Clinical Performance Assessment of Two Silicone Hydrogel Daily Disposable Contact Lenses

STUDY ID:

CLX679-C001

STATISTICAL ANALYSIS PLAN

NCT05725317

Statistical Analysis Plan for CLX679-C001
Title: Clinical Performance Assessment of Two Silicone Hydrogel Daily Disposable Contact Lenses

[redacted]

This version of the Statistical Analysis Plan is based on Version 1.0 of the study protocol.

Executive Summary:

Key Objectives:

The Primary objective of this study is to demonstrate noninferiority (NI) in visual acuity (VA) at distance when wearing [redacted] contact lenses compared to DT1 contact lenses, after approximately 4 days of wear.

Decision Criteria for Study Success:

Success of this study will be based on demonstration of NI in distance VA with [redacted] contact lenses when compared to DTI contact lenses, at Day 4, using a margin of 0.05 on the logMAR scale.

Table of Contents

[redacted]

List of Tables

List of Figures

1 STUDY OBJECTIVES AND DESIGN

1.1 Study Objectives

PRIMARY OBJECTIVE

The primary objective of this study is to demonstrate NI in VA at distance when wearing [redacted] contact lenses compared to DT1 contact lenses, after approximately 4 days of wear.

[redacted]

1.2 Study Description

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

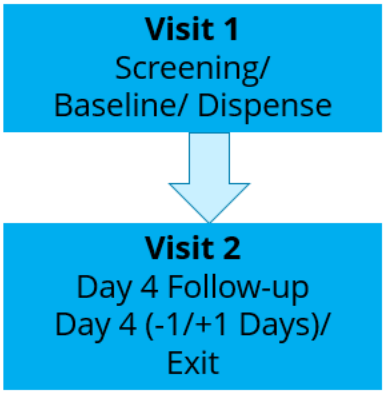
Table 1-1 Study Description Summary

Study Design	Prospective, randomized, [redacted], double-masked, contralateral
Study population	Habitual spherical soft contact lens wearers aged 18 or above, having at least 3 months of contact lens wearing experience, and who wear their habitual contact lenses for at least 5 days per week and at least 10 hours per day. [redacted] Target to complete: 100 [redacted] Planned to enroll: ~110
Number of Sites	~ 7 US
Test Product	[redacted] delefilcon A; LID220365)
Comparator Product	DAILIES TOTAL1® spherical soft contact lenses (DT1; delefilcon A; LID006961)
Planned Duration of	~ 4 days total duration (test and comparator):

Exposure	Test Product: 4 (-1/+1) days Comparator Product: 4 (-1/+1) days
Visits	Visit 1: Screening/Baseline/Dispense [Day 1] Visit 2: Day 4 Follow-up/Exit [Day 4 (-1 /+1)]

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

Qualifying subjects will be randomized in a 1:1 ratio to receive treatment (lens) in contralateral sequence [redacted]

Sequence	EDC/randomization integration system
Sequence 1	LID220365(OD)/LID006961(OS)
Sequence 2	LID006961(OD)/LID220365(OS)

1.4 Masking

This study is double-masked.

[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 analysis 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 first exposure of the study lenses under evaluation in this clinical protocol will be listed as pre-treatment.

For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lens 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.

2.2 Full Analysis Set

The full analysis set (FAS) is the set of all randomized subjects who are exposed to any study lenses [redacted] 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 Deviation and Evaluability Plan (DEP).

3 SUBJECT CHARACTERISTICS AND STUDY CONDUCT SUMMARIES

The following tables will be presented:

- Subject Disposition by Lens Sequence
- Analysis Sets by Lens
- Analysis Sets by Lens Sequence
- Subject Accounting by Lens Sequence
- Demographics by Lens Sequence
- Baseline Characteristics by Lens Sequence [redacted]

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 [redacted] will use the FAS as the primary analysis.

[redacted]

[redacted]

Continuous variables will be summarized using the number of observations, mean, SD, median, minimum, and maximum, as well as confidence intervals (CIs) or confidence limits (CLs) where 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 effectiveness analyses.

