A Multi-Center, Prospective, Randomized, Controlled Clinical Evaluation of the Safety and Effectiveness of the Sight Sciences VISCO™360 Viscosurgical System in Canaloplasty versus Selective Laser Trabeculoplasty in the Reduction of IOP in Primary Open Angle Glaucoma

Protocol Number: SIGHTVISCO-001

Statistical Analysis Plan

Version 1.0

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LIST OF ABBREVIATIONS

AE	Adverse Event
BCVA	Best Corrected Visual Acuity
CIGTS	The Collaborative Initial Glaucoma Treatment Study
IOP	Intraocular Pressure
ISO	International Organization for Standardization
ITT	Intent to Treat
mITT	Modified Intent to Treat
PP	Per Protocol
PRO	Patient Reported Outcomes
SAP	Statistical Analysis Plan
SLT	Selective Laser Trabeculoplasty
SSI	Secondary Surgical Intervention
MD	Visual Field Mean Deviation
PSD	Visual Field Pattern Standard Deviation

1.0 INTRODUCTION

This statistical analysis plan (SAP) describes the statistical methods to be implemented to analyze the data from Protocol SIGHTVISCO-001. Any changes to this plan will be reflected in amendments (to this plan) before the database lock or documented in the clinical study report.

2.0 STUDY OBJECTIVE

The objective of this study is to establish the safety and effectiveness of the Sight Sciences VISCO™360 Viscosurgical System in support of the proposed Indications for Use Statement.

3.0 STUDY DESIGN

This is a multicenter, prospective, single-masked, randomized, controlled trial. Two study groups will be included in the study. The treatment group consists of subjects who undergo canaloplasty with the VISCO™ 360 Viscosurgical System (VISCO360). The control group consists of subjects who undergo Selective Laser Trabeculoplasty (SLT). The clinical examinations and study visit schedules are included in Appendix 1.

A total of approximately **298** subjects will be enrolled and randomized in a 1:1 ratio at up to 10 clinical sites. Only one eye from each eligible subject will be enrolled in the study. If both eyes are eligible, the right eye will be selected for the study.

- VISCO360 Arm: 149 enrolled subjects
- Control Arm: 149 enrolled subjects

Anticipating a **40**% screening failure rate (including baseline IOP failure), up to **497** subjects will undergo screening and baseline exams in order to have at least **298** randomized subjects, and have at least **134** randomized subjects per study group reach the 12-month visit, assuming an annual drop-out rate of 10%.

A minimum enrollment of **10** investigational device subjects per investigator should be sought. No investigator should enroll more than 25% of the total number of investigational device or control subjects. For centers with more than one investigator, the center's total enrollment (investigational or control arm) should not exceed 33% of the total. The randomization of VISCO360 and SLT will be stratified by investigational site and prior history of SLT in the study eye (yes versus no).

Investigational sites for the clinical study will be selected with the goal of obtaining an appropriate balance of gender, minority, and age during the study.

The study will consist of two phases. In the initial phase, 30 subjects will be enrolled and randomized at 3 of the 10 investigational sites. If, among the first 30 randomized subjects, the number of subjects randomized to the VISCO360 is fewer than 20, then an extension request will be submitted to FDA for additional enrollment for the initial phase of the study. When the first 20 subjects randomized to VISCO360 complete the 1-month follow-up examination, safety data will be submitted to the FDA to request approval for expansion to the full population in order to have 298 enrolled and randomized subjects.

4.0 STUDY ENDPOINTS

4.1 Effectiveness Endpoints

4.1.1 Primary Effectiveness Endpoint

The primary effectiveness endpoint is the change in medication-free mean diurnal IOP from baseline at 12 months (i.e. medication-free mean diurnal IOP at 12 months – medication-free mean diurnal IOP at baseline). The medication-free mean diurnal IOP (i.e. average of three medication-free IOP's measured at three different time points) will be calculated for each subject. For each subject, a negative change in mean diurnal IOP value means a reduction; a positive value means an increase.

