STATISTICAL ANALYSIS PLAN

EARLY FEASIBILITY STUDY TO EVALUATE THE SAFETY AND EFFECTIVENESS OF THE ACCURASEE™ FOR SECONDARY IMPLANTATION IN THE CAPSULAR BAG TO CORRECT RESIDUAL REFRACTIVE ERRORS OF PREVIOUS CATARACT SURGERY

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APPENDIX 6: STATISTICAL ANALYSIS PLAN

Protocol Number:	CIIPCL-018
Version:	5.0; July 8, 2021
Protocol Title:	Early Feasibility Study to Evaluate the Safety and Effectiveness of the AccuraSee™ for Secondary Implantation in the Capsular Bag to Correct Residual Refractive Errors of Previous Cataract Surgery
Sponsor:	OnPoint Vision Inc. 6A Liberty, Suite 100 Aliso Viejo, CA. 92656 U.S.A.

APPROVAL SIGNATURES

Product:	AccuraSee Intraocular Pseudophakic Contact Lens
Protocol Number/Amendment:	CIIPCL-018
SAP Version:	5.0
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The individuals signing below have reviewed and approve this statistical analysis plan.

Signature on file — 5/19/23

Lynne Richards
Clinical Affairs Consultant

Date

Signature on file — 5/19/23

Tonya Porter
Regulatory Affairs Consultant

Date

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LIST OF ABBREVIATIONS

AE	Adverse event
ANOVA	Analysis of Variance
BCDVA	Best corrected distance visual acuity
CI	Confidence interval
CS	Contrast sensitivity
ETDRS	Early Treatment Diabetic Retinopathy Study
IOP	Intraocular Pressure
MRSE	Manifest refraction spherical equivalent
QoV	Quality of Vision
SAP	Statistical Analysis Plan
UCDVA	Uncorrected distance visual acuity

1 INTRODUCTION

This Statistical Analysis Plan (SAP) outlines the statistical methods to be implemented within the scope of Protocol CIIPCL-18, entitled "Early Feasibility Study to Evaluate the Safety and Effectiveness of the AccuraSee™ for Secondary Implantation in the Capsular Bag to Correct Residual Refractive Errors of Previous Cataract Surgery." Results of the proposed analyses will become the basis of the clinical study report for this protocol.

The purpose of this plan is to provide specific guidelines from which the analysis will proceed. All planned analyses specified in this document will be performed. Any changes to this plan, in the form of "post hoc" or "data driven" analyses will be identified as such in the final clinical study report. Any changes will either be reflected in amendments to this plan before the database lock or specifically documented in the clinical study report.

2 STUDY OBJECTIVE

The objective of this study is to determine if the intraocular pseudophakic contact lens (IOPCL), referred to as the AccuraSee, corrects residual refractive errors using a plus powered lens in subjects with ocular pathology previously implanted with an AcrySof® IQ monofocal intraocular lens and to confirm its positional stability and adherence relative to the intraocular lens.

The primary objective of this study is to determine the stability of the AccuraSee to successfully adhere to a pseudophakic intraocular lens without rotation or slippage.

The secondary objective of this study is to determine if the AccuraSee can successfully correct refractive errors up to +/- 3.0 diopters (D) in subjects previously implanted with an AcrySof® IQ monofocal intraocular lens.

3 STUDY ENDPOINTS

3.1 Effectiveness Endpoint

3.1.1 Primary Effectiveness Endpoint

The primary effectiveness endpoint identified for this Early Feasibility Study for AccuraSee.

- Proportion of eyes (≥ 50%) able to achieve a stable target refraction within 0.5 D of the intended target. Stability is achieved when there is no change (±0.50 D) in MRSE within two consecutive postoperative visits at 1 month or later visits.

3.1.2 Additional Effectiveness Outcomes

Other important effectiveness outcomes include the following visual acuity measurement:

- Monocular uncorrected distance visual acuity (UCDVA)

These effectiveness outcomes will be summarized descriptively for different lens groups. The differences between preoperative and postoperative results will also be summarized by descriptive statistics. The 95% confidence intervals of mean difference may be provided.

3.2 Safety Endpoints

- Preservation of Best Corrected Distance Visual Acuity (BCDVA)

The preservation of BCDVA is defined as proportion of eyes (< 5%) that lose two or more lines of BCDVA from baseline.

