Clinical Performance of Two Frequent Replacement Silicone Hydrogel Multifocal Contact Lenses

STUDY ID

CLM234-C001

STATISTICAL ANALYSIS PLAN v.1

25 Jun 2024

NCT06469242

Statistical Analysis Plan for CLM234-C001
Title: Clinical Performance of Two Frequent Replacement Silicone Hydrogel Multifocal Contact Lenses

Executive Summary:

Key Objectives:

The primary objective of this study is to evaluate binocular visual acuity (VA) at distance of LID233309 lenses and ACUVUE® OASYS MULTIFOCAL with PUPIL OPTIMIZED DESIGN (Oasys MF) lenses.

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 evaluate binocular VA at distance of LID233309 lenses and Oasys MF lenses.

[redacted]

SAFETY OBJECTIVE

The safety objective is to describe the safety profile of the study products.

1.2 Study Description

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

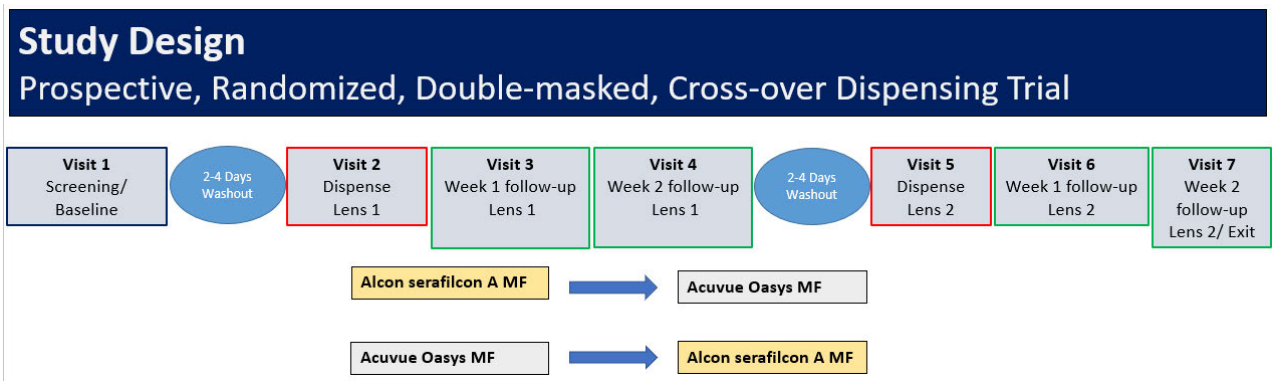
Table 1-1 Study Description Summary

Study Design	Prospective, randomized, bilateral, crossover, double-masked (study lenses)
Study Population	• The subject population consists of volunteer subjects aged ≥ 40 years, frequent replacement soft multifocal contact lens wearers (excluding habitual Oasys MF and habitual daily disposable lens wearers) for at least past 6 months and wear their habitual lenses at least 5 days per week and at least 10 hours per day, [redacted]

	Target to complete: 92 Planned to enroll: ~96
Number of Sites	~8 US
Test Product	Alcon serafilcon A Multifocal contact lenses (serafilcon A; LID233309)
Comparator Product	ACUVUE® OASYS MULTIFOCAL with PUPIL OPTIMIZED DESIGN contact lenses (Oasys MF; senofilcon A)
Planned Duration of Exposure	~28 days total duration (test and comparator): Test Product: 14 days Comparator Product: 14 days
Visits	Prescreening (optional) Visit 1: Screening/Baseline/Lens Fitting Visit 2: Dispense Lens 1 [2 (at least 48 hours) - 4 days after the end of 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 the end of 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*

A study design schematic is depicted in Figure 1-1.

Figure 1-1 Study Design



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

[redacted]

1.4 Masking

This study is double-masked (study lenses).

[redacted]

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], any adverse event (AE) or device deficiency occurring after informed consent and prior to the initial exposure to the study lenses (test or comparator) under evaluation in this clinical protocol will be listed as pretreatment.

For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lenses exposed in the corresponding study 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.

2.2 Full Analysis Set

The full analysis set (FAS) is the set of all randomized subjects who are exposed to any study lenses evaluated in this study,

2.3 Per Protocol Analysis Set

The per protocol (PP) analysis set is a subset of FAS and excludes all data/subjects that have met any of the critical deviation or evaluability criteria identified in the Data Evaluability Plan (DEP).

