Short Title:

Statistical Analysis Plan
CLY935-C007 / NCT04055519

Full Title:

Statistical Analysis Plan
CLY935-C007

Protocol Title:	Clinical Performance Assessment of a Daily Wear Monthly Replacement Soft Silicone Hydrogel Contact Lens
Project Number:	A02491
Protocol TDOC Number:	TDOC-0056720
Author:	[redacted]
	[redacted]
Template Version:	Version 2.0
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 2.0 of the study protocol.

Executive Summary:

Key Objective:

The primary objective of this study is to describe the clinical performance of an investigational silicone hydrogel contact lens over 30 days of daily 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 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, single-masked, bilateral crossover
Study Population	Volunteer subjects aged 18 or over who are habitual spherical weekly/monthly soft contact lens wearers (excluding Biofinity 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. Target to complete: 32; Planned to enroll: ~36
Number of Sites	~3 US
Test Product	LID017569
Control Product	CooperVision® Biofinity® contact lenses (Biofinity)
Duration of Treatment	~ 60 days total duration (test and control) Test Product: ~30 days Control Product: ~30 days
Visits	Visit 1 – Screen/Baseline/ Lens 1: Dispense [Day 1] Visit 2 – Lens 1: Week 1 Follow-up [Day 8 ±2 Days] Visit 3 – Lens 1: Month 1 Follow-up [Day 30 ± 2 days]/Lens 2 – Dispense [Day 1] Visit 4 – Lens 2: Week 1 Follow-up [Day 8 ± 2 days] Visit 5 – Lens 2: Month 1 Follow-up/Exit [Day 30 ± 2 days]

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 sequence assignment. [redacted]

1.4 Masking

This is a single-masked (trial subject) study.

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 lenses exposed in the corresponding lens sequence.

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 by Lens Sequence
- Analysis Set by Lens Sequence
- Analysis Set by Lens
- Subject Accounting by Lens Sequence
- Demographics Characteristics by Lens Sequence
- Baseline Characteristics by Lens Sequence

In addition, the following subject listings will be provided:

- Listing of Subjects Excluded from Protocol Defined Analysis Set
- Listing of Lens Sequence 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 be used for all effectiveness analyses.

Continuous variables will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized with counts and percentages from each category.

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

A listing of selected effectiveness data will also be provided.

4.1 Effectiveness Endpoints

Primary Endpoint

The primary endpoint is distance visual acuity (VA) with study lenses, collected in logMAR, for each eye.

[redacted]

[redacted]

4.2 Effectiveness Hypotheses

Primary Effectiveness

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

[redacted]

4.3 Statistical Methods for Effectiveness Analyses

4.3.1 Primary Effectiveness Analyses

Descriptive statistics (number of observations, mean, standard deviation, median, minimum, maximum) for the logMAR values will be presented.

[redacted]

4.4 Multiplicity Strategy

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

4.5 Subgroup Analyses and Effect of Baseline Factors

It is not expected that demographic or baseline characteristics will have an impact on the study results in this study. No subgroup analyses are planned.

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 (ie, 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.

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. Each AE will be summarized under the exposed lens based upon the event onset date/time, up until the start of the next lens in the crossover sequence.

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

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 [This listing will include all relevant visits within the crossover period]
- Listing of Subjects With Increased Severity by 2 or More Grades in Biomicroscopy Findings [This listing will include all relevant visits within the crossover period]
- 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

[redacted]

8 References

Not Applicable.

9 Revision History

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 2.0 of the study protocol.

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10 Appendix

Table 10–2 Overview of Study Plan

Procedure/ Assessment	Visit 1 Screen / Baseline/ Lens 1: Dispense [Day 1]	Visit 2 Lens 1: Week 1 Follow-up [Day 8 (± 2 days)] $	Visit 3 Lens 1: Month 1 Follow-up [Day 30 (± 2 days)] Lens 2: Dispense [Day 1]		Visit 4 Lens 2: Week 1 Follow-up [Day 8 (± 2 days)] $	Visit 5 Lens 2: Month 1 Follow-up/ Exit^ [Day 30 (± 2 days)]$	Unscheduled Visit
			Follow-up Lens 1$	Dispense Lens 2			
Informed Consent	X						
Demographics	X						
Medical History	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X
Inclusion/ Exclusion	X						
Habitual lens (brand, power*, care)	X						
VA w/ habitual correction* (OD, OS, logMAR distance)	X					X	(X)
[redacted]	[redacted]		[redacted]			[redacted]	
Manifest refraction*	X	(X)	(X)	(X)	(X)	(X)	(X)
BCVA* (OD, OS, logMAR distance with manifest refraction)	X	(X)	(X)	(X)	(X)	(X)	(X)
Biomicroscopy	X	X	X		X	X	X
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Randomization	X						
Dispense study lenses	X			X			(X)
VA w/ study lenses, (OD, OS, logMAR distance)	X	X	X	X	X	X	(X)
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Procedure/ Assessment	Visit 1 Screen / Baseline/ Lens 1: Dispense [Day 1]	Visit 2 Lens 1: Week 1 Follow-up [Day 8 (± 2 days)] $	Visit 3 Lens 1: Month 1 Follow-up [Day 30 (± 2 days)] Lens 2: Dispense [Day 1]		Visit 4 Lens 2: Week 1 Follow-up [Day 8 (± 2 days)] $	Visit 5 Lens 2: Month 1 Follow-up/ Exit^ [Day 30 (± 2 days)]$	Unscheduled Visit
			Follow-up Lens 1$	Dispense Lens 2			
AEs	X	X	X	X	X	X	X
Device deficiencies	X	X	X	X	X	X	X
Exit Form	(X)	(X)	(X)	(X)	(X)	X	(X)

* Source only

$ Subjects are required to wear the study lenses for a minimum of 6 hours on the day of follow-up visits prior to the visit.

Printed By:

Print Date:

[redacted]
