Comparison of Visual Outcomes with Mini-Monovision between a Monofocal and an Adjustable Intraocular Lens

An investigator-initiated clinical trial

1. TITLE PAGE

Protocol Number:	CB-23-02
Amendment Number	Version 1.0
IRB / ERC	Salus IRB 2111 West Braker Lane, Suite 400 Austin, Texas 78758
Sponsor Name & Address:	Clayton Blehm, MD North Georgia Eye Associates 2061 Beverly Rd Gainesville, GA 30501 ***(funding only, this is an investigator-initiated study IIT # 89850521)*** Alcon 6201 South Freeway, Fort Worth, TX 76134-2099, USA
Test Articles:	The Clareon™ Monofocal Intraocular Lens (Toric and Non-Toric) The Light-Adjustable Lens™
Investigator:	Clayton Blehm, MD

2 . INVESTIGATOR AGREEMENT

I confirm that I have read and that I understand this protocol entitled "Comparison of Visual Outcomes with Mini-Monovision between a Monofocal and an Adjustable Intraocular Lens", and understand the use of the study products. I agree to conduct this study in accordance with the requirements of this protocol and also protect the rights, safety, privacy, and well-being of study subjects in accordance with the following:

- The ethical principles that have their origin in the Declaration of Helsinki.
- All applicable laws and regulations, including, without limitation, data privacy laws and regulations.
- Regulatory requirements for reporting serious adverse events defined in Section 13 of this protocol.

Signature of Investigator (Date)

Investigator Name (print or type)

Investigator's Title

Name of Facility

Location of Facility (City)

3. GENERAL INFORMATION

Objective	To compare binocular visual outcomes with light adjustable lens (LAL) vs. Clareon monofocal/toric IOL when both are targeting mini-monovision (-0.75 ~ -1.00 D in the non-dominant eye). The hypothesis is that the Clareon monofocal/toric IOL with mini-monovision will provide non-inferior binocular distance vision compared to LAL mini-monovision (non-inferiority margin: 0.1 logMAR).
Test Article(s)	The Clareon™ Monofocal Intraocular Lens (Toric and Non-Toric) The Light-Adjustable Lens™
Sample size	138 subjects total (69 in each group)
Study Population	Age-related Cataract patients with ≥ 0.75D corneal astigmatism and without previous experience of monovision > -1.00D offset.
Number of sites	One
Study Design	Single center, multi-surgeon, prospective, randomized, comparative study.
Masking	None.
Variables	Primary: Binocular corrected distance visual acuity (CDVA), 3-months postop. Secondary: • Binocular uncorrected distance visual acuity (UDVA), 3-months postop. • Binocular distance-corrected intermediate visual acuity (DCIVA) at 66cm, 3-months postop. • Binocular uncorrected intermediate visual acuity (UIVA) at 66cm, 3-months postop. • Monocular corrected distance visual acuity (CDVA), 3-months postop.

- Monocular uncorrected distance visual acuity (UDVA), 3-months postop.
- Monocular distance-corrected intermediate visual acuity (DCIVA) at 66cm, 3-months postop.
- Monocular uncorrected intermediate visual acuity (UIVA) at 66cm, 3-months postop.

Exploratory:

- Binocular distance-corrected near visual acuity (DCNVA) at 40cm, 3-months postop.
- Binocular uncorrected near visual acuity (UNVA) at 40cm, 3-months postop.
- Monocular distance corrected defocus curve at 3 months post-op for both eyes in LAL group and dominant eye for Clareon group.
- Binocular defocus curve at 3 months post-op (dominant eye: plano corrected, non-dominant: -1.00D)
- Manifest refraction (MRSE, residual sphere, and residual astigmatism) at postoperative day 17-28 and at 3 months post-op.
- Patient reported spectacle usage questionnaire (PRSIQ) at postoperative day 17-28 and at 3 months post-op
- Total ocular, corneal and internal HOA and SA with iTRACE for both eyes in LAL group and dominant eye for Clareon group (Objective depth of focus measurement with iTRACE for each eyes in both groups)
- Number of days and post-op office visits from cataract surgery to routine "release of care visit" (i.e. final lock-in for LAL group, 17-28 days after 2nd eye surgery for Clareon group).

Duration / Follow-up	Preoperative to 3 months postoperative

The study will be registered with clinicaltrials.gov.

