Short Title:

Statistical Analysis Plan
CLD523-E001 /
NCT03459131

Full Title:

Statistical Analysis Plan
CLD523-E001

Protocol Title:	Clinical Evaluation of Two Monthly Contact Lenses
Project Number:	A03261
Protocol TDOC Number:	TDOC-0054838
Author:	[redacted]
	[redacted]
Template Version:	Version 1.0
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 Objective:

The primary objective is to explore overall vision with Biofinity® Energys™ as compared to BIOFINITY lenses after 1 week of wear.

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 is to explore overall vision with BIOFINITY ENERGYS as compared to BIOFINITY lenses after 1 week of wear.

SECONDARY OBJECTIVE

The secondary objective is to evaluate the difference between over-refraction of BIOFINITY ENERGYS as compared to BIOFINITY.

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 to 35 with normal eyes (other than correction for refractive error), currently wearing BIOFINITY (or private label) sphere soft contact lenses on a daily wear basis. Subjects should have at least 3 months of BIOFINITY (or private label) wearing experience, wear these lenses at least 5 days per week and at least 8 hours per day, use digital devices at least 4 hours per day at least 5 days per week, and require contact lenses in a power range from +6.00 to -10.00 DS. Target to complete: 10; Planned to enroll: ~16
Number of Sites	1 US
Test Product	CooperVision® Biofinity® Energys™ soft contact lenses (BIOFINITY ENERGYS)
Control Product	CooperVision® Biofinity® soft contact lenses (BIOFINITY)
Duration of Treatment	Up to 18 days total duration Test Product: 7 days (± 2 days) Control Product: 7 days (± 2 days)
Visits	Visit 1 (Day 0) – Baseline/Fitting Visit 2 (0-7 Days from Visit 1) – Dispense Pair 1

	Visit 3 (7 ± 2 Days from Visit 2) – [Follow-up visit for Pair 1 and Dispensing visit for Pair 2] Visit 4 (7 ± 2 Days from Visit 3) – [Follow-up visit for Pair 2 / Exit]

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 iMedidata Balance.

Subjects will be randomized in a 1:1 manner to receive treatment in crossover sequence, BIOFINITY ENERGYS then BIOFINITY, or BIOFINITY then BIOFINITY ENERGYS, respectively.

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

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 Setby Lens
- Analysis Set by Lens Sequence
- Subject Accounting by Lens Sequence
- Demographics Characteristics by Lens Sequence
- Baseline Characteristics by Lens Sequence

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 one primary endpoint, one secondary endpoint [redacted]. The Safety Analysis Set will serve as the set for all effectiveness analyses.

Continuous variables will be summarized using the number of observations, mean, standard deviation, median, minimum and maximum. Categorical variables will be summarized using counts 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 analysis.