Criteria for Failure to Respond

The medication-free mean diurnal IOP at 12 months will be imputed for subjects who meet the following criteria:

- IOP persistently below 6mmHg (defined as an intraocular pressure below 6mmHg that is present on two consecutive follow-up visits after the three month visit),
- underwent secondary IOP lowering interventions to control IOP (e.g., laser trabeculoplasty, trabeculectomy, shunt or valve placement, iridotomy/iridectomy) prior to the 12-month visit,
- post-operative introduction of an oral carbonic anhydrase inhibitor,[1]
- no diurnal IOP data collected from the available Month 12 visit,
- underwent other secondary surgical interventions (SSI) that could affect IOP, or
- use of ocular hypotensive medication within 4 weeks of the Month 12 washout visit[2]

[1] Does not include use in the perioperative period

[2] If the study subject fails to remember not to use ocular hypotensive medication for the study eye per the required washout period prior to this visit, they can be reinstructed to washout and return for a 12 month washout IOP visit as long as it falls within the specified visit window.

For subjects who meet any of the criteria above, the medication-free mean diurnal IOP at 12 months will be imputed by the mean washout (i.e. medication-free) diurnal IOP at baseline.

It is expected that the follow-up rate will be better than 90% at 12 months postoperatively. Therefore, the primary analyses for the primary and secondary effectiveness endpoints will be based on the available medication-free mean diurnal IOP data at 12 months with the imputation described above. For sensitivity analyses, imputations of the missing 12-month medication-free diurnal IOP will be performed for the subjects that do not meet the criteria above and are discontinued prior to the 12-month visit (Section **9.4.3**).

The mean of change in medication-free mean diurnal IOP from baseline at 12 months will be compared between the VISCO360 group and control group. The corresponding statistical hypotheses are as follows:

$$H_0: \mu_c - \mu_v = 0 \text{ versus } H_A: \mu_c - \mu_v > 0$$

The μ_v and μ_c are the mean change in medication-free mean diurnal IOP changes from baseline at 12-month for the VISCO360 group and control group, respectively. The VISCO360 group will be concluded to be superior to the control group in reducing the IOP if the null hypothesis (H_0) is rejected based on one-sided significance level of 0.025.

4.1.2 Secondary Effectiveness Endpoint

The secondary effectiveness endpoint is the outcome of achieving ≥ 20% reduction in medication-free mean diurnal IOP from baseline at 12 months. Subjects who meet any of the criteria listed in Section **4.1.1** above will be imputed as non-responders (i.e. failures) for this secondary endpoint. Similarly, the primary analyses for the secondary effectiveness endpoint will be based on the available 12-month medication-free mean diurnal IOP with the imputation described above for the subjects meet the criteria listed in Section **4.1.1**. For subjects that do not meet the criteria listed in Section **4.1.1** and are discontinued prior to the 12-month visits, imputations for their missing 12-month medication-free mean diurnal IOP will be performed as the sensitivity analyses.

The proportion of subjects achieving this effectiveness endpoint (12-month IOP responder rate) will be compared between the VISCO360 group and control group. The corresponding statistical hypotheses are as follows:

$$H_0: p_v - p_c = 0 \text{ versus } H_A: p_v - p_c > 0$$

The p_v and p_c are the 12-month IOP response rates for the VISCO360 group and control group, respectively. The VISCO360 will be concluded to be superior to the control group in reducing IOP if H_0 is rejected based on one-sided significance level of 0.025.

Since the formal statistical conclusion for the secondary effectiveness endpoint will be made if and only if the null hypothesis of the primary effectiveness endpoint is rejected, no adjustment for the significance level will be performed for the secondary effectiveness endpoint.

