Short Title:

Statistical Analysis Plan CLE383-C005

Full Title:

Statistical Analysis Plan - US CLE383-C005 / NCT03305770

Protocol Title: DD T2 Daily Disposable Registration Trial

Project Number: CLE383-C005

Reference Number:

Protocol TDOC Number: TDOC-0054027

Author: [redacted]

[redacted]

Template Version: Version 4.0, approved 16MAR2015

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 Objectives:

The primary objective is to demonstrate effectiveness and safety of the Daily Disposable (DD) T2 soft contact lens when worn for daily disposable wear as compared to DAILIES TOTAL1® (DT1) soft contact lens.

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 demonstrate effectiveness and safety of the DD T2 soft contact lens when worn for daily disposable wear as compared to DT1 soft contact lens.

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] controlled, double-masked, parallel-group
Study Population	Volunteer subjects aged 18 or over who are soft contact lens wearers, excluding DT1 habitual 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 8 hours per day. Subjects must require contact lenses in a power range from -1.00 to -6.00 DS. [redacted] Target to complete: 90 subjects (60:30;Test:Control); Planned to enroll: ~99 subjects (66:33; Test:Control)
Number of Sites	~6 (US)
Test Product	DD T2 soft contact lenses
Control Product	DT1 (delefilcon A) daily disposable soft contact lenses
Duration of Treatment	Approximately 3 months
Visits	Visit 1: Baseline/ Screening Visit 2: Dispense (up to 4 days after lens order) Visit 3: Week 1 follow-up (7 -1/+2 days) Visit 4: Week 2 follow-up (15 -1/+3 days) Visit 5: 1-month follow-up (30 -2/+5 days) Visit 6: 2-month follow-up (60 -2/+5 days) Visit 7: 3-month follow-up/Exit (95 -2/+5 days)

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 assignment. Randomization will be implemented in iMedidata BALANCE.

Subjects will be randomized in a 2:1 ratio to receive either DD T2 or DT1 soft contact lenses, respectively. [redacted]

[redacted]

Randomization schedule will be blocked to ensure a balance (2:1) in lens allocation within sites.

1.4 Masking

This study is double-masked.

The following individuals associated with the study will be considered unmasked: unmasked study coordinator(s), lead clinical site manager, clinical site manager, unmasked data manager(s), Interactive Response Technology manager, and randomization specialist.

1.5 Interim Analysis

No interim analyses are planned for this study.

2 Analysis Sets

2.1 All Enrolled

All subjects who have signed the informed consent for the study will be included in the All Enrolled analysis set.

2.2 Enrolled Dispensed

Enrolled Dispensed is a subset of All Enrolled subjects/eyes which have been exposed to study lenses. Lenses from the fitting set used for power determination are not considered study lenses in this context.

2.3 Enrolled Not Dispensed

Enrolled Not Dispensed is a subset of All Enrolled subjects/eyes which have not been exposed to study lenses. Lenses from the fitting set used for power determination are not considered study lenses in this context.

2.4 Completed

The Completed analysis set consists of Enrolled Dispensed subjects/eyes completing the study.

2.5 Discontinued

The Discontinued analysis set consists of Enrolled Dispensed subjects/eyes not completing the study.

3 Subject Characteristics and Study Conduct Summaries

Demographic information (age, sex, ethnicity, and race), [redacted], and habitual lens information will be presented by lens group and overall for the All Enrolled set.

[redacted]

The following tables and listings for study conduct summaries will be presented:

- Accountability by Eyes Enrolled in the Study and Distribution by Status
- Listing of Lens Assignment by Investigator
- Discontinued Subjects Tabulated by Completed Visits and Reason for Discontinuation with Incidence Rates
- Listing of Subjects Discontinued from Study
- Listing of Out-of-Window Visits

4 Effectiveness Analysis Strategy

This study defines one primary endpoint [redacted]. Unless otherwise specified, separate summary tables will be prepared for the Completed and the Discontinued sets with the following distinction:

- Completed Control (eyes/subjects)
- Completed Test (eyes/subjects)
- Discontinued Control (eyes/subjects)
- Discontinued Test (eyes/subjects)

[redacted]

[redacted]

4.1 Effectiveness Endpoints

Primary Endpoint

The primary endpoint is distance visual acuity (VA) with study lenses, collected in Snellen, for each eye. Conversion will be made to 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]