3 SUBJECT CHARACTERISTICS AND STUDY CONDUCT SUMMARIES

The following tables will be presented:

- Subject Disposition by Lens Sequence
- Subject Disposition by Study Lens Sequence
- Analysis Sets by Study Lens
- Analysis Sets by Study Lens Sequence
- Subject Accounting by Lens
- Subject Accounting by Study Lens Sequence
- Demographics by Lens Sequence
- Demographics by Study Lens Sequence
- Baseline Characteristics by Study Lens Sequence [lens brand; hours of digital device use per day; pupil size]

Subject accounting and demographics tables will be summarized on the safety, full, and per protocol analysis datasets. Baseline characteristics will be summarized on the full and per protocol analysis datasets.

In addition, the following subject listings will be provided:

- Listing of Subjects Excluded from Protocol Defined Analysis Sets
- Listing of Lens Sequence Assignment by Investigator
- Listing of Subjects Discontinued from Study

4 EFFECTIVENESS ANALYSIS STRATEGY

This study defines 1 primary effectiveness endpoint, [redacted] effectiveness evaluations will use the FAS as the primary analysis set. [redacted]

[redacted]

[redacted]

Continuous variables will be summarized using the number of observations, mean, standard deviation (SD), median, minimum, and maximum, as well as confidence intervals/limits as applicable. Categorical variables will be summarized with frequencies and percentages from each category.

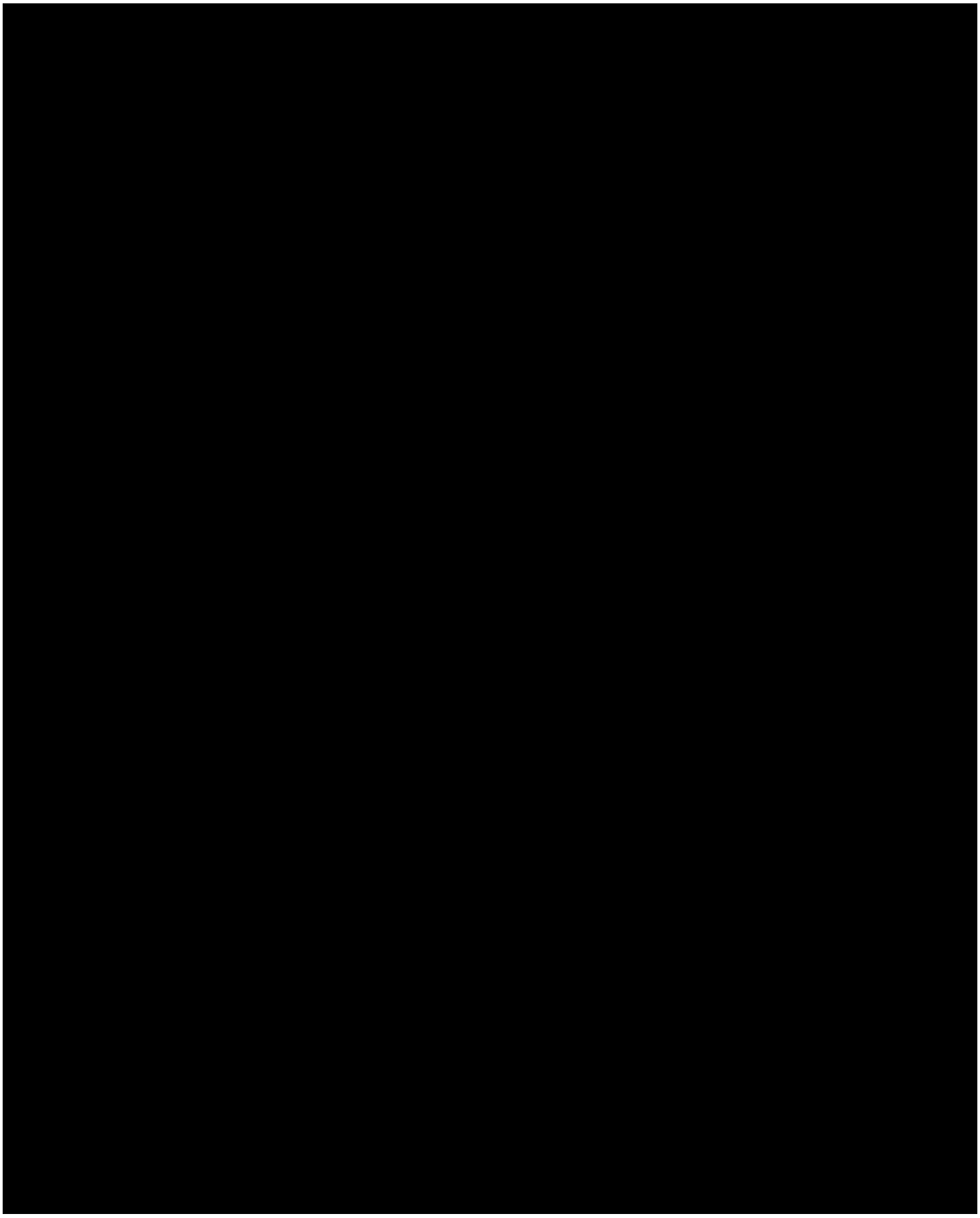
All data obtained in evaluable subjects/eyes will be included in the analysis. No imputation for missing values will be carried out for the primary and key exploratory effectiveness analyses.