4.2 Safety Outcomes

The safety outcomes include all intraoperative or postoperative ocular adverse events (AEs) as listed in Section VII of the study protocol, BCVA changes from baseline, results of slit lamp examination, gonioscopy findings, dilated fundus examination findings, and pachymetry.

4.3 Other Clinical Parameters

A focused questionnaire consisting of 18 questions from the CIGTS "Symptom and Health Problem Chart" (11 Visual Function items and 7 Local Eye items) will be administered. For each subject, the total score is calculated for Visual Function Symptom Impact (range from 0 to 55) and for Local Eye Symptom Impact (range from 0 to 35). No labeling claims will be made based on the PRO's.

5.0 SEQUENCE OF PLANNED ANALYSES

5.1 Interim Analyses/FDA Annual Report Submission

No interim effectiveness analyses will be performed prior to the database closure for the endpoint analysis of 12 month IOP outcomes.

As described in Section 3.0, when the first 20 VISCO360 subjects complete the 1-month examination, an interim analysis of the safety data will be performed using all available data. Descriptive statistics (mean, median, standard deviation, minimum, and maximum for the continuous outcomes; counts and percentages for categorical variables) will be used to summarize data for each of the two study treatment groups. No postoperative IOP, non-diurnal or diurnal, will be analyzed or summarized. However, IOP associated adverse events will be reported.

Only safety data will be summarized for the FDA annual report. As will be the case for the expansion request to FDA, no postoperative IOP, non-diurnal or diurnal, will be analyzed or summarized in annual reports. Any adverse events associated with IOP would be included.

5.2 Pre-Market Submission

When all randomized subjects have either completed the 12-month follow-up examination or have discontinued from the study, the data will be analyzed based on this Statistical Analysis Plan for a premarket FDA submission.

5.3 Final Report

When all randomized subjects have either completed the 24-month or later follow-up examination or have discontinued from the study, the data will be analyzed based on this Statistical Analysis Plan.

6.0 SAMPLE SIZE CALCULATION

The sample size for the primary effectiveness endpoint and the corresponding statistical hypotheses described in Section **4.1.1** is based on the following assumptions and criteria.

- The standard deviation of change in mean diurnal IOP from baseline at 12 months is assumed to be 5.0 mmHg. Per Seymennoglu[3], the mean and standard deviation (SD) of the change in IOP from baseline to 12 months was 5.5 mmHg ± 3.8 mmHg for the pseudophakic eyes with SLT, without additional medications, without SLT retreatments, and without any glaucoma-related secondary surgical intervention. Since the study will evaluate the change in the mean diurnal IOP from baseline after washout to 12 months after washout, the SD of the endpoint is expected to be larger than the published SD of 3.8 mmHg. An SD of 5 mmHg is assumed for the study.
- Significance level is 0.025 (one-sided) and statistical power is 90% at a true mean difference of 2 mmHg.
- Two-sample *t*-test will be used.
- A yearly dropout rate of 10% is considered.
- The randomization ratio for the study is 1:1.

Based on the criteria above, the 12-month sample size for the primary effectiveness endpoint and corresponding statistical hypotheses are **133** VISCO360 and **133** control subjects at 12 months. With the yearly dropout rate of 10%, approximately **296** subjects (**148** VISCO360 and **148** controls) should be randomized.

The sample size calculation for the secondary effectiveness endpoint and the corresponding statistical hypotheses described in Section **4.1.2** is based on the following assumptions and criteria:

[3] Göktuğ Seymenoğlu, MD and Esin F. Baser, MD (2015). Efficacy of Selective Laser Trabeculoplasty in Phakic and Pseduphakic Eyes. J. Glaucoma, 2015;24:105–110.