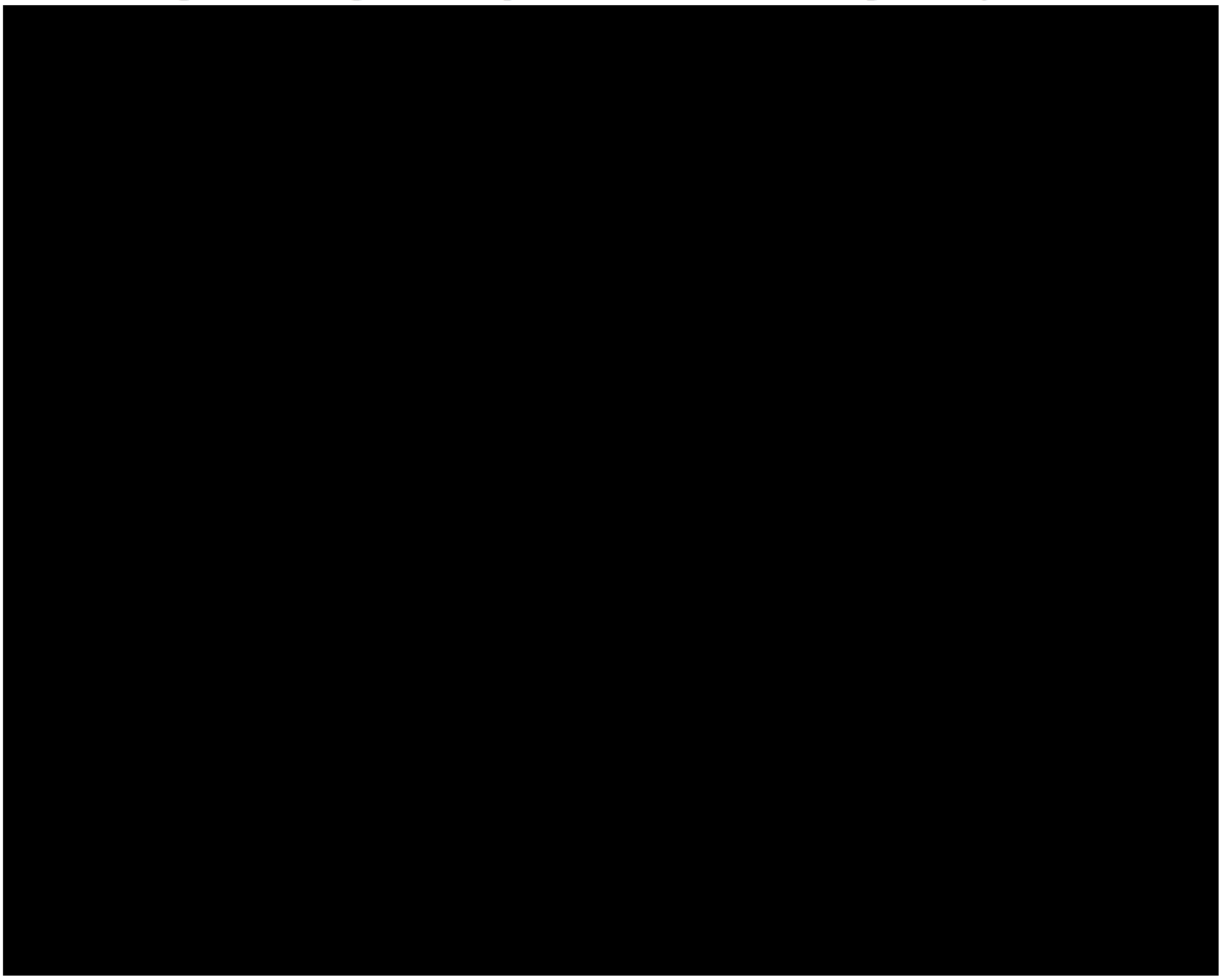
4.3 Statistical Methods for Effectiveness Analyses

4.3.1 Primary Effectiveness Analyses

Summary statistics will be provided at each visit (Dispense, Week 1, Week 2, 1-month, 2-month, 3-month, and all unscheduled visits combined). Descriptive summary statistics will be displayed with counts and percentages on the Snellen categories, and n, mean, standard deviation, median, minimum, and maximum for the converted logMAR values.

In addition, the following will be presented:

- Shift table comparing VA at dispense vs. subsequent visits
- Frequency and percent for VA of 20/30 or better, final VA within 1 line of Dispense, final VA worse than 1 line of Dispense
- Listing for VA changes from Dispense of 2 or more lines during the study



[redacted]

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 Effectiveness

There are no plans to conduct an interim analysis and no criteria by which the study would be terminated early based upon statistical determination.

5 Safety Analysis Strategy

5.1 Safety Endpoints

The safety endpoints are

- Adverse events (AE)
- Biomicroscopy Findings/Slit Lamp Examination
    - 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

Unless otherwise specified, separate summary tables will be prepared for the Completed and the Discontinued sets with the following distinction:

- Completed Control (eyes/subjects)
- Completed Test (eyes/subjects)
- Discontinued Control (eyes/subjects)
- Discontinued Test (eyes/subjects)

Subjects/eyes will be categorized under the actual lens exposed.

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 the study lens (not including fitting lenses). The period for treatment-emergent AE analysis starts from exposure to study lens until the subject completes or is discontinued from the study.

