Short Title:

Statistical Analysis Plan CLL949-C009 / NCT03920280

Full Title:

Statistical Analysis Plan [redacted] CLL949-C009

Protocol Title:	Clinical Evaluation of a Daily Wear Frequent Replacement Silicone Hydrogel Lens
Project Number:	[redacted]
Reference Number:	
Protocol TDOC Number:	TDOC-0056233
Author:	[redacted]
	[redacted]
Template Version:	[redacted]
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 Objectives:

The primary objective is to demonstrate safety and effectiveness of [redacted] soft contact lens when worn for daily wear as compared to BIOFINITY® soft contact lens.

[redacted]

[redacted]

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1 Study Objectives and Design

1.1 Study Objectives

PRIMARY OBJECTIVE

The primary objective is to demonstrate safety and effectiveness of [redacted] soft contact lens when worn for daily wear as compared to Biofinity soft contact lens.

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: 90 subjects (60:30; Test:Control) Planned to enroll: ~120 subjects
Number of Sites	~8 (US)
Test Product	[redacted] soft contact lenses [redacted]
Control Product	CooperVision® BIOFINITY® (comfilcon A) soft contact lenses (Biofinity)
Duration of Treatment	Approximately 3 months
Visits	Visit 1: Screening/Baseline/Dispense (Day 1) Visit 2: Week 1 Follow-up [redacted] Visit 3: Week 2 Follow-up [redacted] Visit 4: Month 1 Follow-up [redacted] Visit 5: Month 2 Follow-up [redacted] Visit 6: 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.

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

1.4 Masking

This study is double-masked.

2 Analysis Sets

2.1 All Enrolled

All subjects who have signed the informed consent for the study will be included in the All Enrolled analysis set.

2.2 Enrolled Dispensed

Enrolled Dispensed is a subset of All Enrolled subjects/eyes that have been exposed to study lenses.

[redacted]

2.4 Completed

The Completed analysis set consists of Enrolled Dispensed subjects/eyes completing the study.

2.5 Discontinued

The Discontinued analysis set consists of Enrolled Dispensed subjects/eyes not completing the study.

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 [redacted]

[redacted]

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

4 Effectiveness Analysis Strategy

This study defines one primary effectiveness endpoint [redacted]. Unless otherwise specified, separate summary tables will be presented for the Completed and the Discontinued analysis sets with the following distinction:

- Completed Control (eyes/subjects)
- Completed Test (eyes/subjects)

- Discontinued Control (eyes/subjects)
- Discontinued Test (eyes/subjects)

No inferential testing will be performed on the effectiveness endpoints, [redacted]

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]

4.2 Effectiveness Hypotheses

Primary Effectiveness

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

[redacted]

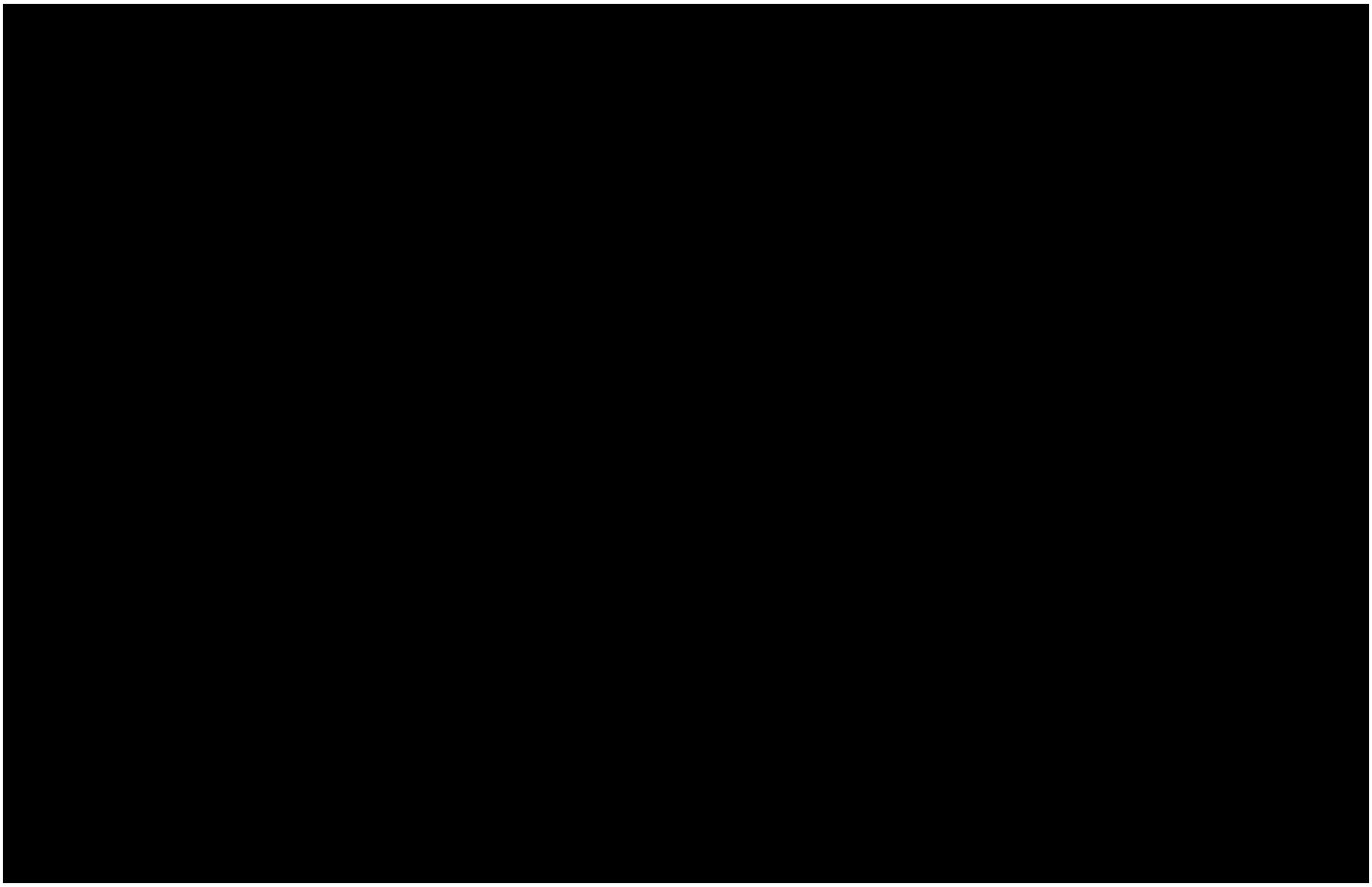
[redacted]