- Successful Delivery of the IOPCL as determined at 7-14 days post-operative

The successful delivery of the IOPCL is defined as no capsular tear, visualize centration between the IOL and IOPCL, no visible damage to either the IOL or IOPCL, and uniform leaflet coverage of all IOPCL haptic tabs.

- Long-term Adherence and Positional Stability

The long-term adherence and positional stability is defined as minimal change (i.e. ± 10 microns) between 1-2 months and 4-6- months as determined by UBM measurements. The open central spacing between the IOL and IOPCL is established and maintained using UBM imaging.

- Adverse Events

The Adverse Events is defined as characterization and incidence of cumulative and persistent intraoperative and post-operative adverse events.

3.3 Other Clinical Outcomes

- Auto-refraction
- Visual acuity parameters (BCDVA)
- Slit lamp examination
- Applanation intraocular pressure (IOP) using Goldmann
- Dilated fundus examination
- Visual symptoms (QoV)

4 STUDY DESIGN

This will be a three (3) center US clinical trial, in which a maximum of 10 subjects will be implanted unilaterally with the AccuraSee IOPCL and followed for 12 months.

The subjects who might be eligible are potentially interested in participating and have provided their informed consent will be examined preoperatively to obtain a medical history and to establish a baseline for their ocular condition. Qualified subjects who provide written consent will be enrolled into the study.

Subjects will undergo IOPCL implantation. Postoperatively, subjects will undergo a complete ophthalmic evaluation at regularly scheduled intervals in accordance with study protocol.

An Investigational Device Exemption (IDE) application will be submitted on clinical outcomes when all enrolled eyes have a chance of reaching the 4-6-month post-operative visit (Postop Form 4).

This study is being conducted in accordance with 21CFR, Parts 50, 54, 56 and 812.42 (U.S.C 282(j)). ISO 14155 Clinical investigation of Medical Devices for Human Subjects, ISO 11979-7, and the ethical principles laid down in the Declaration of Helsinki.

5 ANALYSIS POPULATIONS

The analyses will include the data of all study eyes where implantation of IOPCL was attempted and/or successful.

6 STATISTICAL CONSIDERATIONS

6.1 General Considerations

Descriptive statistics (mean, median, standard deviation, minimum, and maximum) will be used to summarize continuous variables. Frequencies and percentages will be used to summarize categorical variables.

Any analysis not described in this plan will be considered exploratory, and will be documented in the clinical study report (CSR) as a post hoc analysis or a change to the planned analysis.

6.2 Sample Size

Sample size is limited to maximum of 10 subjects (eyes) for this Early Feasibility Study (EFS).

6.3 Randomization and Masking

This study will not be randomized or masked.

6.4 Data Transformations and Derivations

- Age in years (round down) will be calculated using informed consent date and birth date.
- Time variables based on two dates (e.g., Start Date and End Date), will be calculated as (End Date – Start Date) (in days) unless otherwise specified in the planned analysis section. For example, the postoperative day = postoperative visit date – lens implantation date (i.e. surgical date).
- The following unit conversion will be implemented unless otherwise specified:
    - Months = Days / 30.4375
    - Years =Days / 365.25

6.5 Handling of Dropouts and Missing Data

All data analyses will be conducted based on available data. No imputation will be performed.

6.6 Examination of Subgroups

Due to possible subset of eyes implanted having underlying pathology resulting in poor preoperative BCDVA, separate analyses will be provided for effectiveness with this subset of eyes and the remaining eyes without poor preoperative BCDVA.

6.7 Covariates

Covariates are not considered for adjustment in the analyses.

6.8 Timing of Analyses

An interim analysis will be performed when all enrolled subjects either have been seen for their 4-6 month visit, or have earlier exited from the study before the 4-6 month visit, or the visit window has closed for the 4-6 month visit (i.e., missed visit).

Interim safety summaries will be provided for annual reports based on regulatory requirement. Postoperative follow-up through 12 months on all implanted subjects will be completed as per protocol at which the final report analysis will be performed.

7 PLANNED METHODS OF ANALYSES

7.1 Accountability and Disposition

Accountability of the eyes by visit will be provided based on ISO 11979-7:2014(E) for all eyes. Reasons for discontinuation of study will be summarized. The number and percentage of eyes and subjects in each analysis population will be summarized.

7.2 Demographic and Baseline Characteristics

Demographics, preoperative parameters, and operative parameters will be summarized descriptively by mean, standard deviation, median, minimum, and maximum for the continuous outcomes and by count and percentage for the categorical outcomes.

