

A Non-Interventional Study to Evaluate the Effect of Intraocular Lens (IOL) Centration and Tilt on Visual Performance in Patients who have Undergone Clareon® Vivity® IOL Implantation

Short Title: Effect of Intraocular Lens (IOL) Centration and Tilt on Visual Performance with Clareon® Vivity® IOL Implantation

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ABBREVIATIONS USED IN THE PROTOCOL

Abbreviation	Term
AE	Adverse Event
GCP	Good Clinical Practice
IRB	Institutional Review Board
ICF	Informed Consent Form
SAE	Serious Adverse Event
IOL	Intraocular Lens
FLACS	Femtosecond Laser-Assisted Cataract Surgery
USFDA	United States Food and Drug Administration
EDOF	Extended Depth of Focus
HEMA	Hydroxyethylmethacrylate
UBM	Ultrasound Biomicroscopy
AS-OCT	Anterior Segment Optical Coherence Tomography
LED	Light-Emitting Diode
ANSI	American National Standards Institute
IEC	International Electrotechnical Commission
LogMAR	Logarithm of the Minimum Angle of Resolution
EDTRS	Early Treatment Diabetic Retinopathy Study

Abbreviation	Term
BCDVA	Best-Corrected Distance Visual Acuity
UCDVA	Uncorrected Distance Visual Acuity
DCIVA	Distance-Corrected Intermediate Visual Acuity
UCIVA	Uncorrected Intermediate Visual Acuity
MRSE	Manifest Refraction Spherical Equivalent
YAG	Yttrium Aluminum Garnet
LASIK	Laser-Assisted In Situ Keratomileusis
PRK	Photorefractive Keratectomy
AMD	Age-Related Macular Degeneration
MIGS	Microinvasive Glaucoma Surgery
HOA	Higher-Order Aberration
SAS	Statistical Analysis System
USB	Universal Serial Bus
HIPAA	Health Insurance Portability and Accountability Act

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1 INTRODUCTION

1.1 Background and Significance

Cataracts and Treatment Options

A cataract is clouding of the lens in the eye, which leads to blurring of vision and symptoms (e.g., glare and haloes) most notable with night-time driving. Visually significant cataracts are a leading cause of reversible blindness, with common risk factors including older age (~70 years), trauma, diabetes, prior intraocular surgery, and sunlight exposure, to list a few. Surgical approaches to cataract treatment have evolved with technology and innovation, as creation of the intraocular lens (IOL) in the 1950s and phacoemulsification in the late 1960s have prompted today's standard of care, removal of the cataract and implantation of an IOL.^{1,2} Additionally, with the advent of femtosecond laser-assisted cataract surgery (FLACS) and further advancement in IOL technology, reduced postoperative dependence on glasses has become a relatively routine and expected outcome for patients who undergo IOL implantation.³

Intraocular Lenses

A variety of USFDA-approved IOLs are currently available through several manufacturers, though IOL designs are grouped into three basic categories: monofocal, multifocal, and extended depth of focus (EDOF) – all of which may include astigmatism correction with a shape known as toric.

1. Monofocal IOLs: These lenses have a single focal point and provide clear vision at one distance, either far or near. Patients with monofocal IOLs may still need to wear glasses for tasks that require clear vision at intermediate distances or for reading.
2. Multifocal IOLs: These lenses have two or more focal points, which allow patients to see clearly at multiple distances, including far and near. Visual acuity often improves after surgery with multifocal IOLs, but contrast sensitivity may be reduced in comparison to monofocal IOLs.
3. Extended Depth of Focus IOLs: These lenses have a unique optical design that provides a range of intermediate focus, which can improve visual acuity at intermediate distances. EDOF IOLs are an alternative option for patients who prefer not to wear glasses or experience the reduced contrast sensitivity associated with multifocal IOLs.

Numerous studies have been published investigating the quality and performance of the Acrysof® Alcon lens, a popular IOL platform with more than 125 million implantations worldwide over the past 30 years. Within the past year, Alcon has developed Clareon®, a lens made of an advanced hydrophobic acrylic biomaterial incorporating HEMA, or hydroxyethylmethacrylate, which allows a more uniformly distributed and increased water content of the lens (1.5% compared to 0.4% in Acrysof®).⁴ This subtle change in the properties of the water content contributes to improved optical clarity characteristics of the lens such as reduced glistenings. In our investigation, we will assess the Clareon® family of IOLs, specifically the EDOF lenses known as Vivity and Vivity Toric.