- The 12-month IOP response rates for the control group (p_c) is estimated are estimated to be 0.5. Per Seymennoglu, the 12-month IOP response rate was 0.62 for the pseudophakic eyes with SLT, without additional medications, without SLT retreatments, and without any glaucoma-related secondary surgical intervention. Due to the requirement of medication washout in this study, it is expected that the 12-month response rate for the control group of this study is lower than the published 0.62. Therefore, a 12-month response rate of 0.50 is assumed for the control group.
- Significance level is 0.025 (one-sided) and statistical power is 90% at a difference in the responder rate of 0.2. In other words, the power is 90% if the true p_v (the 12-month response rate of the VISCO360 group) is 0.2 and the true p_c is 0.5.
- Fisher's exact test will be used.
- A yearly dropout rate of 10% is considered.
- The randomization ratio for the study is 1:1.

Based on the criteria above, the 12-month sample size for the secondary effectiveness endpoint and corresponding statistical hypotheses are **134** VISCO360 and **134** control subjects at 12 months. With the yearly dropout rate of 10%, approximately **298** subjects (**149** VISCO360 and **149** controls) should be randomized.

Since the sample size for the secondary effectiveness endpoint is larger than that for the first effectiveness endpoint, approximately **298 randomized subjects** will be required for this study. If a 40% screening failure is considered, approximately **497** subjects should be enrolled and screened.

7.0 ANALYSIS POPULATIONS

7.1 Safety Population

The safety analysis population will contain all subjects who are randomized and for whom VISCO360 or SLT is attempted. Subjects will be grouped according to whether they undergo VISCO360 or SLT and not according to their randomization assignment (as randomized). The subjects who have aborted VISCO360 or SLT procedures will be included in the safety analysis population since the procedure has been performed or attempted.

7.2 Intent to Treat and Modified Intent to Treat Populations

The Intent to Treat (ITT) analysis population will include all subjects randomized. Subjects will be grouped according to their randomization assignment (as randomized) regardless if they actually undergo the assigned procedure. The Modified Intent to Treat (mITT) population is a subset of the ITT population. It consists of the ITT subjects that actually undergo the assigned procedure. The mITT population will be used for the primary analyses of the primary and secondary effectiveness endpoints. The ITT population will be also used for the analyses of the primary and secondary effectiveness endpoints as part of the sensitivity analyses.

7.3 Per Protocol Population

The per-protocol (PP) population is the mITT population that also meets all of the following criteria:

- Subject meets all protocol eligibility criteria.
- Subject has the 12-month examination.
- Subject does not have any major protocol deviations that are established before the data review and database closure.
- Subject that assigned to the VISCO360 study arm receive the 360-degree treatment and subjects assigned to the SLT arm receive a least a 180 degree treatment.

The PP population will be used for the analyses of the primary and secondary effectiveness endpoints as part of the sensitivity analyses.

For the analyses on the primary and secondary effectiveness endpoints based on the mITT or PP populations, the analyses will be based on the available 12-month medication-free mean diurnal IOP with the baseline-imputation for subjects who meet the criteria listed in Section **4.1.1**.

8.0 DATA HANDLING

8.1 General Procedure for Data Summary

Descriptive statistics on continuous variables will include mean, standard deviation, median, minimum, and maximum. Confidence intervals for change from baseline will be included for selected endpoints. Categorical variables will be summarized using frequency counts and percentages. Exact confidence intervals for point estimates may be provided. Statistical testing will be one-sided with a significance level of 0.025 or two-sided significance level of 0.05) unless specify otherwise. Data listings of individual subject data may be provided.

8.2 Definition

8.2.1 Baseline

The baseline values are those that are obtained at the closest visit prior to the surgery. The arithmetic difference between the baseline and a post-baseline (post-operative for this study) are as follows:

Change from baseline = (post-baseline value – baseline value)

Percent change from baseline = Change from baseline ÷ baseline value × 100.

8.2.2 Mean Diurnal IOP

In order to determine the mean diurnal intraocular pressure (IOP) measurements, IOP will be taken at 9:00AM ±1.5 hours, 12:00PM ± 1 hour, and 4:00PM ± 2 hours. Each time IOP is measured, two measurements should be taken and the mean recorded on the case report form unless they differ by more than 2mmHg in which case a third measurement is taken and the median value is recorded. The three IOP measurements should then be averaged to determine the mean diurnal IOP.