7.3 Protocol Deviations

Major protocol deviations are those that represent a divergence from the protocol that could have a significant effect on the integrity of the study data, or on the subject's rights, safety, or welfare. Major protocol deviations also include exemptions to the study inclusion/exclusion criteria and will be summarized by category. A list of subjects with major protocol deviations will be presented.

7.4 Effectiveness Analysis

7.4.1 Primary Analyses of the Primary Effectiveness Endpoint

The 4-6 month MRSE value of the primary eyes will be summarized descriptively by mean, standard deviation, median, minimum, and maximum based on the intended refractive target. MRSE stability (i.e., no change [±0.50 D]) within two consecutive postoperative visits at 1 month or later will be calculated.

7.4.2 Additional Effectiveness Analyses

The analysis in section 7.4.1 will be repeated using auto-refraction instead of MRSE for an objective understanding of the change in refraction as this study includes patients with underlying pathology with poor BCDVA, which can impact the reliability of MRSE measurements.

All the available monocular uncorrected distance visual acuity at each protocol specified scheduled visit will be presented for the primary eyes. The categorical presentations will include the visual acuity of 20/16 or better, 20/20 or better, 20/25 or better, 20/32 or better, 20/40 or better, 20/50 or better, 20/63 or better, 20/80 or better, and worse than 20/80.

7.5 Safety Analyses

The safety population will be used to summarize all safety endpoints. No imputation for the missing values will be performed.

7.5.1 Preservation of BCDVA

The analysis of this clinical outcome will be based on the observed data of AccuraSee IOPCL. The number and percent of IOPCL implanted eyes with a BCDVA loss of 2 or more lines from preoperative will be derived.

Additionally, if needed, data listing or summary will be provided for eyes with a BCDVA loss of ≥ 2 lines from the best BCDVA before the corresponding visits.

7.5.2 Successful Delivery of the IOPCL

The analysis of this clinical outcome will be based on the observed data of AccuraSee IOPCL. The number and percent of eyes with successful delivery of the IOPCL will be reported.

7.5.3 Long-term Adherence and Positional Stability

The analysis of this clinical outcome will be based on the observed data of AccuraSee IOPCL. The number and percent of eyes with minimal change (i.e. ± 10 microns) between 1-2 months and 4-6- months established and maintained central spacing between the IOPCL and IOL will be reported.

Long-term adherence and positional stability will also be stratified by the surgical technique (e.g., discrete narrow channels or wider sweeping channels).

7.5.4 Adverse Events

For each adverse event, number and percent of eyes reported with the event will be summarized at each scheduled visit (including intraoperatively) and during the study (i.e. cumulative and persistent).

7.5.5 Other Safety Analyses

7.5.5.1 Best-corrected Distance Visual Acuity

All the available monocular best-corrected distance visual acuity at each protocol specified scheduled visit will be presented for the primary eyes. The categorical presentations will include the visual acuity of 20/16 or better, 20/20 or better, 20/25 or better, 20/32 or better, 20/40 or better, 20/50 or better, 20/63 or better, 20/80 or better, and worse than 20/80.

7.5.5.2 Tonometry

Goldmann measurements of IOP and its change from baseline will be summarized descriptively at each visit.

7.5.5.3 Slit Lamp and Fundus Examination Findings

Numbers and percentages of eyes will be summarized for each of the findings at visit.

7.5.5.4 Visual Symptoms

For each symptom of the Quality of Vision (QoV) at each specified visit, the number and percent of subjects of the findings will be summarized. Additionally, the subscale score and overall score based on the QoV user manual will be calculated for each subject. These subscale score and overall score will be summarized based on mean, standard deviation, minimum, and maximum. Similar descriptive statistics will be prepared for the change in the QoV from preoperative.

8 CHANGES FROM PLANNED ANALYSES

8.1 Changes from the Original Protocol

Version 2.0 – None
Version 3.0 – Add subgroup analyses for effectiveness due to the first 3 eyes having poor preoperative BCDVA with underlying pathology.
Version 4.0 – Updated study objective to match clinical study protocol. Add effectiveness analysis using autorefraction measurements. Revised subgroup analyses for effectiveness to subjects having poor preoperative BCDVA with underlaying pathology (removed first 3 eyes language).
Version 5.0 – Added analysis to evaluate the impact of surgical technique on IOPCL stability.

9 REFERENCES

ISO 11979-7, Ophthalmic implants - Intraocular lenses - Part 7: Clinical investigations, 2014.