The study will be conducted in compliance with the protocol, GCP and applicable regulatory requirements

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5. INTRODUCTION

The Light Adjustable Lens (LAL) is claimed to be the first and only intraocular lens (IOL) that can be customized to patient's satisfaction after cataract and IOL implantation surgery by using UV light treatments to adjust the refractive and visual outcomes. LAL allows cataract patients, even those without monovision experience to try mini-monovision and adjust to their visual satisfaction to provide improved range of vision. Clinically, monovision or mini-monovision with monofocal IOLs has been used to provide some presbyopia mitigation, especially before the invention of modern multifocal and extended depth of focus IOLs.

There is limited data on the visual outcomes for patients with mini-monovision with Light Adjustable Lens (LAL) compared to mini-monovision with a traditional monofocal/toric IOL. Previous studies have shown that the Clareon® intraocular lens (IOL) (Alcon, Fort Worth, Texas, USA) provides good visual outcomes for patients at distance.[1] The purpose of this study is to compare binocular visual outcomes with LAL vs. Clareon monofocal/toric IOL when targeting mini-monovision (-0.75 ~ -1.00D).

6. OBJECTIVE(S)

To compare binocular visual outcomes with LAL vs. Clareon monofocal/toric IOL when targeting mini-monovision (-0.75 ~ -1.00D).

7. SUBJECTS

7.1. Subject Population

Eligible test subjects will be adult normal astigmatic (≥ 0.75D corneal astigmatism) cataract patients presenting for cataract surgery who are considered appropriate candidates for intraocular lens implantation.

A total of 138 subjects at one site will be enrolled (69 per group). Both eyes of a subject must be enrolled. Subjects must meet the inclusion criteria. Prior to enrollment, subjects will be provided information on the study and asked to sign a patient information and consent form to participate. The patient information and consent form will be approved by an appropriate ethics committee.

7.2. Inclusion Criteria

Subjects are eligible for the study if they meet the following criteria:

Note: Ocular criteria must be met in both eyes.

- Adult patients undergoing age-related cataract surgery with expected best-corrected visual outcomes of 20/25 or better
- Regular corneal astigmatism of 0.75D-2.50D
- Dilated pupil diameter of 7mm or greater

7.3. Exclusion Criteria

If any of the following exclusion criteria are applicable to the subject or either eye, the subject should not be enrolled in the study.

- Moderate-severe corneal pathology, irregular astigmatism, preexisting macular disease and other retinal degenerative diseases that is expected to cause future vision loss, glaucoma, severe dry eye disease, history of uveitis, ocular herpes simplex virus, nystagmus, strabismus, zonular laxity or dehiscence, pseudoexfoliation.
- History of corneal refractive and intraocular surgery.
- Patients taking systemic medication that may increase sensitivity to UV light or that may cause toxicity to the retina.

The principal investigator reserves the right to declare a patient ineligible or non-evaluable based on medical evidence that indicates they are unsuitable for the trial.

Pregnancy has a known effect on the stability of refractions and visual acuity. As such, subjects who become pregnant during the study will not be discontinued but their data may be excluded from analyses of effectiveness.

8. STUDY DESIGN

8.1. Study Design

This study is a single center, multi-surgeon, prospective, randomized, comparative study of binocular corrected distance visual acuity (CDVA) after successful bilateral cataract surgery. Subjects will be assessed pre-operatively, operatively and at up to 6 post-operative visits. Clinical evaluations will include administration of patient reported spectacle usage questionnaire (PRSIQ), as well as measurement of monocular and binocular visual acuities at distance, intermediate, and near, defocus curve, manifest refraction, measurement of higher order aberrations.

The primary outcome measure will be the binocular corrected distance visual acuity (CDVA), 3-months postop.

Secondary outcome measures are as follows:

- Binocular uncorrected distance visual acuity (UDVA), 3-months postop.
- Binocular distance-corrected intermediate visual acuity (DCIVA) at 66cm, 3-months postop.
- Binocular uncorrected intermediate visual acuity (UIVA) at 66cm, 3-months postop.
- Monocular corrected distance visual acuity (CDVA), 3-months postop.
- Monocular uncorrected distance visual acuity (UDVA), 3-months postop.

- Monocular distance-corrected intermediate visual acuity (DCIVA) at 66cm, 3-months postop.
- Monocular uncorrected intermediate visual acuity (UIVA) at 66cm, 3-months postop.