8.2.3 Day 0 and Study Day

The Day 0 is the surgery day. The study day is defined as the study date – date of surgery. A positive study day is for a post-surgery date; a negative study day is for a pre-surgery date.

8.2.4 Visit Windows

Visit	Window
Screening	Day -45 to -2
Baseline	Day -15 to -1, after completion of medication washout
Surgery/SLT Procedure	Day 0 (up to -72 hours)
1 Day Postop	Day 1
1 Week Postop	Day 5-9
1 Month Postop	Day 21-35
3 Months Postop	Day 70-98
6 Months Postop	Day 150 –210
12 Months Postop	Day 330 – 420
12 Month Washout	Day 330 – 420, after completion of medication washout
18 Months Postop	Day 510 – 600
24 Months Postop	Day 690 – 780

8.2.5 Washout

For subjects taking hypotensive medications at screening and 12 months after surgery, the minimum wash-out periods are specified in the study protocol.

8.2.6 Age Calculation

Age will be calculated for each subject by (Date of Surgery – Date of Birth + 1) ÷ 365.25 and rounded down to the nearest integer. For subjects enrolled but not undergoing surgery, the age will be calculated by (Date of Screening – Date of Birth + 1) ÷ 365.25 and rounded down to the nearest integer, if necessary.

8.3 Handling of Missing or Incomplete Data

8.3.1 Missing Primary and Secondary Effectiveness Outcomes

For the primary and secondary effectiveness endpoints, the imputed values described in Sections **4.1.1** and **4.1.2** will be performed for the missing endpoints.

8.3.2 Partial Dates

For incomplete dates such as AE or medication start date or stop date, the imputed dates described in the table below will be used.

Imputation Rules for Partial Adverse Event or Concomitant Medication Start and Stop Dates

Date	Missing	Imputation	Exception
Start Date	Day	01	Default to Study Day 0 (day of first injection procedure) if an event starts in the same year and month as Study Day 0
	Day/Month	01Jan	Default to Study Day 0 if an event starts in the same year as Day 0
Stop Date	Day	Last day of the month	Default to the End of Study Date if the imputed event stop date is after the End of Study Date or before start day of the event
	Day/Month	31DEC	

8.3.3 Missing AE Severity or Relationship to Surgical Procedure

The "severe" will be assigned to the missing AE severity level. The "definitely related" will be assigned to the missing AE relationship to the corresponding surgical procedure.

8.3.4 Safety Outcomes

No imputation will be performed for the safety outcomes other than the cases described in Sections **8.3.2** and **8.3.3**.

8.4 Multiplicity Adjustment

The statistical tests for the primary and secondary effectiveness endpoints will be performed by the hierarchical approach (Section **4.1.2**). The interim analyses specified in Section 5.1 are for safety data only. No other multiplicity adjustment will be performed.

9.0 STATISTICAL METHODS

9.1 General Principles of Data of Data Analyses

The primary effectiveness data analyses will be based on the mITT population. The effectiveness analyses based on the ITT and PP populations will also be performed. The safety data will be summarized based on the safety population.

The statistical analyses will be reported using summary tables and figures. Continuous variables will be summarized with means, standard deviations, medians, minimums, and maximums, and the number of non-missing observations for each study group. Other selected percentiles such as 25^{th} and 75^{th} percentiles may be presented. Categorical variables will be summarized by count and percentage of subjects in the corresponding categories.