A listing of select effectiveness data will also be provided.

4.1 Effectiveness Endpoints

Primary Effectiveness Endpoint

The primary endpoint is binocular High Contrast/High Illumination (HC/HI) distance (4 m) VA with study lenses at Week 1, collected on 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.

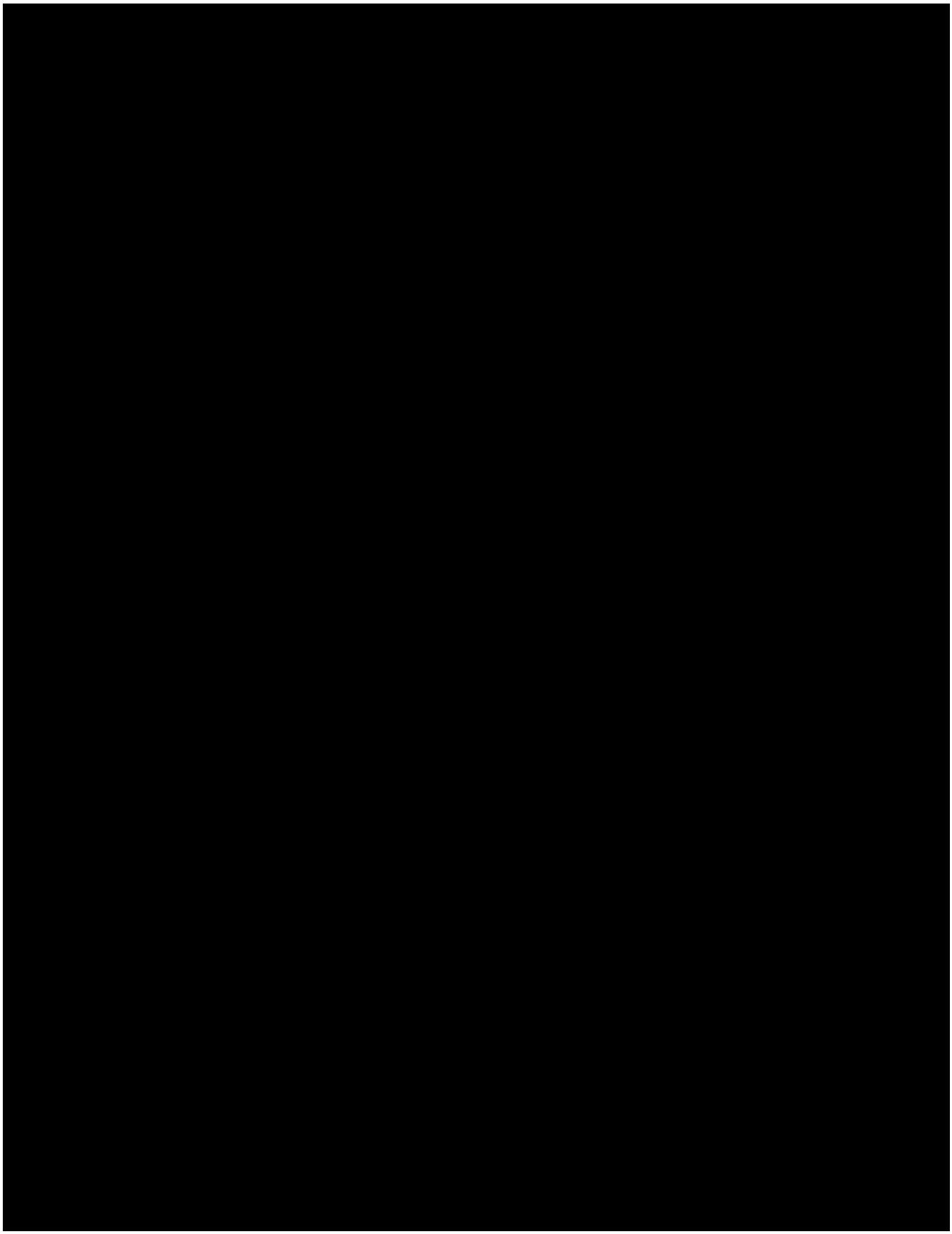
[redacted]

4.3 Statistical Methods for Effectiveness Analyses

Primary Effectiveness

At Week 1, descriptive statistics will be provided as number of observations, mean, SD, median, minimum, and maximum, along with a two-sided 95% confidence interval. Similarly, for Dispense and Week 2.