Exploratory outcome measures are as follows:

- Binocular distance-corrected near visual acuity (DCNVA) at 40cm, 3-months postop.
- Binocular uncorrected near visual acuity (UNVA) at 40cm, 3-months postop.
- Monocular distance corrected defocus curve at 3 months post-op for both eyes in LAL group and dominant eye for Clareon group.
- Binocular defocus curve at 3 months post-op (dominant eye: plano corrected, non-dominant: -1.00D)
- Manifest refraction (MRSE, residual sphere, and residual astigmatism) at postoperative day 17-28 and at 3 months post-op.
- Patient reported spectacle usage questionnaire (PRSIQ) at postoperative day 17-28 and at 3 months post-op
- Total ocular, corneal and internal HOA and SA with iTRACE for both eyes in LAL group and dominant eye for Clareon group (Objective depth of focus measurement with iTRACE for each eyes in both groups).
- Number of days and post-op office visits from cataract surgery to routine "release of care visit" (i.e. final lock-in for LAL group, 17-28 days after 2nd eye surgery for Clareon group).

8.2. Methods Used to Minimize Bias

Patient selection will be based on the patient's interest and the surgeon's opinion as to whether they are a suitable candidate for IOL implantation. Subjects will be randomized to treatment groups.

The measurement of visual acuity will be conducted in a systematic fashion to minimize bias. Individuals conducting visual acuity measures will be instructed to perform the same testing in the same fashion for all subjects, with the same level of encouragement to subjects. Questionnaire instructions will be provided to all patients in a similar manner.

All data collection will be completed through provided Case Report Forms (CRFs) or computer files generated by automated test equipment. All site personnel involved in the study will be trained in regard to conducting study-specific procedures.

8.3. Method of Assigning Subjects to Treatment Arms

Subjects will be assigned to the Clareon monofocal or the LAL treatment groups in a 1:1 ratio using the method of randomly permuted blocks.

9. STUDY PROCEDURE

9.1. Informed Consent / Subject enrollment

No subject will be enrolled into the study who does not meet the inclusion/exclusion criteria and does not sign the current approved informed consent document. Informed consent will be obtained prior to collecting any data for the study. The original signed documents will be maintained by the investigator as a permanent part of the subject's medical records. A signed copy will be provided to the subject.

9.2. Visits and Examinations

Subjects will participate in eight study visits, one eye per visit for bilateral surgery. Visits will include an uptake visit, two operative visits, and up to 6 total postoperative visits (Visit numbers 1-8 below). The visit schedule, complete with window and associated CRF forms, are displayed in Table 9.2-1. Details of each study visit, including testing to be conducted, are provided below.

Table 9.2-1. Visit Schedule

Visit Number	Visit Name	Visit Window	Group	CRF Number
1	Preoperative	-90 to 0 days from surgery	L,C	1
2,2a	Operative	0 from surgery	L,C	2,2a
3	Follow Up Visit and LAL with UV treatment #1	POD 17-28	L,C	3
4	LAL with UV treatment #2 or lock-in #1	POD 24-42	L	4
5	LAL with UV treatment #3 or lock-in #1 or lock-in #2	POD 31-56	L	5
6	LAL with lock-in #1 or LAL lock-in #2 (if needed)*	POD 38-63	L	6
7	LAL with lock-in #2 (if needed)*	POD 45-70	L	7
8	Final Visit	POD 90 ± 14 days	L,C	8

C = Clareon Group; L = LAL Group; POD = postoperative day
*Note that visits 6 and 7 may not be necessary as not all subjects need 3 UV treatments, but each subjects will need 2 lock-ins.

9.2.1. Preoperative

At the preoperative exam, subjects will be consented, qualified for the study (compared with inclusion/exclusion criteria), and assigned a study ID/subject number. Subject numbers will be assigned sequentially at each site in the order of enrollment. Pre-operative qualification should take place no more than 90 days prior to surgery.

A medical history will be taken and exams will include the tests described below:

- manifest refraction,
- visual acuity

In addition, all site-specific, routine, usual standard of care preoperative measures should be undertaken.

Measurements should be made as described in section 9.3 below.

9.2.2. Operative (Surgery)

All subjects will undergo cataract surgery with implantation of either the Clareon or LAL IOL. The surgeon's usual standard of care with regard to treatment and medication will be used for all study subjects.