9.2 Subject Enrollment and Disposition

9.2.1 Subject Disposition

Subject disposition will be summarized for all randomized subjects by the two study groups, VISCO360 versus Control (SLT) groups, separately. The summary will include the number and percentage (based on total number of subjects randomized) of subjects in each of the following categories:

- ITT population
- mITT population
- PP Population
- Safety population
- Available at 12 months
- Discontinued prior to the 12 months examination
- Discontinued prior to the 24 months examination
- Completed the 24 months examination

The number of subjects who are enrolled but not randomized will also be provided.

9.2.2 Subject Status by Study Visit

For the ITT population, PP population, and Safety population, subject accountability will be prepared based on Table A.1 of ISO 11979-7, 2006.

9.3 Demographics and Preoperative Characteristics

Subject demographics (age, race/ethnicity and gender) will be summarized by study group for the ITT, PP, and Safety populations using descriptive statistics. Age will be summarized as a continuous variable and categorized into the four groups based on the observed quartiles.

The baseline medicated IOP and washout (unmedicated) IOP will be summarized by study groups for the ITT and PP populations. They will be treated as continuous variables. Additionally, number and percentage of subjects will be presented for four unmedicated IOP groups based on the observed quartiles. For the four subgroups, the number of glaucoma medications in use at enrollment will be prepared for each of the study groups using descriptive statistics for categorical variables.

The above data summaries will be stratified by study site.

Medical and Ocular history will be summarized for each study group by number and percentage of subjects in the ITT population.

9.4 Effectiveness Endpoints Analyses

9.4.1 Primary Analysis for Primary Effectiveness Endpoint

The primary analysis of the primary effectiveness objective described in Section 4.1.1 will be based on the mITT population. The medication-free mean diurnal IOP change from baseline at 12 months will be calculated for each study eye. As described in Section 4.1.1, for subjects meeting the criteria listed in Section 4.1.1, their 12-month medication-free mean diurnal IOP will be imputed by the baseline medication-free diurnal IOP. In order to assess the pattern of the distribution, box-plots will be prepared for the medication-free mean diurnal IOP and its change from baseline for each of the two study groups.

The descriptive statistics (such as mean, standard deviation, median, minimum, and maximum) of the medication-free mean diurnal IOP and the change from baseline and the 95% confidence interval of the mean will be calculated for each of the two study groups. A two-sample t-test with a one-sided significance level of 0.025 will be used to test the statistical hypotheses described in Section 4.1.1. The two-sided 95% confidence interval based on the t-distribution will also be provided for the mean difference in the medication-free mean diurnal IOP between the two study groups.

9.4.2 Primary Analysis for Secondary Effectiveness Endpoint

The percent change in medication-free mean diurnal IOP from baseline at 12 months will be calculated for each study eye as follows:

% change = (12-month medication-free mean diurnal IOP – baseline medication-free mean diurnal IOP) ÷ (baseline medication-free mean diurnal IOP) × 100%.

Histograms of the percent change in medication-free mean diurnal IOP from baseline at 12 months will be prepared for the two study groups separately. The number and percent of subjects achieving ≥ 20% reduction in medication-free mean diurnal IOP from baseline at 12 months (12-month IOP responder rate) will be calculated. The exact 95% confidence interval of the 12-month IOP responder rate will be calculated by the binomial distribution. For subjects who meet any of the criteria listed in Section 4.1 above, the non-responder (i.e. failure) will be imputed. An ones-side Fisher's exact test with a significance level of 0.025 will be used to compare the 12-month IOP responder rates between the two study groups. A 95% confidence interval of the difference in the 12-month IOP responder rate between the two study groups will be derived by the 2-sample normal distribution.

[redacted]

[redacted]

The scatter plots of the 12-month medication-free mean diurnal IOP versus the baseline medication-free mean diurnal IOP along with a 45º line will be provided. The scatter plot of the percent change in medication-free mean diurnal IOP from baseline to 12 months versus the baseline medication-free mean diurnal IOP will also be provided. The Box plots of the change and percent change in medication-free mean diurnal IOP from baseline to 12 months will be prepared for each category of the covariates.