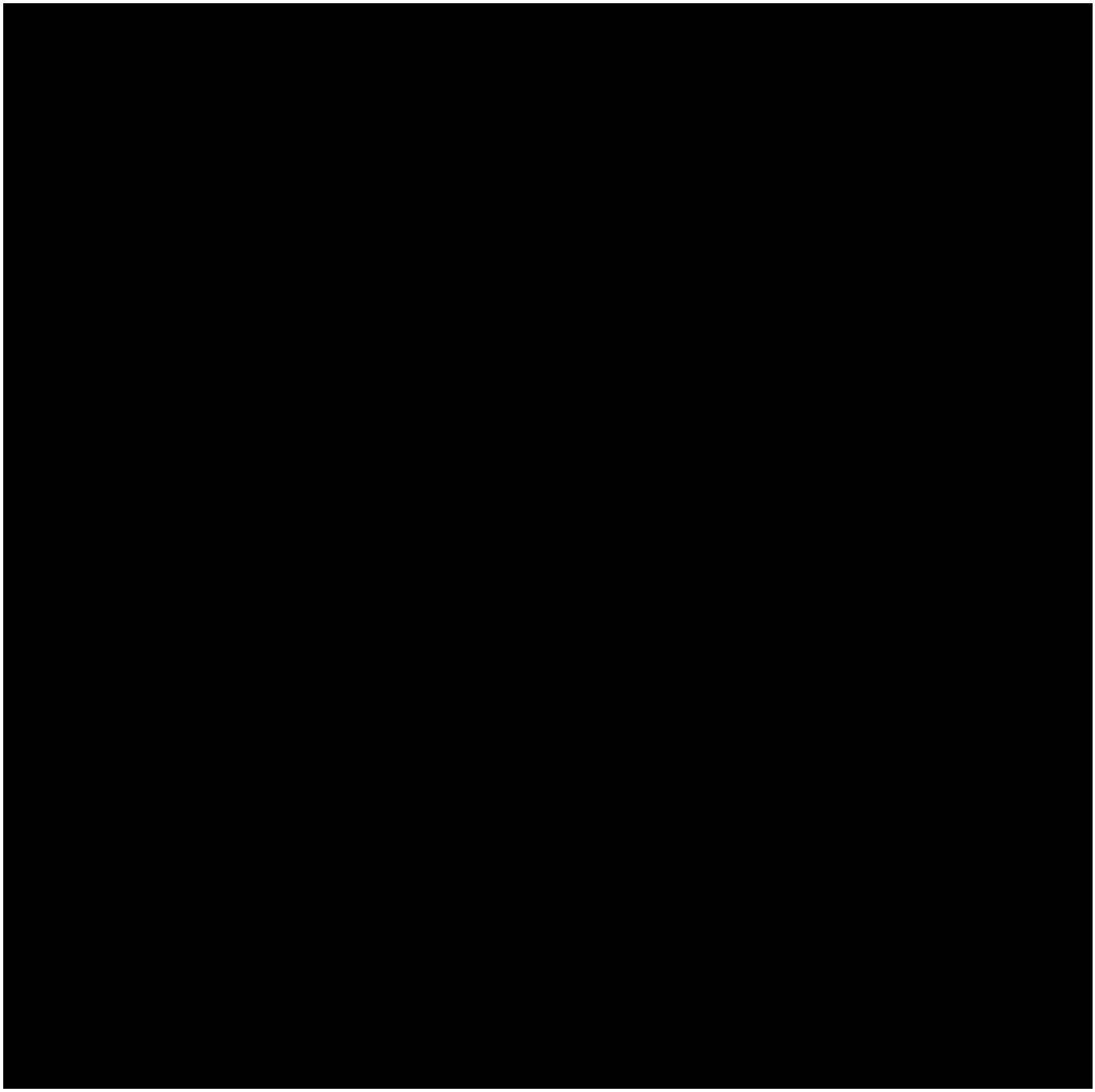
For all planned inferential analyses, alternative models/methods may be considered, for instance, if convergence cannot be achieved.