Decentration and Tilt

Two key parameters measured in this study include decentration and tilt and their impact on visual outcomes. IOL tilt is defined as the angle between the IOL axis and a reference axis while IOL decentration is defined as the distance between the IOL center and a reference axis. In published literature, there is variability in which reference axis is utilized. For instance, pupillary axis, corneal vertex, and visual axis have all been used as reference axes in several studies. Methods of measuring IOL tilt and decentration include Purkinje and Scheimpflug imaging as well as ultrasound biomicroscopy (UBM) and anterior segment optical coherence tomography (AS-OCT).⁵

In this study, Tomey Corporation's CASIA2 AS-OCT will be used to directly measure IOL tilt and decentration. Results published in literature have shown that tilt greater than 3° or decentration greater than 0.3 mm has a negative impact on the quality of vision and, subsequently, patient satisfaction.⁵ In the FDA registration study, Clareon® IOLs illustrated excellent mechanical stability, however no studies have been performed assessing the effects of decentration and tilt of the Clareon® Vivity® and Vivity® Toric lenses on visual outcomes. If decentration and tilt measured in this study exceed parameters previously deemed visually significant, assessment of their impact on visual performance will determine whether this newer technology will be more forgiving with less-negative outcomes.

1.2 Risk Assessment

The potential risks to subjects in this study will likely be similar to those experienced in regular patient care.

Patients may experience discomfort during study examinations that utilize the EDTRS Sloan chart, RT-1 phoropter, iTrace wavefront aberrometer, or CASIA2 AS-OCT.

Patients will experience exposure to light-emitting diode (LED) light and laser diode light during examinations that utilize the CASIA2 AS-OCT.⁶ The CASIA2 AS-OCT device conforms to American National Standards Institute (ANSI) Z80.36:2021 standards for Light Hazard Protection for Ophthalmic Instruments, and the energy level emitted from the device to patients is considered safe by the USFDA when used in accordance with approved labeling.^{6,7} Patients will experience exposure to laser diode light during examinations that utilize the iTrace wavefront aberrometer.^{8,9} The iTrace wavefront aberrometer conforms to International Electrotechnical Commission (IEC) 60825-1:2014 standards for Safety of Laser Products, and the energy level emitted from the device to patients is considered safe by the USFDA when used in accordance with approved labeling.

Mydriasis, or pupil dilation, will be performed prior to measurements of IOL decentration and tilt as well as measurements of coma and spherical higher-order aberrations (HOAs).

Tropicamide 1% ophthalmic solution will be administered to dilate the pupils of patients who undergo these examinations. Tropicamide 1% ophthalmic solution is approved by the USFDA for use in accordance with labeling.^{10,11} Labeled indications for use of tropicamide 1% ophthalmic solution include mydriasis and cycloplegia for diagnostic procedures.¹¹ Potential adverse drug reactions to tropicamide 1% ophthalmic solution include transient stinging, blurred vision, photophobia, superficial punctate keratitis, dryness of the mouth, tachycardia, headache, allergic reactions, nausea, vomiting, pallor, central nervous system disturbances, and muscle rigidity. Use of tropicamide 1% ophthalmic solution is contraindicated in persons showing hypersensitivity to any component of this preparation. Tropicamide 1% ophthalmic solution may interfere with the antihypertensive action of carbachol, pilocarpine, or ophthalmic cholinesterase inhibitors.

2 ETHICS

2.1 Good Clinical Practice (GCP)

This study will be conducted in accordance with Good Clinical Practice (GCP), in accordance

with the United States Code of Federal Regulations, Title 21, Part 50 (21CFR50). The study will be conducted in compliance with the protocol.

All potential protocol deviations or violations must be reported to the IRB immediately. A protocol deviation or violation is defined as a violation of the GCP guidelines regarding the study protocol, which is likely to significantly affect the safety of the subjects in the study or the scientific validity of the study. Study staff involved in conducting this study will be qualified by education, training, and experience to perform their respective tasks and this study will not use study staff where there has been scientific misconduct or fraud (e.g., loss of medical licensure, debarment).

2.2 Institutional Review Board (IRB)

Before initiation of the study, the investigator must have received IRB approval for the protocol, ICF, subject recruitment materials (e.g., advertisements), and any other written information to be provided to subjects.

During the clinical study, any amendment to the clinical trial protocol must be submitted to the IRB before implementation, unless the change is necessary to eliminate an immediate hazard to the subjects, in which case the IRB should be promptly informed. The IRB should also be informed of any event likely to impact the safety of subjects in the clinical trial. The investigator must send a progress report to the IRB at least annually, as well as a summary of the clinical trial's outcomes at the end of the clinical trial.

2.3 Informed Consent

The investigator will ensure that the ICF includes all elements required by GCP and applicable regulatory requirements, as well as follow the ethical principles within the Declaration of Helsinki. The investigator will ensure that the ICF is reviewed and approved by the IRB prior to use in a clinical trial.

