Short Title:

Statistical Analysis Plan
CLE383-P003 / NCT04527978

Full Title:

Statistical Analysis Plan
CLE383-P003

Protocol Title: Clinical Comparison of 2 Daily Disposable Contact Lenses – Pilot Study 1

[redacted]

Protocol TDOC Number: TDOC-0057752

[redacted]

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 of this study is to evaluate the overall performance of PRECISION1™ (verofilcon A) Soft Contact Lenses (PRECISION1) when compared to Bausch + Lomb Biotrue® ONEday (Biotrue ONEday).

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 the overall performance of PRECISION1 contact lenses when compared to Biotrue ONEday.

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, parallel group, crossover, double-masked, [redacted]
Study Population	Volunteer subjects aged 18 or over who are habitual spherical soft contact lens wearers (excluding current/previous PRECISION1, Biotrue ONEday and DAILIES TOTAL1® 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 10 hours per day. [redacted] Target to complete: 52 [redacted] Planned to enroll: ~72
Number of Sites	~4 US
Test Product	PRECISION1 (verofilcon A) Soft Contact Lenses (PRECISION1)
Control Product	Bausch + Lomb Biotrue® ONEday (Biotrue ONEday)
Duration of Treatment	~ 16 days total duration (test and control) Test Product: ~ 8 days Control Product: ~ 8 days

Visits	Visit 1 (Day 0) – Screening/Baseline/Dispense Lens 1 Visit 2 [Day 8 (-0/+3 Days)] – Week 1 Follow-up Lens 1/Dispense Lens 2 Visit 3 [Day 8 (-0/+3 Days)] – Week 1 Follow-up Lens 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 the Electronic Data Capture (EDC)/randomization integration system.

[redacted]

1.4 Masking

The study is double-masked.

[redacted]

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

[redacted]

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 Characteristics by Lens Sequence
- Baseline Demographics 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

[redacted]

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

4.1 Effectiveness Endpoints

Primary Endpoint

The primary endpoint is distance visual acuity (VA) with study lenses, collected in logMAR, for each eye.

[redacted]

[redacted]

- [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
- [redacted]
- [redacted]
  - [redacted]
  - [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

4.2 Effectiveness Hypotheses

Primary Effectiveness

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

[redacted]

[redacted]

4.3 Statistical Methods for Effectiveness Analyses

4.3.1 Primary Effectiveness Analyses

Descriptive statistics will be presented by lens [redacted]

[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

- 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, Visit 1 for Period 1 and Visit 2 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 when a subject exits the study will be accounted for in the reporting.

[redacted]

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

[redacted]

[redacted]

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 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 Sample Size and Power Calculations

No formal sample size calculation is provided given the descriptive and pilot nature of the study.

7 References

Not Applicable.

8 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.

9 Appendix

Table 9–1 Overview of Study Plan

Procedure / Assessment	[redacted]	**Visit 1** Screening/Baseline/ Dispense Lens 1 [redacted]	**Visit 2** Week 1 Follow-up Lens 1 ‡ / Dispense Lens 2	**Visit 3** Week 1 Follow-up Lens 2 ‡ / Exit	**Unscheduled Visit / Early Exit**
		[redacted]	8 -0/+3 days after Visit 1 [redacted]	8 -0/+3 days after Visit 2	**N/A**
Informed Consent	-	✓	-	-	-
Demographics	-	✓	-	-	-
Medical History	-	✓	✓	✓	✓
Concomitant Medications	-	✓	✓	✓	✓
Inclusion/Exclusion	-	✓	-	-	-
[redacted]					
[redacted]					
[redacted]					
[redacted]					
Biomicroscopy	-	✓	✓	✓	✓
[redacted]					
[redacted]					
[redacted]					
Randomize	-	✓	-	-	-
Dispense (provide) study lenses	-	✓	✓	-	(✓)

VA (logMAR distance) with study lenses, OD, OS	-	-	✓	✓	-
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
AEs	-	✓	✓	✓	✓
Device Deficiencies	-	✓	✓	✓	✓
Exit Form	-	(✓)	(✓)	(✓)	(✓)

[redacted]

‡ subjects will be required to wear the study lenses for 10 (-2/+6) hours at the follow-up visits;

[redacted]