A listing of select effectiveness data will also be provided.

4.1 Effectiveness Endpoints

Primary Effectiveness Endpoint

The primary endpoint is distance VA with study lenses (dispensed power) at Day 4, collected for each eye in logMAR.



[redacted]

4.2 Effectiveness Hypotheses

Primary Effectiveness

The null and alternative hypotheses are formulated in terms of the predefined margin of 0.05 for noninferiority:

H_0: $\mu_{(T)} - \mu_{(C)} \geq 0.05$

H_a: $\mu_{(T)} - \mu_{(C)} < 0.05$

where $\mu_{(T)}$ and $\mu_{(C)}$ denote the mean distance VA at Day 4 for Cassini and DT1, respectively, on the logMAR scale.

[redacted]

4.3 Statistical Methods for Effectiveness Analyses

4.3.1 Primary Effectiveness Analysis

A mixed effects repeated measures model will be utilized to test these hypotheses. The model will include terms for lens, visit, lens by visit interaction, sequence, and habitual lens brand stratum (DT1, non-DT1). Within-subject correlation due to the contralateral design will also be accounted for in the model. Lens difference[redacted]) and the corresponding one-sided 95% upper confidence limit will be computed at Day 4. Noninferiority in distance VA will be declared if the upper confidence limit is less than 0.05.

[redacted]

[redacted]

4.6 Interim Analysis for Effectiveness

No interim analysis is planned [redacted]

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:

- AEs
- 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 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 the time of their study exit will be accounted for in the reporting.

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

- Pre-treatment AE: an event that occurs after signing informed consent but prior to exposure to study lenses.

- Treatment-emergent: an event that occurs from first exposure to study lenses until the subject exists from the study.

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 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

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

[redacted]

7 SAMPLE SIZE AND POWER CALCULATIONS

[redacted]

Sample size required to demonstrate NI (one-sided α=0.05) for VA [redacted]

Endpoint	**SD Paired Difference (CLX679-E001)**	**N**		**NI or EQV margin**
		80% power	90% power	
Visual Acuity	0.0567 (Overall)	10	14	0.05 logMAR (NI)

[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 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 Day 4 Follow-up / Exit	Early Exit	Unscheduled Visit
	Day 1	Day 4 (-1/+1 Day)	N/A	N/A
Informed Consent	X			
Demographics	X			
Medical History	X	X	X	X
Concomitant Medications	X	X	X	X
Inclusion/Exclusion	X			
Habitual lens (brand, power)	X			
VA with habitual correction (OD, OS, Snellen distance)	X	X	X	(X)
Keratometry	X			
Manifest refraction	X	(X)	(X)	(X)
BCVA with manifest refraction (OD, OS, logMAR distance)	X	(X)	(X)	(X)

Procedure / Assessment	Visit 1 Screening / Baseline / Dispense	Visit 2 Day 4 Follow-up / Exit	Early Exit	Unscheduled Visit
	Day 1	Day 4 (-1/+1 Day)	N/A	N/A
Biomicroscopy	X	X	X	(X)
[redacted]				
Determine and record study lenses power (dispensed power, OD, OS)	X			
VA with study lenses (dispensed power) (OD, OS, logMAR distance)	X	X	(X)	(X)
[redacted]				

Procedure / Assessment	Visit 1 Screening / Baseline / Dispense	Visit 2 Day 4 Follow-up / Exit■	Early Exit	Unscheduled Visit
	Day 1	Day 4 (-1/+1 Day)	N/A	N/A
[redacted]				
Unplanned lens replacement with reason		(X)		(X)
AEs	X	X	X	X
Device deficiencies	X	X	X	X

Procedure / Assessment	Visit 1 Screening / Baseline / Dispense	Visit 2 Day 4 Follow-up / Exit	Early Exit	Unscheduled Visit
	Day 1	Day 4 (-1/+1 Day)	N/A	N/A
Exit Form	(X)	X	X	(X)

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

[redacted]