All patients will undergo bilateral femtosecond laser assisted cataract surgery (with ORA in the Clareon group). Surgeries will be completed 1 week apart with the non-dominant eye being the first eye. Surgeries will include femtosecond laser arcuate keratotomy or Clareon monofocal/toric IOL power calculation targeting (dominant eye: Plano ± 0.25D; non-dominant eye: -0.75 ~ -1.00D). Personalized lens constants for Clareon and Clareon toric will be used with Barrett Universal II formula, Barrett toric calculator and will consider the results from Hill RBF. If discrepancy between ORA and Barrett Universal II, will adjust to first minus on sphere that ORA recommends and will adjust one T power up or down based on ORA.

LAL patients will have a pre-op target of closest to +0.25D calculated with the Barrett Universal II formula. LAL patients will undergo UV treatment until targeted refractive outcomes are achieved (dominant eye: plano ± 0.25D; non-dominant eye: -0.75 ~ -1.00D).

Surgical findings will be recorded and any adverse events/serious adverse events (AEs/ SAEs) occurring during surgery will be noted at this visit. Any other problems during surgery and comments regarding surgery will be documented.

Any subject whose surgery is not completed successfully will be documented in the appropriate case report form. These subjects will be monitored for safety but clinical performance data may be excluded from the analysis.

9.2.3. Postoperative Day 17 to 28
All routine, usual standard of care postoperative measures should be undertaken. In addition, the subject will undergo VA, manifest refraction, PRSIQ questionnaire, and iTrace testing in accordance with the specifications below (Section 9.3). Adverse events will be monitored.

9.2.4. Postoperative UV Treatments
LAL patients will undergo UV treatment until targeted refractive outcomes are achieved (dominant eye: plano ± 0.25D; non-dominant eye: -0.75 ~ -1.00D). All routine, usual standard of care postoperative measures should be undertaken. In addition, the subject will undergo VA, manifest refraction, and iTrace testing (Section 9.3) at these visits. Any device deficiencies or adverse events will be monitored.

9.2.5. Postoperative Day 90
All routine, usual standard of care postoperative measures should be undertaken. In addition, the subject will undergo VA, manifest refraction, defocus curve, PRSIQ questionnaire, and iTrace testing (Section 9.3). Any device deficiencies or adverse events will be monitored.

9.2.6. Exit Procedures
In the event of premature exit from the study, all study related examinations should be completed where possible. The Exit CRF should be completed, noting that the subject did not complete the study and the reason for premature study exit. If no premature exit from the study occurs, the Exit CRF should be completed at the end of Visit 7 (Postoperative Day 90).

9.3. Study Methods and Measurements

All routine testing and basic eye examinations should be carried out at each study visit. Abnormalities should be recorded in the CRF "Comment" section. Specific study examination procedures are outlined below.

9.3.1. Manifest Refraction
Perform a manifest refraction with a high contrast logMAR chart under photopic lighting conditions (>85 cd/m^2). Document refraction results with sphere, cylinder and axis readings. If uncorrected visual acuity is not improved by manifest refraction, use zero for sphere and cylinder and draw a line through the blank for the axis.

Note: Each subject should be manually refracted to his/her best correction by an ophthalmologist, optometrist, or a skilled technician using a phoropter or trial lenses.

9.3.2. Visual Acuity (VA)

To obtain logMAR VA, ask subjects to begin reading the chart at the smallest row where all letters are easily distinguishable. Have subjects continue to read rows with smaller letters and encourage subjects to guess at all letters in a line if at least one correct response was given on the previous row. Request subjects read rows until no letters on a row are read correctly or until all letters on a row are too indistinguishable to even be guessed.

While the subject is reading the chart, record the number of letters on each line read incorrectly by the subject. The last line from which the subject read at least one letter correctly is recorded as the baseline logMAR VA. The actual logMAR VA is calculated using the baseline logMAR VA line and the number of letters read incorrectly.

Distance VA
Measure distance visual acuity using a high contrast logMAR ETDRS chart under photopic lighting (>85 cd/m2) at a distance of 4 m.

Intermediate VA
Have the subject view an appropriately-scaled high-contrast logMAR ETDRS Visual Acuity Chart at 66 cm. Visual acuity determined with the chart will be recorded and scored.