[redacted]



[redacted]

4.4 Multiplicity Strategy

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

[redacted]

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 pretreatment AEs, between-treatment AEs, and treatment-emergent AEs as defined below:

- Pretreatment: 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 Ocular Serious Treatment-Emergent Adverse Events
- Incidence of Ocular Significant Nonserious Treatment-Emergent Adverse Events
- Incidence of All Nonocular Treatment-Emergent Adverse Events
- Incidence of All Nonocular Serious 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 Eyes With Other Biomicroscopy Findings
- Listing of Eyes With Conjunctival Compression/Indentation or Chemosis
- Listing of Eyes With Increased Severity by 2 or More Grades in Biomicroscopy Findings
- Listing of Eyes 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
- Listing of Between-Treatment Device Deficiencies

6 ANALYSIS STRATEGY FOR OTHER ENDPOINTS

Not Applicable.

7 SAMPLE SIZE AND POWER CALCULATIONS

Although inferential testing is not planned for the primary and effectiveness endpoints, expected precision of the observed results is provided for the chosen sample size of 92, [redacted]

Visual Acuity

With the assumed SD of 0.12, a two-sided 95% CI for the mean of distance visual acuity based on t-statistics, coverage probability of 0.85 will extend 0.027 (~1 Snellen letter) from the observed mean.

[redacted]

8 REFERENCES

Not applicable.

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 2.0 of the study protocol.

10 APPENDIX

Table 10-1 Schedule of Study Procedures and Assessments

		Fitting Lens 1 (Fit Period 1) and Fitting Lens 2 (Fit Period 2)	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unscheduled Visit
		Visit 1 Screening/ Baseline/ Lens Fitting	Visit 2 Dispense Lens 1	Visit 3 Week 1 Follow-up Lens 1	Visit 4 Week 2 Follow- up Lens 1	Visit 5 Dispense Lens 2	Visit 6 Week 1 Follow-up Lens 2	Visit 7 Week 2 Follow-up Lens 2/Exit		
Procedure/ Assessment	**Pre-screening**		**Day 1** [Visit 2 must occur after washout with habitual spectacles, 2 (at least 48 hours) - 4 days after the end of Visit 1]	(7 -0/+1 days after Visit 2)	(7 -0/+1 days after Visit 3)	**Day 1** [Visit 5 must occur after washout with habitual spectacles, 2 (at least 48 hours) - 4 days after the end of Visit 4]	(7 -0/+1 days after Visit 5)	(7 -0/+1 days after Visit 6)		
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								

		Fitting Lens 1 (Fit Period 1) and Fitting Lens 2 (Fit Period 2)	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unscheduled Visit
		Visit 1 Screening/ Baseline/ Lens Fitting	Visit 2 Dispense Lens 1	Visit 3 Week 1 Follow-up Lens 1	Visit 4 Week 2 Follow- up Lens 1	Visit 5 Dispense Lens 2	Visit 6 Week 1 Follow-up Lens 2	Visit 7 Week 2 Follow-up Lens 2/Exit		
Procedure/ Assessment	**Pre-screening**		**Day 1** [Visit 2 must occur after washout with habitual spectacles, 2 (at least 48 hours) - 4 days after the end of Visit 1]	(7 -0/+1 days after Visit 2)	(7 -0/+1 days after Visit 3)	**Day 1** [Visit 5 must occur after washout with habitual spectacles, 2 (at least 48 hours) - 4 days after the end of Visit 4]	(7 -0/+1 days after Visit 5)	(7 -0/+1 days after Visit 6)		
[redacted]	[redacted]	[redacted]								
[redacted]		[redacted]								
Keratometry* (OD, OS)		X								
[redacted]		[redacted]								
VA w/ habitual correction (OD, OS, logMAR distance and near)*		X						X	X	(X)
Manifest refraction*		X	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