For the primary effectiveness endpoint, two-way ANOVA with study group, one of the factors listed above, and the interaction between the study group and the factor will be used to check the possible covariate effects. For the secondary effectiveness endpoints, the Gail-Simon test will be performed. A p-value of 0.15 will be used for evaluating the possible covariate effects. It should be noted that the subgroups of these covariates will be re-examined and may be re-categorized or eliminated due to small sample size (if there are < 10 subjects within each subgroup).

9.4.5 Investigational Site Poolability

It should be noted that, for the primary effectiveness analyses, the data from all study investigational sites will be pooled based on the criteria of Meinert[4] (1986): all study investigational sites will conduct the study under a uniform protocol with well-defined study eligibility criteria; the data collection will be monitored for study protocol compliance across all study sties; all study sites will be in U.S. and will use the same method to collect clinical study data. The possible differences that may be observed among different sites during the study reflect the variability in the overall study populations and/or the clinical practices.

As described in Section 9.3, the demographic and preoperative characteristics summaries will be stratified by the study sites in order to evaluate possible clinically meaningful differences among different study sites. To evaluate possible statistical differences in the effectiveness outcomes among different sites, the two-way ANOVA and Gail-Simon test will be performed as described in Section 9.4.4. These statistical comparisons will be evaluated for clinical relevance. If there are statistically insignificant findings and some sites are small (< 10 subjects), the small sites will be pooled into the large sites that are geographically close, and the ANOVA or Gail-Simon test will be performed again.

[4] Meinert, C. (1986), *Clinical Trials: Design, Conduct and Analysis*, Oxford University Press Inc.

[redacted]

9.5 Safety Analysis

All safety analyses will be performed on the Safety population based on all available data

9.5.1 Adverse Event

Adverse events (AEs) will be classified as intraoperative or postoperative. The number and the percent of subjects reporting at least 1 adverse event of a given type will be summarized by study group. The corresponding 95% confidence interval of the percentage will be calculated by binomial distribution. Additionally, the number of reports and the proportion of events (the total number of events divided by the total number of subjects) of each type of AEs will be provided.

For each AE, the number and the percent of subjects reported with the event will be summarized by the severity level. For subjects with multiple reports of the same type of AE, the maximum severity will be used. Similarly, the AE relationship to the procedure will be summarized for the two study group separately. For subjects with multiple reports of the same type of AE, the closest relationship to the procedure will be used.

9.5.2 Best Corrected Visual Acuity (BCVA)

The number and percent of subjects reporting with BCVA of 20/20 or better, 20/25 or better, 20/32 or better, 20/40 or better, worse than 20/40 to 20/80, worse than 20/80 to 20/200, and worse than 20/200 at each visit will be summarized for the two study groups separately. The number and percent of subjects reporting BCVA of increase ≥ 2 lines (10 letters), increase 2 lines, increase ≥ 1 line to < 2 lines, within 1 line change, decrease ≥ 1 line to < 2 lines, decrease 2 lines, and decrease ≥ 2 lines at each postoperative visit will be calculated for the two study groups separately.

9.5.3 Other Safety Analyses

The number and percent of subjects reported with each kind of slit lamp findings, gonioscopy findings, dilated fundus examination findings, and pachymetry at each visit will be provided for the two study groups separately.

The descriptive statistics for the continuous variables will be derived for the visual field mean deviation (MD) and pattern standard deviation (PSD), and pachymetry.

9.6 Analysis on PRO Data

The total score is calculated for Visual Function Symptom Impact (range from 0 to 55) and for Local Eye Symptom Impact (range from 0 to 35) will be calculated for each subject at baseline, 3 months, 12 months, and 24 months. The change in these total scores from baseline to the postoperative visits will be derived for each subject. Descriptive statistics for the continuous variables will be used to summarize these total scores at each visit for the two study groups separately. No inferential statistics will be provided since no labeling claims will be made based on the results.

[redacted]

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