4.3 Statistical Methods for Effectiveness Analyses

4.3.1 Primary Effectiveness Analyses

Summary statistics will be provided at each visi [redacted] the converted logMAR values will be provided.

[redacted]



5 Safety Analysis Strategy

Unless otherwise specified, separate summary tables will be presented for the Completed and the Discontinued analysis sets with the following distinction:

- Completed Control (eyes/subjects)
- Completed Test (eyes/subjects)
- Discontinued Control (eyes/subjects)
- Discontinued Test (eyes/subjects)

Subjects/eyes will be categorized under the actual lens exposed.

5.1 Safety Endpoints

The safety endpoints include the following:

- 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

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 [redacted] 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 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 Visit 1 to 6 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]

8 References

[redacted]

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 10-1 Schedule of Study Procedures and Assessments

Procedure/ Assessment	Visit 1 Screening/ Baseline/ Dispense	Visit 2 Week 1 Follow-up	Visit 3 Week 2 Follow-up	Visit 4 Month 1 Follow-up	Visit 5 Month 2 Follow-up	Visit 6 Month 3 Follow-up/Exit	Early Exit	USV
	Day 1	Day 7 [redacted]	Day 15 [redacted]	Day 30 [redacted]	Day 60 [redacted]	Day 95 [redacted]		
Informed Consent	✓	-	-	-	-	-	-	-
Demographics	✓	-	-	-	-	-	-	-
Medical History	✓	✓	✓	✓	✓	✓	✓	(✓)
Concomitant Medications	✓	✓	✓	✓	✓	✓	✓	(✓)
Inclusion/ Exclusion	✓	-	-	-	-	-	-	-
Habitual lens information (brand / manufacturer, modality, power, wear success, habitual lens care brand)	✓	-	-	-	-	-	-	-
VA w/ habitual correction (OD,OS Snellen distance)	✓	-	-	-	-	✓	✓	(✓)
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Procedure/ Assessment	Visit 1 Screening/ Baseline/ Dispense	Visit 2 Week 1 Follow-up	Visit 3 Week 2 Follow-up	Visit 4 Month 1 Follow-up	Visit 5 Month 2 Follow-up	Visit 6 Month 3 Follow-up/Exit	Early Exit	USV
	Day 1	Day 7	Day 15	Day 30	Day 60	Day 95		
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Biomicroscopy	✓	✓	✓	✓	✓	✓	✓	(✓)
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Randomize	✓	-	-	-	-	-	-	-
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
IP Dispense	✓	✓	(✓)	(✓)	(✓)	-	-	(✓)
VA w/ study lenses (OD, OS Snellen distance)[1]	✓	✓	✓	✓	✓	✓	✓	(✓)
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Printed By:

Print Date:

Procedure/ Assessment	Visit 1 Screening/ Baseline/ Dispense	Visit 2 Week 1 Follow-up	Visit 3 Week 2 Follow-up	Visit 4 Month 1 Follow-up	Visit 5 Month 2 Follow-up	Visit 6 Month 3 Follow-up/Exit	Early Exit	USV
	Day 1	Day 7 [redacted]	Day 15 [redacted]	Day 30 [redacted]	Day 60 [redacted]	Day 95 [redacted]		
[redacted]								

Procedure/ Assessment	Visit 1 Screening/ Baseline/ Dispense	Visit 2 Week 1 Follow-up	Visit 3 Week 2 Follow-up	Visit 4 Month 1 Follow-up	Visit 5 Month 2 Follow-up	Visit 6 Month 3 Follow-up/Exit	Early Exit	USV
	Day 1	Day 7 [redacted]	Day 15 [redacted]	Day 30 [redacted]	Day 60 [redacted]	Day 95 [redacted]		
[redacted]								
AEs	✓	✓	✓	✓	✓	✓	✓	(✓)
Device deficiencies	✓	✓	✓	✓	✓	✓	✓	(✓)
Exit Form	(✓)	(✓)	(✓)	(✓)	(✓)	✓	✓	(✓)

[redacted]

a) All follow-up visits should be scheduled at least 4 hours after lens insertion [redacted]

[redacted]