Descriptive summaries (counts and percentages) for ocular and nonocular AEs will be presented by Medical Dictionary for Regulatory Activities (MedDRA) Preferred Terms (PT). Serious AEs and significant nonserious ocular AEs will be noted. Additionally, relationship to lens will be identified in all AE tables. Unit of presentation for ocular AEs will be eye and nonocular AEs will be subject.

Individual subject listings will be provided for both pre-treatment and treatment-emergent AEs, where any AE leading to study discontinuation will be indicated.

5.3.2 Biomicroscopy Findings/Slit Lamp Examination

Biomicroscopy assessment will be performed at all study visits, including Visit 1 to 7 and unscheduled visits. The reporting unit for each biomicroscopy finding will be eye.

A summary of grade category counts and percentages will be presented for each parameter at each scheduled visit and all unscheduled visits combined. [redacted]

5.3.3 Device Deficiencies

A frequency table showing counts for each treatment-emergent Device Deficiency category will be presented. In addition, listings for treatment-emergent and pre-treatment device deficiencies will be provided.

[redacted]

[redacted]

8 References

1. Premarket Notification (510(k)) Guidance Document for Daily Wear Contact Lenses
2. ISO 11980:2012 Ophthalmic optics - Contact lenses and contact lens care products - Guidance for clinical investigations

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, Baseline/ Screening (Day 0)	Visit 2, Dispense study lenses	Visit 3, Week 1 follow-up	Visit 4, Week 2 follow-up	Visit 5, 1-month follow-up	Visit 6, 2-month follow-up	Visit 7, 3-month follow-up/ exit	USV
		Up to 4 days after lens order (Day 1 of lens wear)	7 days (-1/+2 days) from the Dispense visit	15 days (-1/+3 days) from the Dispense visit	30 days (-2 days /+5 days) from the Dispense visit	60 days (-2 days /+5 days) from the Dispense visit	95 days (-2 days /+5 days) from the Dispense visit	
Informed Consent	✓	-	-	-	-	-	-	-
Demographics	✓	-	-	-	-	-	-	-
Medical History	✓	-	-	-	-	-	-	-
Concomitant Medications	✓	✓	✓	✓	✓	✓	✓	(✓)
Inclusion/ Exclusion	✓	-	-	-	-	-	-	-
[redacted]								
VA w/ habitual correction (Snellen distance)	✓	✓	-	-	-	-	✓	(✓)
[redacted]								
Biomicroscopy	✓	✓	✓	✓	✓	✓	✓	(✓)
[redacted]								
Order subject's study lenses	✓	-	-	-	-	-	-	-

Procedure/ Assessment	**Visit 1, Baseline/ Screening (Day 0)**	**Visit 2, Dispense study lenses**	**Visit 3, Week 1 follow-up**	**Visit 4, Week 2 follow-up**	**Visit 5, 1-month follow-up**	**Visit 6, 2-month follow-up**	**Visit 7, 3-month follow-up/ exit**	**USV**
		Up to 4 days after lens order (Day 1 of lens wear)	7 days (-1/+2 days) from the Dispense visit	15 days (-1/+3 days) from the Dispense visit	30 days (-2 days /+5 days) from the Dispense visit	60 days (-2 days /+5 days) from the Dispense visit	95 days (-2 days /+5 days) from the Dispense visit	
Dispense or provision of study lenses	-	✓	-	-	✓	✓	-	(✓)
VA w/ study lenses (Snellen distance)	✓	✓	✓	✓	✓	✓	✓	(✓)
[redacted]								

Procedure/ Assessment	**Visit 1, Baseline/ Screening (Day 0)**	**Visit 2, Dispense study lenses**	**Visit 3, Week 1 follow-up**	**Visit 4, Week 2 follow-up**	**Visit 5, 1-month follow-up**	**Visit 6, 2-month follow-up**	**Visit 7, 3-month follow-up/ exit**	**USV**
		Up to 4 days after lens order (Day 1 of lens wear)	7 days (-1/+2 days) from the Dispense visit	15 days (-1/+3 days) from the Dispense visit	30 days (-2 days /+5 days) from the Dispense visit	60 days (-2 days /+5 days) from the Dispense visit	95 days (-2 days /+5 days) from the Dispense visit	
[redacted]								
AEs	✓	✓	✓	✓	✓	✓	✓	(✓)
Device deficiencies	✓	✓	✓	✓	✓	✓	✓	(✓)
Exit Form	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)

(✓) assessment performed as necessary, eg, decrease of visual acuity by 2 lines or more with investigational products.

USV = Unscheduled Visit

[redacted]

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
09/22/2017 15:55:11	[redacted]	[redacted]
09/22/2017 15:58:03	[redacted]	[redacted]
09/22/2017 19:17:20	[redacted]	[redacted]