Short Title:

Statistical Analysis Plan
CLL949-C004 / NCT03560141

Full Title:

Statistical Analysis Plan
CLL949-C004

Protocol Title:	Clinical Performance of a Silicone Hydrogel Following One Night of Extended Wear
Project Number:	[redacted]
Protocol TDOC Number:	TDOC-0054558
Author:	[redacted]
	[redacted]
Template Version:	[redacted]
Approvals:	See last page for electronic approvals.
Job Notes:	

This is the second revision (Version 3.0) of the Statistical Analysis Plan for this study. This version of the Statistical Analysis Plan is based on Version 3.0 of the study protocol.

Executive Summary:

Key Objectives:

The primary objective is to obtain [redacted] insights to safety and performance of [redacted] soft contact lenses when worn in an extended wear modality compared to the Biofinity® soft contact lenses.

[redacted]

[redacted]

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1 Study Objectives and Design

1.1 Study Objectives

PRIMARY OBJECTIVE

The primary objective is to obtain [redacted] insights to safety and performance of [redacted] soft contact lenses when worn in an extended wear modality compared to the Biofinity soft contact lenses.

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, controlled, double-masked, contralateral
Study Population	Volunteer subjects aged 18 or over who are soft contact lens wearers, excluding Biofinity habitual wearers, have at least 3 months of contact lens wearing experience, and who wear their habitual lenses at least 5 days per week in either a daily wear or extended wear modality. Subjects who wear their habitual lenses in a daily wear modality (ie, not extended wear) should wear their habitual lenses at least 12 hours per day. [redacted] Pregnant and breastfeeding women are excluded from this study. Target to complete: 10; Planned to enroll: ~12
Number of Sites	~1 (US)
Test Product	[redacted] soft contact lenses (LID011121)
Control Product	Biofinity® (comfilcon A) soft contact lenses
Duration of Treatment	Subjects will wear the lenses in an extended wear modality (ie, while awake and asleep) for one overnight only
Visits	Visit 1, Day 1: Screening/Baseline/Dispense Visit 2, Day 1: Follow-Up prior to sleeping (≥ 4 hours after Dispense) Visit 3, Day 2: Follow-Up (0 to 10 mins upon eye opening) Visit 4, Day 2: 1 Hour Follow-Up/Exit (-30/+60 mins after Visit 3)

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 1:1 ratio to receive [redacted] and Biofinity contralaterally in one of the sequences below:

Sequence 1: [redacted] (OD) / Biofinity (OS)
Sequence 2: Biofinity (OD) / [redacted] (OS)

1.4 Masking

This study is double-masked.

[redacted]

[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 eyes exposed to any study lenses evaluated in this study. For treatment-emergent safety analyses, eyes will be categorized under the actual study lens exposed at the time of the clinical assessment.

3 Subject Characteristics and Study Conduct Summaries

Demographic information (age, sex, ethnicity, and race) and habitual lens information will be tabulated.

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 serve as the primary set for all effectiveness analyses.

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.

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, Follow-up prior to sleeping, Follow-up, 1 Hour Follow-up). [redacted]

[redacted]

[redacted]

5 Safety Analysis Strategy

5.1 Safety Endpoints

The safety endpoints are

- Adverse events (AE)
- Biomicroscopy Findings/Slit Lamp Examination
    - 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 the safety analysis set as 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 the study lens. The period for treatment-emergent AE analysis starts from exposure to study lens 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 nonserious 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. 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.

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]

