Short Title:

Statistical Analysis Plan
CLY935-C008 / NCT04403542

Full Title:

Statistical Analysis Plan
CLY935-C008

Protocol Title:	Pilot Clinical Performance of a Silicone Hydrogel Lens for Up to Six Nights of Extended Wear
[redacted]	[redacted]
Protocol TDOC Number:	TDOC-0056933
Author:	[redacted]
	[redacted]
[redacted]	[redacted]
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 is to assess initial safety and performance of the [redacted] soft contact lens [redacted] when worn in an extended wear modality (ie, up to 6 nights/7 days of continuous wear) as compared to the BIOFINITY® soft contact lens (Biofinity).

[redacted]

[redacted]

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1 Study Objectives and Design

1.1 Study Objectives

PRIMARY OBJECTIVE

The primary objective is to assess initial safety and performance of the [redacted] soft contact lens when worn in an extended wear modality (ie, up to 6 nights/7 days of continuous wear) as compared to the Biofinity soft contact lens.

1.2 Study Description

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

Table [redacted]1 Study Description Summary

Study Design	Prospective, randomized, controlled, double-masked, contralateral
Study Population	Volunteer subjects aged 18 or over who are adapted 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 in an extended wear modality a minimum of 1 night per week. Subjects must require contact lenses in a power range from -1.00 to -6.00 D. Pregnant and breastfeeding women are excluded from this study. Target to complete: 30 Planned to enroll: ~36
Number of Sites	~3 (US)
Test Product	[redacted] soft contact lenses (LID018869) [redacted]
Control Product	CooperVision® BIOFINITY® (comfilcon A) soft contact lenses (Biofinity)
Duration of Treatment	Up to 6 nights/7 days of continuous wear
Visits	Visit 1, Day 1: Screening/Baseline/Dispense Visit 2, Day 2: Next Day Follow-up [≤ 4 hours after awakening] Visit 3, Day 7: Week 1 Follow-up/Exit [7 days (-1 day) of lens wear (ideally within 4 hours of awakening)]

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. Randomization will be implemented in the Electronic Data Capture (EDC)/randomization integration system.

Subjects will be randomized in a 1:1 ratio to receive treatment with [redacted] or Biofinity in one eye and the other lens in the fellow eye, as indicated below:

Sequence 1: [redacted] (OD)/Biofinity (OS)

Sequence 2: Biofinity (OD)/[redacted] (OS)

1.4 Masking

This is a double-masked study.

[redacted]

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, when applicable, from the corresponding lens sequence at the time of clinical assessment.

3 Subject Characteristics and Study Conduct Summaries

Demographic information (age, sex, ethnicity, and race) will be tabulated by lens sequence and overall.

The following tables and listings for study conduct summaries will be presented:

- Subject Disposition by Lens Sequence
- Analysis Set by Lens
- Subject Accounting by Lens Sequence
- Listing of Lens Sequence Assignment by Investigator
- Listing of Subjects Discontinued from Study
- Listing of Out-of-Window Visits

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.

4.1 Effectiveness Endpoints

Primary Endpoint

The primary endpoint is distance visual acuity (VA) with study lenses, collected in Snellen, for each eye. Conversion will be made to the logMAR scale.

[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

Summary statistics will be provided at each visit (Dispense, Next Day Follow-up, Week 1 Follow-up). Descriptive summary statistics will be displayed with counts and percentages on the Snellen categories, and n, mean, standard deviation, median, minimum, and maximum for the converted logMAR values.

[redacted]

[redacted]

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. Each AE will be summarized under the exposed lens based upon the event onset date/time.

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

Biomicroscopy assessment will be performed at all study visits. The reporting unit for each biomicroscopy finding will be eye.

A summary of grade category counts and percentages will be presented for each parameter at each scheduled visit. Findings collected during unscheduled visits will be presented in a subject listing. Furthermore, a listing of “Other" slit lamp findings will also be provided.

Additionally, for each biomicroscopy parameter, counts and percentages of eyes that experience an increase of ≥ 2 grades from baseline (Visit 1) to any subsequent visit will be presented, together with a supportive listing.

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]

7 Sample Size and Power Calculations

Given the early pilot nature of the study, sample size/power calculation is not relevant.

8 References

Not Applicable.

9 Revision History

Revision 1

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.