		Fitting Lens 1 (Fit Period 1) and Fitting Lens 2 (Fit Period 2)	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unscheduled Visit
		Visit 1 Screening/ Baseline/ Lens Fitting	Visit 2 Dispense Lens 1	Visit 3 Week 1 Follow-up Lens 1	Visit 4 Week 2 Follow- up Lens 1	Visit 5 Dispense Lens 2	Visit 6 Week 1 Follow-up Lens 2	Visit 7 Week 2 Follow-up Lens 2/Exit		
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[redacted]										
Biomicroscopy		X	X	X	X	X	X	X	X	X
Randomization		X								
[redacted]		[redacted]								

		Fitting Lens 1 (Fit Period 1) and Fitting Lens 2 (Fit Period 2)	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unscheduled Visit
		Visit 1 Screening/ Baseline/ Lens Fitting	Visit 2 Dispense Lens 1	Visit 3 Week 1 Follow-up Lens 1	Visit 4 Week 2 Follow- up Lens 1	Visit 5 Dispense Lens 2	Visit 6 Week 1 Follow-up Lens 2	Visit 7 Week 2 Follow-up Lens 2/Exit		
Procedure/ Assessment	**Pre-screening**		**Day 1** [Visit 2 must occur after washout with habitual spectacles, 2 (at least 48 hours) - 4 days after the end of Visit 1]	(7 -0/+1 days after Visit 2)	(7 -0/+1 days after Visit 3)	**Day 1** [Visit 5 must occur after washout with habitual spectacles, 2 (at least 48 hours) - 4 days after the end of Visit 4]	(7 -0/+1 days after Visit 5)	(7 -0/+1 days after Visit 6)		
[redacted]		[redacted]								
[redacted]		[redacted]								
Determine and record study lens power to be dispensed		X								
Dispense study lenses*			X	X		X	X			(X)
[redacted]			X	X (Old & New)	X	X	X (Old & New)	X	(X)	(X)

		Fitting Lens 1 (Fit Period 1) and Fitting Lens 2 (Fit Period 2)	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unscheduled Visit
		Visit 1 Screening/ Baseline/ Lens Fitting	Visit 2 Dispense Lens 1	Visit 3 Week 1 Follow-up Lens 1	Visit 4 Week 2 Follow- up Lens 1	Visit 5 Dispense Lens 2	Visit 6 Week 1 Follow-up Lens 2	Visit 7 Week 2 Follow-up Lens 2/Exit		
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[redacted]										
[redacted]			X	X (Old & New)	X	X	X (Old & New)	X	(X)	(X)
VA (logMAR) with study lenses at • Distance (4 m; OD, OS, OU) [redacted]			X	X (Old & New)	X	X	X (Old & New)	X	(X)	(X)

		Fitting Lens 1 (Fit Period 1) and Fitting Lens 2 (Fit Period 2)	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unscheduled Visit
		Visit 1 Screening/ Baseline/ Lens Fitting	Visit 2 Dispense Lens 1	Visit 3 Week 1 Follow-up Lens 1	Visit 4 Week 2 Follow- up Lens 1	Visit 5 Dispense Lens 2	Visit 6 Week 1 Follow-up Lens 2	Visit 7 Week 2 Follow-up Lens 2/Exit		
Procedure/ Assessment	**Pre-screening**		**Day 1** [Visit 2 must occur after washout with habitual spectacles, 2 (at least 48 hours) - 4 days after the end of Visit 1]	(7 -0/+1 days after Visit 2)	(7 -0/+1 days after Visit 3)	**Day 1** [Visit 5 must occur after washout with habitual spectacles, 2 (at least 48 hours) - 4 days after the end of Visit 4]	(7 -0/+1 days after Visit 5)	(7 -0/+1 days after Visit 6)		
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[redacted]										

		Fitting Lens 1 (Fit Period 1) and Fitting Lens 2 (Fit Period 2)	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unscheduled Visit
		Visit 1 Screening/ Baseline/ Lens Fitting	Visit 2 Dispense Lens 1	Visit 3 Week 1 Follow-up Lens 1	Visit 4 Week 2 Follow- up Lens 1	Visit 5 Dispense Lens 2	Visit 6 Week 1 Follow-up Lens 2	Visit 7 Week 2 Follow-up Lens 2/Exit		
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					(Collect & Review Calendar)			(Collect & Review Calendar)	(Collect & Review Calendar)	
[redacted]			[redacted]	[redacted]		[redacted]	[redacted]			[redacted]
Collect worn study lenses*				X	X		X	X	X	(X)
[redacted]								[redacted]	[redacted]	
AEs		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)	(X)	(X)	(X)	X	X	

[redacted]