Comparison of Clinical Performance of Two Monthly Replacement Toric Soft Contact Lenses

STUDY ID

CLV201-P003

STATISTICAL ANALYSIS PLAN

NCT06165627

Statistical Analysis Plan for CLV201-P003
Title: Comparison of Clinical Performance of Two Monthly Replacement Toric Soft Contact Lenses

This version of the Statistical Analysis Plan is based on Version 3.0 of the study protocol.

Executive Summary:

Key Objectives:

The primary objective of this study is to evaluate the clinical performance of TOTAL30™ for Astigmatism (T30fA) soft contact lenses as compared to Biofinity® Toric soft contact lenses.

Decision Criteria for Study Success:

Decision criteria for study success are not applicable for this study.

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[redacted]

1 STUDY OBJECTIVES AND DESIGN

1.1 Study Objectives

PRIMARY OBJECTIVE

The primary objective of this study is to evaluate the clinical performance of T30fA soft contact lenses as compared to Biofinity Toric 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 [redacted], bilateral crossover, double-masked
Study Population	• Volunteer subjects aged 18-45 years of age. • Current habitual toric soft contact lens wearers, with at least 3 months of contact lens wearing experience (excluding any Biofinity Toric soft habitual contact lens wearers, Alcon Toric contact lens wearers, and habitual daily disposable lens wearers). • Wear habitual lenses at least 5 days per week and at least 12 hours per day during the past 3 months. [redacted] • To qualify, subjects must be able to wear contact lenses within a range of sphere & cylinder power and axes (Sphere: -0.50 D to -6.00 D in 0.25 D steps; Cylinder: -0.75 D and -1.25 D; Axis: 10º, 80º, 90º, 100º, 170º, 180º). [redacted] Target to complete: 60 Planned to enroll: ~66
Number of Sites	~5

	United States
Test Product(s)	TOTAL30 for Astigmatism soft contact lenses (T30fA; lehfilcon A)
Comparator Product(s)	CooperVision Biofinity Toric soft contact lenses (Biofinity Toric; comfilcon A) (No Biofinity Toric XR)
Planned Duration of Exposure	~60 days total duration (test and comparator) Test Product: 30 (-1/+3) days Comparator Product: 30 (-1/+3) days
Visits	Visit 1: Screen/Baseline/Lens Fitting Visit 2: Dispense Lens 1 (2 Days [at least 48 hours] – 4* Days) Visit 3: Day 30 Follow-up Lens 1 (Day 30 [-1/+ 3 Days]) Visit 4: Dispense Lens 2 (2 Days [at least 48 hours] – 4* Days) Visit 5: Day 30 Follow-up Lens 2/Exit (Day 30 [-1/+ 3 Days]) * Washout period with habitual spectacles only after Visit 1 and 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 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 crossover sequence as follows:

Sequence 1: T30fA/Biofinity Toric

Sequence 2: Biofinity Toric/T30fA

[redacted]

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 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 lens sequence.

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, [redacted]]

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 effectiveness endpoint [redacted]. All effectiveness evaluations will use the safety analysis set as the primary analysis set.

Continuous variables will be summarized using the number of observations, mean, standard deviation (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.