The Investigator, or a person designated by the Investigator, should fully inform the subject of all pertinent aspects of the clinical trial including the purpose, potential risks, required procedures, etc. in which they volunteer to participate. All subjects should be informed about the study in a language and at a level they are able to understand. In circumstances where consent cannot be

given to subjects, their legally acceptable representatives must be clearly and fully informed about the purpose, potential risks, required procedures, etc. regarding the clinical trial in which the subject will participate.

Prior to a subject's participation in the clinical trial, the written ICF should be signed and dated personally by the subject or by the subject's legally acceptable representative and by the person who conducted the informed consent discussion. A copy of the signed and dated written ICF will be provided to the subject.

3 HYPOTHESIS

Null Hypothesis: Monocular distance corrected visual acuity is not associated with intraocular lens (IOL) decentration or tilt.

Alternative Hypothesis: Monocular distance corrected visual acuity is associated with IOL decentration or tilt.

4 STUDY DESIGN

4.1 Description

This is a non-interventional, single center, multi-surgeon, observational study. The study population will include individuals implanted with Clareon® Vivity® and Vivity® Toric IOLs. IOL implantations reviewed will range from the earliest performed (May 2022) onward, until 100 implanted patients (200 eyes) are reached. Potential subjects will be consented, then retrospective chart review of pre-operative and operative implantation data will occur and postoperative data will be collected (1 or more months post-operation) via examination (see [Section 4.4](#) for additional details).

The relationship of decentration and tilt to all visual acuity endpoints will be analyzed, as described in [Section 5.6](#). Decentration and tilt of the IOL will be measured with the CASIA2 AS-OCT (Tomey Corp). Visual acuities will be measured in logarithm of the minimum angle of resolution (logMAR) units using the Early Treatment Diabetic Retinopathy Study (EDTRS) Sloan chart under photopic conditions. Monocular best-corrected distance visual acuity (BCDVA) (4 m) and uncorrected distance visual acuity

(UCDVA) (4 m) will be measured at 100% contrast. Monocular BDCVA will also be measured at 25% contrast as an exploratory endpoint. Monocular distance-corrected intermediate visual acuity (DCIVA) (66 cm) and monocular uncorrected intermediate visual acuity (UCIVA) (66 cm) will be measured at 100% contrast.

Manifest refraction/manifest refraction spherical equivalent (MRSE) (D) will be measured using the RT-1 phoropter (Marco). Mesopic pupil size (mm) will also be measured. Coma and spherical HOAs of the cornea (μm) will be measured using the iTrace wavefront aberrometer (Tracey Technologies).

4.2 Study Population

4.2.1 Study Subjects and Approximate Number of Subjects

This is a single-center study which will include the participation of approximately 100 subjects (200 eyes).

4.2.2 Eligibility Criteria

Inclusion Criteria:

Subjects must meet each of the following inclusion criteria to be eligible for enrollment into the study:

1. Age $\geq$ 18 years
2. History of adult cataract and uneventful, refractive cataract surgery with Clareon[®] Vivity[®] or Vivity[®] Toric IOL implantation with MRSE within ± 1.00 D
3. Willing to undergo an eye exam with pupil dilation

Exclusion Criteria:

Subjects presenting with any of the following exclusion criteria will not be eligible for enrollment into the study:

1. Moderate to severe posterior capsule opacification (2+ or more)
2. Yttrium aluminum garnet (YAG) laser capsulotomy within 1 month prior to enrollment
3. Laser-assisted in situ keratomileusis (LASIK) or photorefractive keratectomy (PRK) within the one year prior to IOL implantation or any time after IOL implantation

4. Any previous ocular surgery (excluding YAG, LASIK, PRK)
5. Clinically significant ocular pathology; severe diabetic retinopathy, age-related macular degeneration (AMD), glaucoma, severe dry eye, irregular astigmatism, zonular weakness, pseudoexfoliation, ocular trauma
6. Any additional procedure(s) at the same time as the Vivity implantation including but not limited to microinvasive glaucoma surgery (MIGS)
7. Women who are pregnant at the time of screening (based on self-reported history)
8. Medical or other problems which in the opinion of the investigator will render study participation unsafe

4.3 Study Duration

4.3.1 Approximate Duration of Subject Participation

Subjects will actively participate in the study for approximately one day.

Discontinuation will be based upon investigator's clinical determination and/or by subject decision. All subjects are free to terminate their participation in the study at any time, and the details regarding discontinuation will be recorded.

4.3.2 Withdrawal documentation

The subject may withdraw consent at will at any time. The subject's request to withdraw from the trial must always be respected. In case of withdrawal, the investigator will record the reason for subjects' withdrawal.