Near VA
Have the subject view an appropriately-scaled high-contrast logMAR ETDRS Visual Acuity Chart at 40 cm. Visual acuity determined with the chart will be recorded and scored.

9.3.3 Defocus Curve
Perform monocular distance corrected (corrected to plano) and binocular defocus curve (dominant eye: plano corrected, non-dominant: -1.00) with a high contrast logMAR chart under photopic lighting conditions (>85 cd/m^2). Conduct testing with the manifest distance refraction in place in a phoropter. Add an over-correction of +1.0 D and record VA. Reduce the correction by +0.5 D and retest and record VA. Reduce the correction by +0.25 D and retest and record VA. Add an over-correction of -2.50 D and record VA. Remove over-correction in 0.5 D increments while testing VA at each step (also be sure to record the VA at -0.25 D). The procedure ends with VA testing at a 0.0 D over-correction (best-corrected distance refraction).

9.3.3 Questionnaires
The Patient reported spectacle usage questionnaire (PRSIQ) will be administered to subjects. The administrator should ensure the subjects understand the nature of the questions but should not interpret them for the subject.

9.4. Unscheduled Visits

Unscheduled exams may be conducted at the discretion of the Investigator with all relevant information from the exam recorded in the source documents and on the Unscheduled Visit pages within the CRF booklet.

9.5. Discontinued Subjects

Discontinued subjects are those who do not have an exit visit or who come into the office to be exited prior to the scheduled final study visit. Subjects may be discontinued from the study at any time if, in the opinion of the investigator, their continued participation in the study poses a risk to their health. The reasons for discontinuation include:

a. Adverse event;
b. Lost to follow-up;
c. Subject decision unrelated to an adverse event;
d. Protocol violation;
e. Treatment failure;
f. Other.

To ensure the safety of all subjects who discontinue prior to Visit 8, investigators should assess each subject and, if necessary, advise them of any therapies and/or medical procedures that might be needed to maintain their health. Any changes in medical health and/or use of concomitant medications should also be captured.

10. ANALYSIS PLAN

10.1. Analysis Data Sets

All subjects who are enrolled in the study will be evaluated for safety. Efficacy analyses will be performed based on data from those eyes where uncomplicated cataract surgery with IOL implantation was completed.

10.2. Statistical Methodology

A summary of the data will be prepared for all measurement time points.

10.2.1. Within-treatment Changes

For variables measured on a continuous scale, these summaries will include the sample size, as well as the mean, standard deviation, median, minimum, and maximum. For variables measured on a categorical scale, summaries will provide the number and percentage of eyes in each category. These summaries will be provided for all eyes completing the study.

Differences between parametric variables will be compared using a two-sample t-test. Differences between categorical variables will be compared using the 2-sample test for equality of proportions.

For non-inferiority testing, if the upper boundary of the 95th confidence interval is not greater than 0.1 logMAR, non-inferiority will be claimed.

The step-down methodology will be used on the non-inferiority endpoints in the following order:

1) Binocular CDVA
2) Binocular DCIVA
3) Binocular UDVA
4) Binocular UIVA

The correlation of total ocular and internal HOAs (especially SA) with monocular DCIVA will be evaluated using regression modelling. Findings from these models will provide an indication of whether any HOAs are statistically significantly associated with post-op DCIVA, and the strength of any such association.

10.3. General Statistical Considerations

The statistical analyses will be performed using R, version 4.2.2 or higher. Any statistical tests of hypotheses will employ a level of significance of alpha=0.05.

11. SAMPLE SIZE JUSTIFICATION

Assuming a difference in mean visual acuity between groups of 0.05 logMAR[2] and a pooled standard deviation of 0.1 logMAR, the study would require a sample size of: 69 subjects for each group (total sample size of 138 subjects), to achieve a power of 90% and alpha = 0.05.

There is significant uncertainty in the assumptions for mean difference between groups and pooled standard deviation. Therefore, blinded sample size re-estimation is planned. One interim analysis will be conducted after enrollment of 30 subjects in each group (60 subjects total) to re-estimate the sample size.

One interim analysis will look at the variability in each group (biostatistician should be blinded to the groups). Using these values, the required sample size will be re-estimated.

12. CONFIDENTIALITY/PUBLICATION OF THE STUDY

The existence of this Study is confidential and should not be discussed with persons outside of the Study. Results will be submitted for publication and presentation at national and/or international meetings. A manuscript will be submitted to peer-review journals for publication but there is no guarantee of acceptance.

