Clinical Performance of Two Reusable Silicone Hydrogel Contact Lenses

STUDY ID:

CLL949-E005

STATISTICAL ANALYSIS PLAN

NCT05431478

Statistical Analysis Plan for CLL949-E005
Title: Clinical Performance of Two Reusable Silicone Hydrogel Contact Lenses

Author: [redacted]
Trial Statistician

[redacted].

Executive Summary:

Key Objectives:

The objective of this study is to assess the clinical performance of two reusable silicone hydrogel contact lenses when worn on a daily wear modality.

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 objective of this study is to assess the clinical performance of two reusable silicone hydrogel contact lenses when worn on a daily wear modality.

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 crossover, double-masked
Study Population	Volunteer subjects aged 18 or over who are habitual spherical soft contact lens wearers (excluding current/previous ACUVUE OASYS® 2 Week with HYDRACLEAR® PLUS (AOHP) habitual lens wearers and daily disposable 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. [redacted] Target to complete: 60 Planned to enroll: ~68
Number of Sites	~5 US
Test Product(s)	Alcon serafilcon A contact lenses (serafilcon A; LID022821)
Comparator Product(s)	ACUVUE OASYS® 2 Week with HYDRACLEAR® PLUS (AOHP; senofilcon A)
Planned Duration of Exposure	~28 days total duration (test and comparator) plus wash-out: Test Product: ~14 days Comparator Product: ~14 days
Visits	Prescreening (optional) Visit 1 – Screening/Baseline Visit 2 – Dispense Lens 1 [2 (at least 48 hours) - 4 days after Visit 1*]

	Visit 3 – Week 1 Follow-up Lens 1 [7 -0/+1 days after Visit 2] Visit 4 – Week 2 Follow-up Lens 1 [7 -0/+1 days after Visit 3] Visit 5 – Dispense Lens 2 [2 (at least 48 hours) - 4 days after Visit 4*] Visit 6 – Week 1 Follow-up Lens 2 [7 -0/+1 days after Visit 5] Visit 7 – Week 2 Follow-up Lens 2/Exit [7 -0/+1 days after Visit 6] ** Washout period with habitual spectacles only after Visit 1 and after Visit 4*

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 manner to receive treatment (lens) in crossover sequence as follows:

Sequence	EDC/randomization integration system	Lens Name
Sequence 1	LID022821/AOHP	Alcon serafilcon A/AOHP
Sequence 2	AOHP/LID022821	AOHP/Alcon serafilcon A

1.4 Masking

This study is double-masked.

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, [redacted]

[redacted] 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
- Analysis Set by Lens Sequence
- Subject Accounting by Lens Sequence
- Demographics by Lens Sequence
- Baseline Characteristics by Lens Sequence [lens brand; lens power; lens solution; habitual lens wear and rewetting drop usage, best corrected visual acuity; keratometry readings]

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 1 primary [redacted] effectiveness endpoint. The Safety Analysis Set will be used for all effectiveness analyses.

Select effectiveness endpoints will also be summarized by period.

Continuous variables will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized with frequencies 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 select effectiveness data will also be provided.

4.1 Effectiveness Endpoints

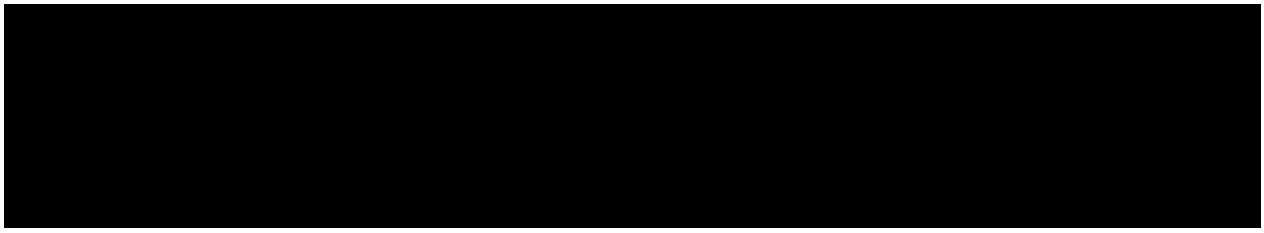
Primary Effectiveness Endpoint

The primary effectiveness endpoint is visual acuity (VA) with study lenses at Week 1 Follow-Up, collected at distance for each eye in logMAR.

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

Primary Effectiveness

Descriptive statistics will be provided, at each visit. Summary by period will also be generated.

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 demographics 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

The focus of the safety analysis will be a comprehensive descriptive assessment of occurrence of adverse events as well as the other listed parameters. Therefore, no inferential testing will be done for the safety analysis.

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. For biomicroscopy data, baseline will be defined as Visit 2 for Period 1 and Visit 5 for Period 2. 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 the time of their study exit will be accounted for in the reporting.