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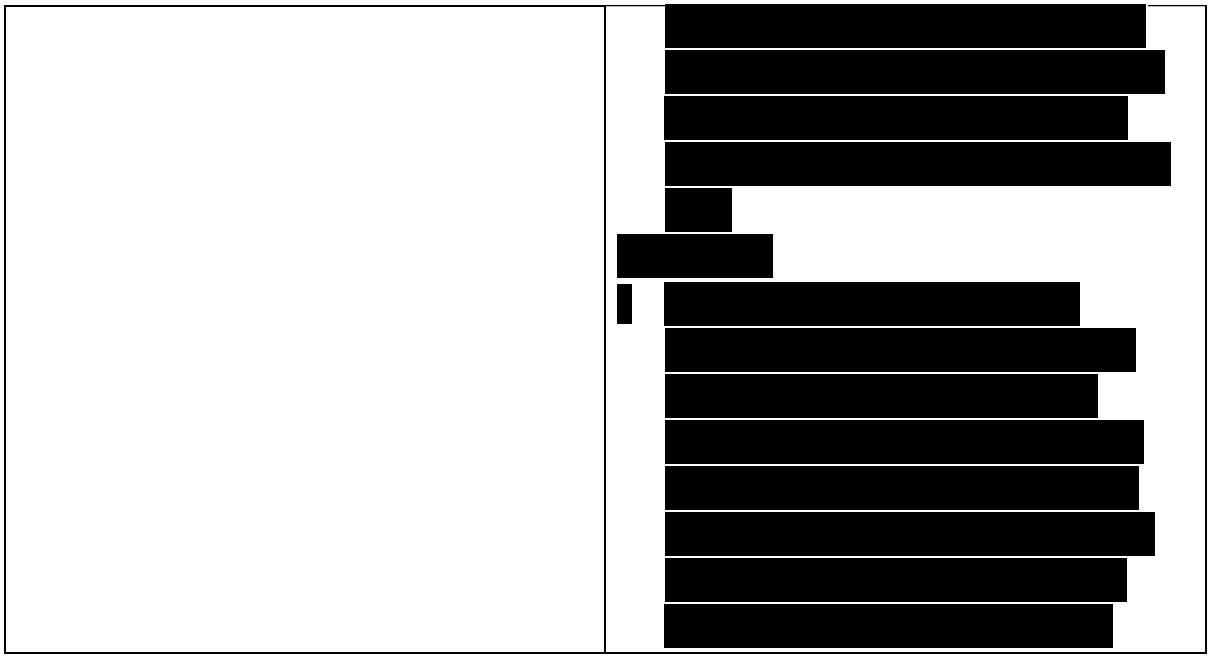
[redacted]	[redacted] [redacted] [redacted]



9 Appendix

Table 9–2 Schedule of Study Procedures and Assessments

Procedure/ Assessment	**Visit 1, Day 1: Screening/ Baseline/ Dispense**	**Visit 2, Day 1: Follow-up prior to sleeping** ≥ 4 hours after Dispense	**Visit 3, Day 2: Follow-up 0 to 10 mins upon eye opening•** ~7:30am	**Visit 4, Day 2: 1 Hour Follow-up/ Exit** (-30/+60 mins after Visit 3)	**Unsched Visit**
		Instruct the subject to retire on Day 1 so that he/she sleeps in the lenses ~7-10 hours.	Visit 3 to occur immediately upon eye opening on Day 2. Subjects will be escorted to the slit-lamp with eyes closed.		
Informed Consent	✓	-	-	-	-
Demographics	✓	-	-	-	-
Medical History	✓	-	-	-	-
Concomitant Medications	✓	(✓)	(✓)	(✓)	(✓)
Inclusion/ Exclusion	✓	-	-	-	-

Procedure/ Assessment	**Visit 1, Day 1: Screening/ Baseline/ Dispense**	**Visit 2, Day 1: Follow-up prior to sleeping** ≥ 4 hours after Dispense	**Visit 3, Day 2: Follow-up 0 to 10 mins upon eye opening•** ~7:30am	**Visit 4, Day 2: 1 Hour Follow-up/ Exit** (-30/+60 mins after Visit 3)	**Unsched Visit**
Habitual lens (brand, power)	✓	-	-	-	-
VA w/ habitual correction (Snellen distance, OD,OS)*	✓	-	-	✓	(✓)
[redacted]	■	■	■	■	■
[redacted]	■	■	■	■	■
[redacted]	■	■	■	■	■
Biomicroscopy	✓	✓‡	✓‡	✓‡ ✓for Exit	✓
Dispense study lenses	✓	-	-	-	-
VA w/ study lenses (Snellen distance, OD, OS)	✓	✓	✓	✓	✓
[redacted]	■	■	■	■	■
[redacted]	■	■	■	■	■
[redacted]	■	■	■	■	■
[redacted]	■	■	■	■	■
[redacted]	■	■	■	■	■

Procedure/ Assessment	**Visit 1, Day 1: Screening/ Baseline/ Dispense**	**Visit 2, Day 1: Follow-up prior to sleeping** ≥ 4 hours after Dispense	**Visit 3, Day 2: Follow-up 0 to 10 mins upon eye opening•** ~7:30am	**Visit 4, Day 2: 1 Hour Follow-up/ Exit** (-30/+60 mins after Visit 3)	**Unsched Visit**
[redacted]					
[redacted]					
[redacted]					
AEs	✓	✓	✓	✓	✓
Device deficiencies	✓	✓	✓	✓	✓
Exit Form	(✓)	(✓)	(✓)	(✓)	(✓)

*source only

[redacted]

[redacted]