All study data will be collected on appropriate Case Report Forms (CRFs). No protected health information will be included on the forms. CRFs will be retained in the patient's file for a minimum period of 3 years. Collected information will only be used for purposes of this study and no information will be sold to third parties. The following people will have access to your study records:

- Study Doctor and staff involved with the study
- Study Monitor or Auditor

- Sponsor Company or Research Institution
- Review boards or accrediting agencies
- Other State or Federal Regulatory Agencies

The de-identified data may be shared with other researchers for future analysis.

13. QUALITY COMPLAINTS AND ADVERSE EVENTS

All subjects will be monitored for adverse events over the course of the study. A place to record any adverse event is included on each case report form.

13.1. General Information

An Adverse Event (AE) is any untoward medical occurrence in a subject who is administered. a study treatment regardless of whether or not the event has a causal relationship with the treatment. An AE, therefore, can be any unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the study treatment, whether or not related to the treatment. In clinical studies, an AE can include an untoward medical occurrence occurring at any time, including run-in or washout periods, even if no study treatment has been administered.

13.2. Monitoring for Adverse Events

At each visit, after the subject has had the opportunity to spontaneously mention any problems, the Investigator should inquire about AEs by asking if the patient has any problems.

13.3. Procedures for Recording and Reporting AEs and SAEs

Subsequent to signing an informed consent form, all untoward medical occurrences that occur during the course of the study must be documented on an Adverse Event Form (AEF). A separate AEF must be filled out for each event. When possible, signs and symptoms indicating a common underlying pathology should be documented as one comprehensive event. For each recorded event, the AE documentation must include the onset date, outcome, resolution date (if event is resolved), intensity (i.e., severity), any action with study treatment taken as a result of the event, and an assessment of the adverse event’s relationship to the study treatment.

Nonserious Adverse Events

A nonserious AE is defined as any untoward change in a subject's medical health that does not meet serious criteria noted below (e.g., is not life-threatening, does not require hospitalization, does not prolong a current hospitalization, is not disabling, etc.). All adverse events must be reported regardless of whether or not they are related to the study treatment.

For nonserious adverse events, an AEF containing all available information will be collected on a routine basis and submitted to the Medical Monitor at the close of the study.

Serious Adverse Events

A serious adverse event (SAE) is defined as any adverse experience that meets any of the following criteria:

- Results in death.
- Is life-threatening.
  NOTE: Life-threatening means that the subject was at immediate risk of death from the reaction as it occurred; i.e., it does not include a reaction which hypothetically might have caused death had it occurred in a more severe form.
- Requires inpatient hospitalization or prolongation of existing hospitalization.
  NOTE: In general, hospitalization signifies that the individual remained at the hospital or emergency ward for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an out-patient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred, the event should be considered serious.
- Results in persistent or significant disability/incapacity. Disability is defined as a substantial disruption of a person's ability to conduct normal life functions.
  NOTE: The term disability means a substantial disruption of a person's ability to conduct normal life functions. This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, or accidental trauma (e.g., sprained ankle) which may interfere or prevent everyday life functions but do not constitute a substantial disruption.
- Is an important medical event. An important medical event is an event that may not result in death, be life-threatening, or require hospitalization but may be considered an SAE when, based upon appropriate medical judgment, it may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in the definitions for SAEs. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in subject hospitalization, or the development of drug dependency or drug abuse.
  All available information on a serious adverse event(s) and any other associated AE, if applicable, must be forwarded to the study coordinator for forwarding to the Medical Monitor immediately (i.e., within one working day of the Investigator's or site's knowledge of the event) as follows:
  - In studies utilizing EDC (electronic data capture), all available information for the SAE and any associated AE(s) must be entered immediately into the EDC system.
  - Additional information for any applicable event is to be reported as soon as it becomes available.

In addition to the reporting of serious adverse events to the study Medical Monitor, the SAE must be reported to the IRB / IEC according to their requirements.

The investigator must document all adverse device events (serious and nonserious but related) and all serious adverse events (related and unrelated) on the Adverse Device Effect and Serious Adverse Event Form. Any device quality complaints will also be documented.

- **Both the Quality Complaint Form and the Adverse Device Effect and Serious Adverse Event Form must be e-mailed immediately to the study coordinator.**
- **Additional relevant information is to be reported as soon as it becomes available.**

Study coordinator contact information is provided below.