Presentation of AEs will be separated into pre-treatment AEs, between-treatment AEs, and treatment-emergent AEs as defined below:

- Pre-treatment: an event that occurs after signing informed consent but prior to exposure to study lenses
- Between-treatment: an event that occurs one day after last exposure to Period 1 study lenses but prior to exposure to Period 2 study lenses
- Treatment-emergent: an event that occurs from exposure to Period 1 study lenses until subject exits from the study, excluding those classified as between-treatment

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
- Listing of All Ocular Between-Treatment Adverse Events
- Listing of All Nonocular Between-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 Conjunctival Compression/Indentation or Chemosis
- Listing of Subjects With Increased Severity by 2 or More Grades in Biomicroscopy Findings
- Listing 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 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. [redacted]

[redacted]

10 APPENDIX

Table 10-1 Schedule of Study Procedures and Assessments

		Lens 1 (Period 1)				Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening / Baseline**	**Visit 2 Dispense Lens 1** [2 (at least 48 hours) - 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)]	**Visit 3 Week 1 Follow-up Lens 1** [7 -0/+ 1 days after Visit 2]	**Visit 4 Week 2 Follow- up Lens 1** [7 -0/+ 1 days after Visit 3)]	**Visit 5 Dispense Lens 2** [2 (at least 48 hours) - 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	**Visit 6 Week 1 Follow-up Lens 2** [7 -0/+ 1 days after Visit 5]	**Visit 7 Week 2 Follow-up Lens 2 /Exit** [7 -0/+ 1 days after Visit 6)]	**Early Exit**	**Unscheduled Visit**
Informed Consent		X								
Demographics		X								
Medical History*		X	X	X	X	X	X	X	X	X
Concomitant Medications*		X	X	X	X	X	X	X	X	X
Inclusion/ Exclusion		X								
Habitual lens (brand, lens power, lens care)		X								
[redacted]										

		Lens 1 (Period 1)				Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening / Baseline**	**Visit 2 Dispense Lens 1** [2 (at least 48 hours) - 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)]	**Visit 3 Week 1 Follow-up Lens 1** [7 -0/+ 1 days after Visit 2]	**Visit 4 Week 2 Follow- up Lens 1** [7 -0/+ 1 days after Visit 3)]	**Visit 5 Dispense Lens 2** [2 (at least 48 hours) - 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	**Visit 6 Week 1 Follow-up Lens 2** [7 -0/+ 1 days after Visit 5]	**Visit 7 Week 2 Follow-up Lens 2 /Exit** [7 -0/+ 1 days after Visit 6)]	**Early Exit**	**Unscheduled Visit**
[redacted]										
VA w/ habitual correction[+] (OD, OS, logMAR distance)*		X						X	(X)	(X)
[redacted]										
Manifest refraction*		X	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
[redacted]										
Biomicroscopy		X	X	X	X	X	X	X	X	X

		Lens 1 (Period 1)				Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening / Baseline**	**Visit 2 Dispense Lens 1** [2 (at least 48 hours) - 4 days after Visit 1 (Washout period with habitual spectacles only after	**Visit 3 Week 1 Follow-up Lens 1** [7 -0/+ 1 days after Visit 2]	**Visit 4 Week 2 Follow- up Lens 1** [7 -0/+ 1 days after Visit 3)]	**Visit 5 Dispense Lens 2** [2 (at least 48 hours) - 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	**Visit 6 Week 1 Follow-up Lens 2** [7 -0/+ 1 days after Visit 5]	**Visit 7 Week 2 Follow-up Lens 2 /Exit** [7 -0/+ 1 days after Visit 6)]	**Early Exit**	**Unscheduled Visit**
[redacted]										
Randomization		X								
Dispense study lenses			X	X		X	X			(X)
VA w/ study lenses (OD, OS, logMAR distance)			X	X	X	X	X	X	(X)	(X)

		Lens 1 (Period 1)				Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening / Baseline**	**Visit 2 Dispense Lens 1** [2 (at least 48 hours) - 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)]	**Visit 3 Week 1 Follow-up Lens 1** [7 -0/+ 1 days after Visit 2]	**Visit 4 Week 2 Follow- up Lens 1** [7 -0/+ 1 days after Visit 3)]	**Visit 5 Dispense Lens 2** [2 (at least 48 hours) - 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	**Visit 6 Week 1 Follow-up Lens 2** [7 -0/+ 1 days after Visit 5]	**Visit 7 Week 2 Follow-up Lens 2 /Exit** [7 -0/+ 1 days after Visit 6)]	**Early Exit**	**Unscheduled Visit**
[redacted]										

		Lens 1 (Period 1)				Lens 2 (Period 2)				
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[redacted]										

		Lens 1 (Period 1)				Lens 2 (Period 2)				
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[redacted]										
Unplanned lens replacement with reason			(X)	(X)	(X)	(X)	(X)			(X)
AEs [α]		X	X	X	X	X	X	X	X	X
Device deficiencies		X	X	X	X	X	X	X	X	X
Exit Form								X	X	

(X) assessment performed as necessary, e.g., reduction of VA by 2 lines or more with investigational product (IP)