[redacted]

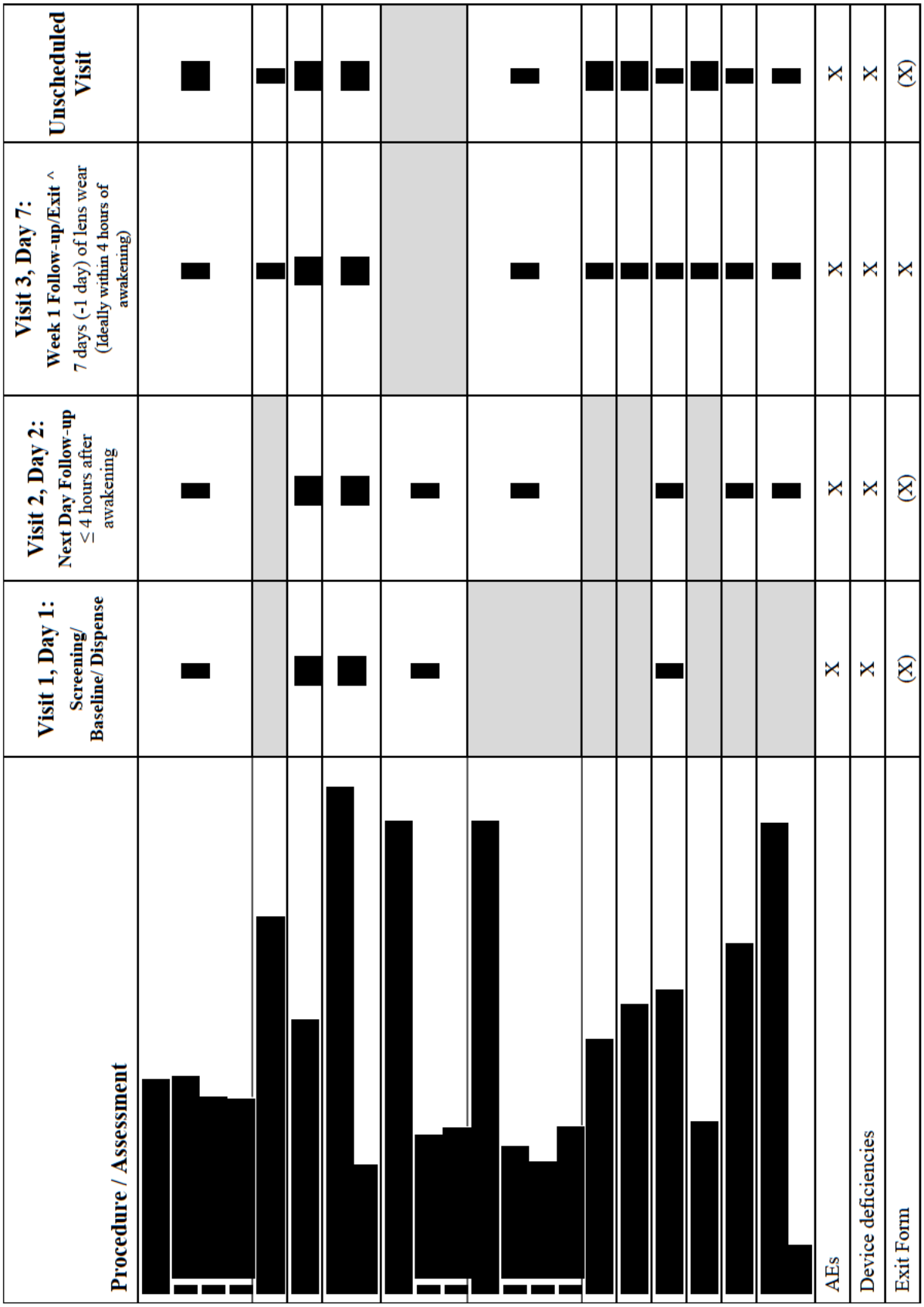
[redacted]

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

10 Appendix

Table [redacted].–2 Overview of Study Plan

Procedure / Assessment	Visit 1, Day 1: Screening/ Baseline/ Dispense	Visit 2, Day 2: Next Day Follow-up ≤ 4 hours after awakening	Visit 3, Day 7: Week 1 Follow-up/Exit ^ 7 days (-1 day) of lens wear (Ideally within 4 hours of awakening)	Unscheduled Visit
Informed Consent	X			
Demographics	X			
Medical History (including pregnancy*)	X	X	X	X
Concomitant Medications	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]
Biomicroscopy (without study lenses)	X	X	X	X
Randomize	X			
IP Dispense	X			(X)
VA w/ study lenses (OD, OS, Snellen distance)	X	X	X	(X)
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]



Procedure / Assessment	Visit 1, Day 1: Screening/ Baseline/ Dispense	Visit 2, Day 2: Next Day Follow-up ≤4 hours after awakening	Visit 3, Day 7: Week 1 Follow-up/Exit ^ 7 days (-1 day) of lens wear (Ideally within 4 hours of awakening)	Unscheduled Visit
AEs	X	X	X	X
Device deficiencies	X	X	X	X
Exit Form	(X)	(X)	X	(X)

[redacted]

^ Any subject who exits early from the study (excluding screen failures) must undergo all procedures outlined in Visit 3, as applicable.

[redacted]