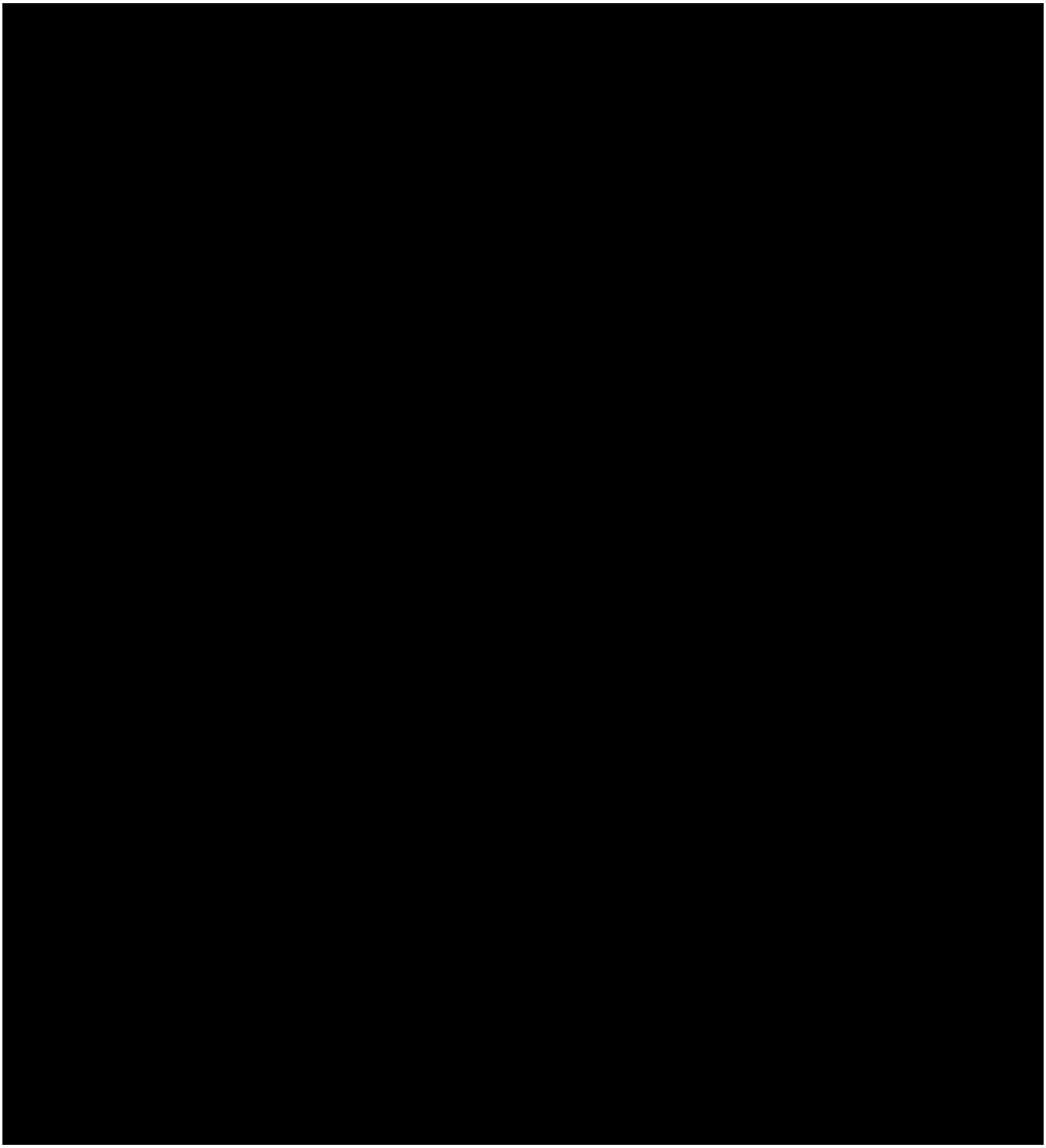
All data obtained in evaluable subjects/eyes will be included in the analysis. No imputation for missing values will be carried out for effectiveness analyses.

A listing of select effectiveness data will also be provided.

4.1 Effectiveness Endpoints

Primary Effectiveness Endpoint

The primary effectiveness endpoint is distance visual acuity (VA) with study lenses at Day 30, collected 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

4.3.1 Primary Effectiveness Analyses

Descriptive statistics of distance VA with study lenses at Day 30 will be provided as number of observations, mean, SD, median, minimum, and maximum, in logMAR.

[redacted]

4.4 Multiplicity Strategy

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

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

- AEs
- Biomicroscopy Findings
    - Limbal hyperemia
    - Bulbar hyperemia
    - Corneal staining
    - Conjunctival staining
    - Palpebral conjunctival observations
    - Conjunctival compression/indention
    - Corneal epithelial edema
    - Corneal stromal edema
    - Corneal vascularization
    - Corneal infiltrates
    - Chemosis
    - 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 4 for Period 2. Safety variables will besummarized 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 of 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 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 Pretreatment Adverse Events
- Listing of All Nonocular Pretreatment 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.

[redacted]

8 REFERENCES

Not applicable.

