment Adverse Events
- Listing of All Nonocular Pre-Treatment Adverse Events

5.3.2 Biomicroscopy Findings/Slit Lamp Examination

The following tables and supportive listings will be provided:

- Frequency and Percentage for Biomicroscopy Findings by Visit
- Incidence of Increased Severity by 2 or More Grades in Biomicroscopy Findings
- Listing of Subjects With Other Biomicroscopy Findings
- Listing of Subjects With Increased Severity by 1 Grade in Biomicroscopy Findings
- Listing of Subjects With Increased Severity by 2 or More Grades in Biomicroscopy Findings
- Listings of Subjects with Infiltrates

5.3.3 Device Deficiencies

The following tables and supportive listings will be provided:

- Frequency of Treatment-Emergent Device Deficiencies
- Listing of Treatment-Emergent Device Deficiencies
- Listing of Device Deficiencies Prior To Treatment Exposure

6 Analysis Strategy for Other Endpoints

Not applicable.

7 Sample Size and Power Calculations

No formal sample size calculation is provided given the pilot and descriptive nature of the study.

8 References

Not applicable.

9 Revision History

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

10 Appendix

Table 100–1 Overview of Study Plan

Procedure/ Assessment	**Visit 1** **Screen / Baseline / Dispense**	**Visit 2** **1-Week Follow-up** [Day 8 (-1/+2 days) minimum 6 hrs after insertion)]	**Visit 3** **2-Week Follow-up** [Day 15 (±2 days)]	**Visit 4** **1-Month Follow-up/Exit** [Day 30 (-4/+2 days)]	**Early Exit**	**Unscheduled Visit**
Informed Consent	✓	--	--	--	--	--
Demographics	✓	--	--	--	--	--
Medical History	✓	✓	✓	✓	✓	✓
Concomitant Medications	✓	✓	✓	✓	✓	✓
Inclusion/ Exclusion	✓	--	--	--	--	--
Habitual lens (brand, power) and lens care	✓	--	--	--	--	--
[redacted]						
Keratometry readings*	✓	--	--	✓	✓	--
Manifest refraction*	✓	(✓)	(✓)	✓	✓	(✓)
BCVA (OD, OS, Snellen distance with manifest refraction)*	✓	(✓)	(✓)	✓	✓	(✓)
Biomicroscopy	✓	✓	✓	✓	✓	✓
Dispense study lenses	✓	(✓)	(✓)	--	--	(✓)

Procedure/ Assessment	**Visit 1 Screen / Baseline / Dispense**	**Visit 2 1-Week Follow-up** [Day 8 (-1/+2 days) minimum 6 hrs after insertion)]	**Visit 3 2-Week Follow-up** [Day 15 (±2 days)]	**Visit 4 1-Month Follow-up/Exit** [Day 30 (-4/+2 days)]	**Early Exit**	**Unscheduled Visit**
VA w/ study lenses (OD, OS, logMAR distance), (OU* as necessary) ^	✓	✓	✓	✓	✓	(✓)
[redacted]						

Procedure/ Assessment	**Visit 1 Screen / Baseline / Dispense**	**Visit 2 1-Week Follow-up** [Day 8 (-1/+2 days) minimum 6 hrs after insertion)]	**Visit 3 2-Week Follow-up** [Day 15 (±2 days)]	**Visit 4 1-Month Follow-up/Exit** [Day 30 (-4/+2 days)]	**Early Exit**	**Unscheduled Visit**
AEs	✓	✓	✓	✓	✓	✓
Device deficiencies	✓	✓	✓	✓	✓	✓
[redacted]						
Exit Form	(✓)	(✓)	(✓)	✓	✓	(✓)

(✓) assessment performed as necessary, eg, decrease of VA by 2 lines or more with investigational product (IP)
* Source only
^ If subject fitted with monovision, near eye must have distance over-refraction in place to assess VA.

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
07/12/2018 19:47:12	[redacted]	Biostatistics
07/12/2018 20:29:46	[redacted]	CDMA PL
07/12/2018 22:29:34	[redacted]	Global Device Medical Safety
07/13/2018 17:43:27	[redacted]	biostatistics