Myopia Assessment of Two Manufacturing Processes for Myopia Management Lenses (MAPLE)

Protocol Number: CPRO-1908-001

Sponsor: SightGlass Vision, Inc.

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STATISTICAL ANALYSIS PLAN SUMMARY

STATISTICAL CONSIDERATIONS

1. Statistical Hypotheses

The null and alternative hypotheses for this study are: The null and alternative primary hypotheses for this study are:

H_o: $\mu_T - \mu_C \geq 0.03$ versus H_A: $\mu_T - \mu_C < 0.03$

Here μ indicates the mean change in axial length between baseline and 6 months.

2. Sample Size Determination

The study is sized to ensure an adequate power at an overall alpha level of 0.05 for treatment comparisons in axial length change from baseline at 6 months. Assuming axial length change from baseline has a standard deviation (SD) of approximately 0.31 mm at 12 months[28]. Therefore, it can be assumed that the SD at 6 months (SD_{6m}) is ≤ 0.31 mm. It has also been assumed that there will be no difference in mean AL change between the test and control lens types.

Power	80%
SD at 6m (each eye)	0.095
Between-eye correlation	0.85
SD of DDAL	0.053
True Difference in DDAL	0.00 mm
Equivalent/NI Margin	0.03 mm

Assuming a drop-out rate of 10-20%, a study of 50-60 subjects achieves 98% power to detect non-inferiority using a one-sided t-test when the margin of non-inferiority is 0.03 mm and the true difference between the treatments is 0.00 mm. The data are drawn from a single population with a standard deviation of 0.053 and the significance level (alpha) of the test is 0.050.

3. Populations for Analyses

The study data will be analyzed in one of the following analysis populations:

The **Per-Protocol (PP)** population will include all randomized subjects who follow the protocol without any major deviation(s) that could impact the integrity of the data. Reasons for exclusion from the PP population may include:

- use of the incorrect study spectacles
- poor compliance with the wearing regimen.

The **Safety** population will include all randomized subjects who use any of the study devices. Subjects will be grouped for analysis based on the actual device used.

4. STATISTICAL ANALYSES

4.1 GENERAL APPROACH

The analyses will be performed once all data have been entered into the EDC, cleaned and the database has been locked.

Descriptive summaries will include mean, standard deviation, median, and range for continuous variables and counts and percentages for categorical variables. Two-sided 95% confidence intervals (CIs) will be provided for the means and percentages. For key outcome measures, the difference between each of the test arms versus the control and the 95% CI of the difference will be computed.

All statistical analysis will be performed using SAS® (Version 9.4 or higher, SAS Institute Inc., Cary, NC, USA). Some graphical tools (such as EXCEL, PowerPoint) may be used to generate figures.

4.2 ANALYSIS OF THE STUDY CONDUCT

The number of subjects who are enrolled, discontinue (early discontinuation of treatment or early termination from the study), and complete the study (through 6 months after randomization) will be tabulated.

Reasons for early discontinuation of the treatment or early termination of from the study will be listed and summarized by treatment arm. Any eligibility criteria exceptions and other protocol deviations will also be summarized by treatment arm.

4.3 ANALYSIS OF TREATMENT COMPARABILITY

Demographic and baseline characteristics such as age, gender and race will be summarized for all randomized subjects. Other baseline characteristics such as baseline axial lengths will be summarized for all randomized subjects by treatment.

4.4 ANALYSIS OF THE PRIMARY EFFICACY ENDPOINTS

The main analysis of the primary efficacy outcome measures (i.e., change from baseline in axial length) will be on the PP population.

A mixed effect model including the following terms will be used to analyze the difference in change in axial length between treatments: treatment, order, age, gender, and treatment-by-order interaction as factors, and the baseline axial length as a covariate. Estimates for the mean change from baseline at 6 months will be calculated from the model [i.e., least-squared (LS) means]. The standard error and 95% confidence interval (CI) of the LS mean will be provided. The difference in LS mean change from baseline between the test and the control lens and the corresponding 95% CI will be derived from the model. If the upper limit of the CI is less than the non-inferiority bound of 0.03 mm, then the hypothesis of the test lens being non-inferior to the control lens will be met. Also, the p-values for testing the pairwise differences in LS means against a zero value will be computed based on t-tests.

4.5 Safety Analyses

Adverse events will be tabulated by incidence overall, by device related, maximum severity, and those resulting in study discontinuation. Serious adverse events will be listed. Data summarized as well as additional collected data will be provided in supporting line listings. Ocular assessments such as BCVA, biomicroscopic slit lamp, ophthalmoscopy results and other findings will be summarized descriptively.

4.6 Missing Data

All possible efforts will be made to minimize missing data rate as missing data may potentially bias the outcome of the statistical analyses and the subsequent estimation of the magnitude of the treatment effect. Due to having only one follow-up visit, it would not be appropriate to impute missing data. Therefore, the efficacy analysis will be completed on the PP population.

4.7 Planned Interim Analyses

There will be no interim analyses during this study.