Table 13.3.-1:
Contact Information for the Study

Study Staff (Coordinator)	Business Phone	e-mail	24-hour Office Phone
Maryann Thomas	770-532-4444	mthomas@gainesvilleeye.com	770-532-4444

Further, depending upon the nature of the adverse event (serious or nonserious) or quality complaint being reported, the study sponsor may request copies of applicable portions of the subject's medical records. The investigator must also report all adverse events and quality complaints according to the relevant IRB requirements.

12.3.1 Intensity and Causality Assessments

For every adverse event and quality complaint, the investigator must assess the causality as Related or Not Related to the medical device under investigation. An assessment of causality will also be performed by the Medical Monitor utilizing the same definitions, as shown below:

Causality

Related — An adverse event or quality complaint classified as related may be either definitely related or possibly related where a direct cause and effect relationship with the medical device has not been demonstrated, but there is a reasonable possibility that the adverse event or quality complaint was caused by the medical device.

Not Related	An adverse event or quality complaint classified as not related may either be definitely unrelated or simply unlikely to be related (i.e., there are other more likely causes for the adverse event or quality complaint).

Where appropriate, the investigator must assess the intensity (severity) of the adverse event as mild, moderate, or severe based on medical judgment with consideration of any subjective symptom(s), as defined below:

Intensity (Severity)

Mild	An adverse event is mild if the subject is aware of but can easily tolerate the sign or symptom.
Moderate	An adverse event is moderate if the sign or symptom results in discomfort significant enough to cause interference with the subject's usual activities.
Severe	An adverse event is severe if the sign or symptom is incapacitating and results in the subject's inability to work or engage in their usual activities.

The investigator must document any action taken (i.e., medication, intervention, or treatment plan) and outcome of the adverse event or quality complaint when applicable.

13.4. Follow-Up of Adverse Events and Quality Complaints

The investigator is responsible for adequate and safe medical care of subjects during the study and for ensuring that appropriate medical care and relevant follow-up procedures are maintained after the study. Any additional data from these follow-up procedures must be documented and available to the study coordinator who, with the Medical Monitor, will determine when the data need to be documented on the CRFs.

13.5. Safety Analyses

The type, severity, duration and frequency of reported ocular adverse events will be tabulated. Adverse events will also be summarized for events that were considered treatment-related.

14. GCP, ICH and ETHICAL CONSIDERATIONS

This study will be conducted in compliance with Good Clinical Practices (GCPs), including International Harmonization (ICH) Guidelines, and in general, consistent with the 1996 version of the Declaration of Helsinki. In addition, all applicable local, state and federal requirements will be adhered to.

This study is to be conducted in accordance with Institutional Review Board regulations. The investigator will obtain appropriate IRB/ethics committee approval prior to initiating the study.

The study will be registered with clinicaltrials.gov.

14.1 Confidentiality

The data collected will be data typical for the procedure(s) when performed on eyes outside the study. Any data collected will become part of the patient's clinical record. The data will be subject to the same privacy and confidentiality as other data in the clinical record.

Only the principal investigator, research consultant and clinic staff will have access to the data collected. All data shared outside the practice will be de-identified; patients' protected health information will not be available and will not be reported in any analyses or publications. No data will be sold to third parties. De-identified data may be used for future research.

15. STANDARD EVALUATION PROCEDURES

Table 15.1. Proposed Visits and Study Assessments

(visits are by patient, with both eyes tested)