10 APPENDIX

Table 10-1 Schedule of Study Procedures and Assessments

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screen/Baseline/ Lens Fitting	**Visit 2 Dispense Lens 1**	**Visit 3 Day 30 Follow-up Lens 1**	**Visit 4 Dispense Lens 2**	**Visit 5 Day 30 Follow-up Lens 2/Exit**	**Unscheduled visit**	**Early Exit**
Procedure/Assessment		**Day 1 [2 Days (at least 48 hours)-4 Days Washout period with habitual spectacles only after Visit 1]**	**Day 30 (-1/+3) Days**	**Day 1 [2 Days (at least 48 hours)-4 Days Washout period with habitual spectacles only after Visit 3]**	**Day 30 (-1/+3) Days**	**N/A**	**N/A**
Informed Consent	X						
Demographics	X						
Medical History	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X
Habitual lens information (brand, lens power*, lens care*)	X						
VA with habitual correction (spectacles or contact lenses) (OD, OS, Snellen distance)*	X				X	(X)	X
Keratometry (OD, OS)*	X						
Manifest refraction*	X	(X)	(X)	(X)	(X)	(X)	(X)
BCVA* (OD, OS, logMAR distance with manifest refraction)	X	(X)	(X)	(X)	(X)	(X)	(X)
Biomicroscopy	X	X	X	X	X	X	X

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screen/Baseline/ Lens Fitting	**Visit 2 Dispense Lens 1**	**Visit 3 Day 30 Follow-up Lens 1**	**Visit 4 Dispense Lens 2**	**Visit 5 Day 30 Follow-up Lens 2/Exit**	**Unscheduled visit**	**Early Exit**
Procedure/Assessment		**Day 1 [2 Days (at least 48 hours)-4 Days Washout period with habitual spectacles only after Visit 1]**	**Day 30 (-1/+3) Days**	**Day 1 [2 Days (at least 48 hours)-4 Days Washout period with habitual spectacles only after Visit 3]**	**Day 30 (-1/+3) Days**	**N/A**	**N/A**
[redacted]							
Inclusion/Exclusion	X						
Lens Fitting (Test and Comparator) fitting and evaluation* (logMAR VA and lens fitting assessments)	X						
Determine study lens power parameters*	X						
Randomization	X						
Determine final study lens power parameters to be dispensed		X		X			
Dispense study lenses*		X		X			
[redacted]							

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screen/Baseline/ Lens Fitting	**Visit 2 Dispense Lens 1**	**Visit 3 Day 30 Follow-up Lens 1**	**Visit 4 Dispense Lens 2**	**Visit 5 Day 30 Follow-up Lens 2/Exit**	**Unscheduled visit**	**Early Exit**
Procedure/Assessment		**Day 1 [2 Days (at least 48 hours)-4 Days Washout period with habitual spectacles only after Visit 1]**	**Day 30 (-1/+3) Days**	**Day 1 [2 Days (at least 48 hours)-4 Days Washout period with habitual spectacles only after Visit 3]**	**Day 30 (-1/+3) Days**	**N/A**	**N/A**
[redacted]							
VA w/study lenses (OD, OS, logMAR distance)		X	X	X	X	(X)	(X)

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screen/Baseline/ Lens Fitting	Visit 2 Dispense Lens 1	Visit 3 Day 30 Follow-up Lens 1	Visit 4 Dispense Lens 2	Visit 5 Day 30 Follow-up Lens 2/Exit	Unscheduled visit	Early Exit
Procedure/Assessment		Day 1 [2 Days (at least 48 hours)-4 Days Washout period with habitual spectacles only after Visit 1]	Day 30 (-1/+3) Days	Day 1 [2 Days (at least 48 hours)-4 Days Washout period with habitual spectacles only after Visit 3]	Day 30 (-1/+3) Days	N/A	N/A

[redacted]

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screen/Baseline/ Lens Fitting	**Visit 2 Dispense Lens 1**	**Visit 3 Day 30 Follow-up Lens 1**	**Visit 4 Dispense Lens 2**	**Visit 5 Day 30 Follow-up Lens 2/Exit**	**Unscheduled visit**	**Early Exit**
Procedure/Assessment		**Day 1 [2 Days (at least 48 hours)-4 Days Washout period with habitual spectacles only after Visit 1]**	**Day 30 (-1/+3) Days**	**Day 1 [2 Days (at least 48 hours)-4 Days Washout period with habitual spectacles only after Visit 3]**	**Day 30 (-1/+3) Days**	**N/A**	**N/A**
Lens Wear Calendar *		Dispense	Collect	Dispense	Collect		Collect
Collect Worn Lenses *			X		X	(X)	X
[redacted]							
Adverse Events	X	X	X	X	X	X	X
Device deficiencies	X	X	X	X	X	X	X
Exit Form	(X)	(X)	(X)	(X)	X		X

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

* Source only and transferred to the sponsor upon request

[redacted]