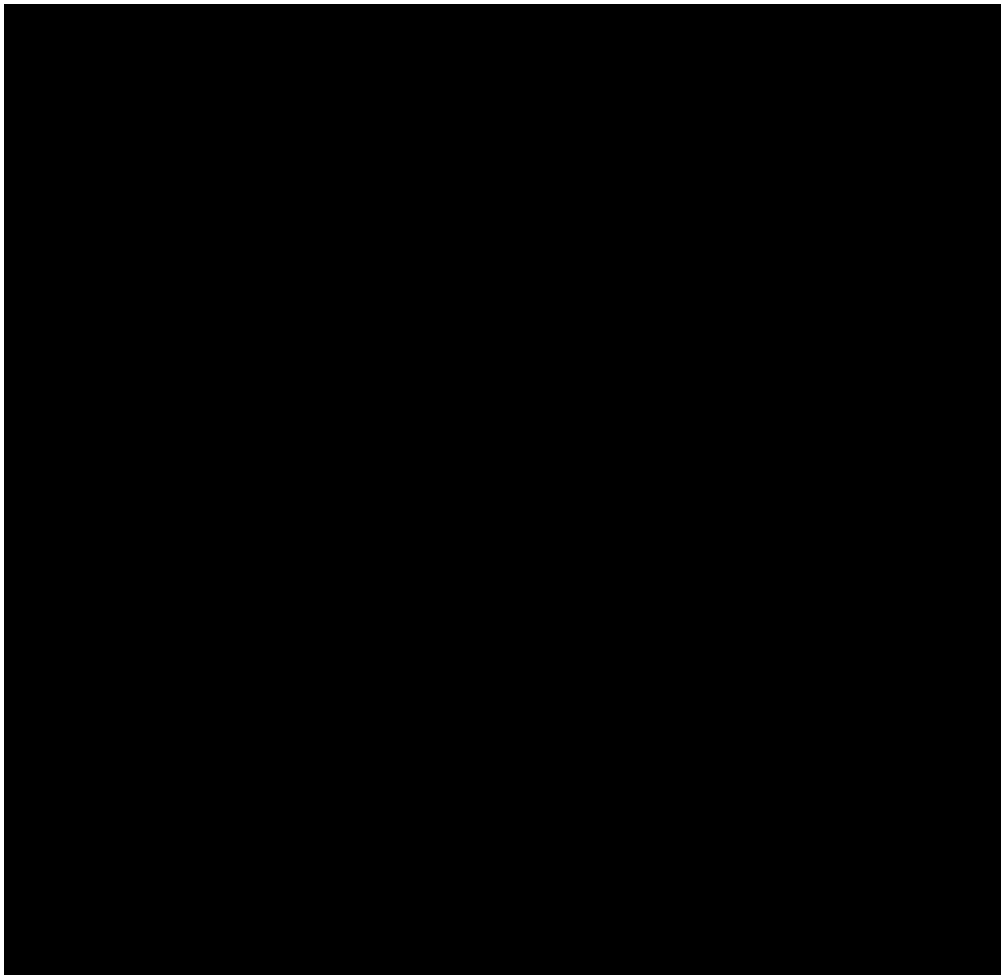
4.1 Effectiveness Endpoints

Primary Endpoint

The primary endpoint is subjective rating of overall vision after 1 week of wear, collected binocularly on a scale of 1 (Poor) to 10 (Excellent).

Secondary Endpoint

The secondary endpoint is over-refraction, collected in diopters for each eye at Dispense.



4.2 Effectiveness Hypotheses

Primary Effectiveness

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

Secondary Effectiveness

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

[redacted]

4.3 Statistical Methods for Effectiveness Analyses

4.3.1 Primary Effectiveness Analyses

Descriptive statistics for both continuous and categorical (subcategories: 1-2, 3-4, 5-6, 7-8, 0-10) variables will be provided.

4.3.2 Secondary Effectiveness Analyses

Descriptive statistics for both continuous and categorical variables will be provided.

[redacted]

4.4 Multiplicity Strategy

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

4.5 Subgroup Analyses and Effect of Baseline Factors

It is not expected that demographic or baseline characteristics will have an impact on the study results in this study. No subgroup analyses are planned.

4.6 Interim Analysis for Efficacy

No interim analyses are planned for this study.

5 Safety Analysis Strategy

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 on Visit 2 (or Visit 1 if both visits occur on the same date). Safety variables will be summarized descriptively.

5.3.1 Adverse Events

The applicable definition of an Adverse Event 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 study lenses. The period for treatment-emergent AE analysis starts from exposure to study lenses until the subject completes or is discontinued from the study. Each AE will be summarized under the exposed lens based upon the event onset date/time, up until the start of the next lens in the crossover sequence.

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

5.3.2 Biomicroscopy Findings/Slit Lamp Examination

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 Increased Severity by 1 Grade in Biomicroscopy Findings
- Listing of Subjects With Increased Severity by 2 or More Grades in Biomicroscopy Findings
- Listings 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 pilot and 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. This version of the Statistical Analysis Plan is based on Version 1.0 of the study protocol.

10 Appendix

Table 10–1 Overview of Study Plan

Procedure/ Assessment	Pre-screening	Visit 1	Visit 2 0-7 days from V1	Visit 3 7 (±2) days from V2		Visit 4 7 (±2) days from V3	Unscheduled Visit	Early Exit
		Baseline / Fitting	Dispense Pair 1	Follow-up Pair 1	Dispense Pair 2	Follow-up Pair 2 / Exit		
Digital Use Time	✓*			✓		✓	✓	✓
Informed Consent		✓						
Demographics		✓						
Medical History		✓	✓	✓		✓	✓	✓
Concomitant Medications		✓	(✓)	(✓)		(✓)	(✓)	(✓)
Inclusion/Exclusion		✓						
Habitual lens* (brand, power) / Lens care* (brand) / Re-wetting drops* (Brand / usage)		✓						
Manifest refraction*		✓	(✓)	(✓)		(✓)	(✓)	(✓)
BCVA (OD, OS, Snellen distance with manifest refraction) *		✓	(✓)	(✓)		(✓)	(✓)	(✓)
Biomicroscopy		✓	✓	✓		✓	✓	✓
Dispense study lenses / Rx			✓		✓			
Over-refraction (OD, OS)			✓		✓			
VA w/ study lenses (OD, OS, OU, Snellen distance,)			✓	✓	✓	✓	(✓)	✓
[redacted]								

Procedure/ Assessment	**Pre-screening**	**Visit 1**	**Visit 2** 0-7 days from V1	**Visit 3** 7 (±2) days from V2		**Visit 4** 7 (±2) days from V3	**Unscheduled Visit**	**Early Exit**
		Baseline / Fitting	**Dispense Pair 1**	**Follow-up Pair 1**	**Dispense Pair 2**	**Follow-up Pair 2 / Exit**		
AEs		✓	✓	✓		✓	✓	✓
Device deficiencies		✓	✓	✓		✓	✓	✓
Exit Form		(✓)	(✓)	(✓)		(✓)	(✓)	✓

(✓) assessment performed as necessary, eg, decrease of VA by 2 lines or more with investigational product (IP)
* Source only

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
03/01/2018 16:21:48	[redacted]	[redacted]
03/01/2018 16:26:07	[redacted]	[redacted]
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