Activity	Pre-operative	Operative	Postoperative					
	Visit 1	Visit 2a,2b	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8
			POD 17-28	POD 24-42	POD 31-56	POD 38-63	POD 45-70	POD 90
Informed Consent	L,C							
Demographics	L,C							
General Information: Medical History	L,C							
Surgery		L,C						
Manifest refraction	L,C		L,C	L	L	L	L	L,C
Monocular uncorrected distance VA	L,C		L,C	L	L	L	L	L,C
Monocular corrected distance VA	L,C		L,C	L	L	L	L	L,C
Binocular uncorrected and best-corrected distance VA			L,C	L	L	L	L	L,C
Monocular uncorrected and best distance-corrected intermediate VA (66cm)			L,C	L	L	L	L	L,C
Binocular uncorrected and best distance-corrected intermediate VA (66cm)			L,C	L	L	L	L	L,C
Monocular uncorrected and best distance-corrected near VA (40cm)			L,C	L	L	L	L	L,C
Binocular uncorrected and best distance-corrected near VA (40cm)			L,C	L	L	L	L	L,C
Monocular Distance Corrected Defocus Curve								L,C
Binocular Defocus Curve (Dominant eye: plano corrected, non-dominant: -1.00D)								L,C
PRSIQ questionnaire			L,C					L,C
Total ocular, corneal and internal HOA and SA with iTRACE (Both eyes in LAL group and dominant eye for Clareon group)			L	L	L	L	L	L,C
Number of days and post-op office visits from cataract surgery to routine "release of care visit" (i.e. final lock-in for LAL group, 17-28 days after 2nd eye surgery for Clareon group)								L,C
Monitor for Adverse Events and Device Deficiencies		L,C	L,C	L,C	L,C	L,C	L,C	L,C
Complete Exit Form[1]								L,C

C = Clareon Group; L = LAL group

[1] Complete Exit Form upon termination of subject participation, or at Visit 8, whichever occurs first.

16. DATA CONFIDENTIALITY

No protected health information (PHI), including the patient's name and date of birth, will be collected; to ensure this, no PHI information is permitted to be entered on any of the Case Report Forms (CRFs). Subjects will only be identified by subject IDs and identities will be removed at the initial visit so that there is no further need to protect or destroy the information. Collected information will only be used for purposes of this study and no information will be sold to third parties. The non-PHI information collected may be used for future research, though there is currently no plan to do so.

17. FINANCIAL AND INSURANCE INFORMATION/STUDY RELATED INJURIES

Every effort to prevent study-related injury will be taken by the Study Doctor and staff. In the event a patient is injured as a direct result of the study while following the Study Doctor's instructions and the study requirements, the patient will be instructed to contact his or her doctor immediately. The Study Doctor is to treat the injured subject as needed for those injuries caused directly by this research study. In the event of injury or illness caused by or occurring during a subject's participation in this research study, all charges for medical care provided to the subject will be billed to his or her insurance company. The Study Doctor or Sponsor does not offer to cover the medical care costs for injuries or illnesses that are not caused directly by the research study. The Sponsor does not offer to provide any other compensation, unless specifically agreed to elsewhere in this document. This information will be provided to each study subject before the start of the study in the consent form.

18. STUDY ENDPOINT CRITERIA

18.1. Patient Completion of Study

If a study patient has completed the final visit (Visit 8) of the study, he/she is considered to have completed the study.

18.2. Patient Discontinuation

Each study patient may voluntarily discontinue the study at any time they choose. Study patients who cannot complete the study for administrative reasons (e.g., non-compliance, failure to meet visit schedule, etc.) will be discontinued from the study. Study patients discontinued during the enrollment phase (prior to surgery) of the study will be replaced.

18.3. Patient Termination

A study patient will be terminated if the study patient develops any severe adverse event that may be related to the study. A study patient will receive appropriate treatment at the discretion of the investigator. Notification of termination will be clearly documented. These study patients are considered to have completed the study and will not be replaced.

18.4. Study Termination

The investigator with appropriate notification may terminate the study. If, after clinical observations, the investigator feels that it may be unwise to continue the study, he may stop the study.

18.5. Study Completion

The study will be complete when all enrolled patients have completed Visit 8 or have been terminated from the study.

19. SUMMARY OF RISKS AND BENEFITS

19.1. Summary of risks

The risks with this study are similar to those for any patient receiving cataract surgery and IOL implantation.[1,2] There is no increased risk associated with the proposed study.

19.2. Summary of benefits

Studies of Clareon and LAL IOLs have demonstrated that patients are likely to have relatively good visual outcomes.[1,2]

Subjects may be compensated up to $200 for completing the study.

REFERENCES

1. Blehm C, Hall B. Evaluation of visual outcomes and 3-month refractive stability of a new hydrophobic acrylic intraocular lens. *Clinical Ophthalmology.* 2023;17:1859-1864.
2. Moshirfar M, Henrie MK, Payne CJ, Hansen AM, Ronquillo YC, Hoopes PC. Comparing visual outcomes of light adjustable intraocular lenses in patients with and without prior history of corneal refractive surgery. *J Refract Surg.* 2023;39(5):311-318.