4.3.3 Approximate Duration of Study

This study is anticipated to be completed within approximately 7 months after study initiation, including subject enrollment, data collection, and analysis.

4.4 Procedures

The following procedures will be performed at the times shown in the Schedule of Activities:

- Subject consent and enrollment
- Retrospective chart review

- Monocular BCDVA (4 m) and UDCVA (4 m) (logMAR) measurements at 100% contrast under photopic conditions
- Monocular DCIVA (66cm) and UCIVA (66cm) (logMAR) measurements at 100% contrast under photopic conditions
- Monocular BCDVA (4 m) (logMAR) measurement at 25% contrast under photopic conditions
- Manifest refraction/MRSE (D) measurement
- Mesopic pupil size (mm) measurement
- Dilated IOL decentration (mm) and tilt (°) measurement
- Dilated corneal coma and spherical HOA (μm) measurements

Demography

Demography will be recorded at Visit 1 and will consists of:

- Date of birth
- Sex
- Ethnicity
- Race

Targeted Medical History

Targeted medical history will be recorded at Visit 1. Medical history includes medical events that the subject has experienced in the past, not including past surgeries or procedures. Medical events of interest include all ophthalmic conditions and respective treatments. Surgical history will also be recorded at Visit 1. Surgical history includes surgeries or procedures the subject has experienced in the past. All ophthalmic surgeries or procedures will be included in the surgical history. There must be medical records present in the subject's source documents to verify the subject's medical history.

4.5 Study Schedule

Procedure	Visit 1 (Screening / Enrollment)
Consent and enrollment	X

Retrospective chart review	X
Demography	X
Targeted medical history	X
Monocular BCDVA (4 m), UDCVA (4 m), DCIVA (66cm), and UCIVA (66cm) (logMAR) measurements at 100% contrast under photopic conditions	X
Manifest Refraction/MRSE (D) measurement	X
Mean monocular BDCVA (4 m) (logMAR) measurement at 25% contrast under photopic conditions	X
Mesopic pupil size (mm) measurement	X
Dilated IOL decentration (mm) and tilt (°) measurement	X
Dilated corneal coma and spherical HOA (μm) measurements	X

4.6 Study Endpoints

4.6.1 Primary Endpoints

- Monocular BCDVA (4 m) (logMAR)

4.6.2 Secondary Endpoints

- Decentration of IOL (mm)
- Tilt of IOL (°)
- Monocular UCDVA (4 m) (logMAR)
- Monocular DCIVA (66 cm) (logMAR)
- Monocular UCIVA (66 cm) (logMAR)
- Manifest refraction/MRSE (D)

4.6.3 Exploratory Endpoint

- Mean Photopic low contrast (25%) monocular BDCVA (4 m) (logMAR)
- Mesopic pupil size (mm)
- HOAs (coma and spherical) of the cornea (μm)

4.7 Data Analysis

4.7.1 Statistical Analysis Plan

The study will describe (with supporting visualization, as relevant) the patient population, including measures of the primary exposures of interest (decentration, tilt), and the outcomes (visual acuity measure(s), including monocular BCDVA) across study subjects. These descriptions will include the mean, standard deviation, median and range.

The study will explore unadjusted associations between exposures and outcomes of interest, followed by adjusted associations between exposures and outcomes of interest, in each case following a similar approach. For example, for the primary outcome, the study will first measure the association of monocular BCDVA and decentration; and, separately, measure the association between monocular BCDVA and tilt, using simple linear regression, with transformation (e.g., log, square, etc) of the exposure variable, if indicated by the data. The study will then fit a multiple linear regression model taking the form:

$$E(Y_i) = \beta_0 + \beta_1 D_i + \beta_2 T_i (+ \beta_{1..j,i} X_{1..j,i}) + \varepsilon_i$$

In which $E(Y_i)$ represents the expected outcome (monocular BCDVA) for patient i , D_i indicates decentration (in mm) for patient i , T_i represents tilt (in degrees) for subject i , $X_{j,i}$ represents a vector of additional covariates ($n=j$) (e.g., Manifest refraction/MRSE, mesopic pupil size, higher order aberrations) for subject i , and ε_i represents the error, assumed to be $N(0, 1)$. β_1 and β_2 are the parameters of interest, representing the independent association of decentration and tilt, respectively, on the outcome. To control the family-wise error rate for multiple comparisons in each model, the Holm-Bonferroni method will be applied. Each visual acuity outcome (see section 4.5.2) will be modelled in a similar fashion, exchanging the dependent variable (Y_i) in the model, and if necessary, adjusting covariates included in the model.

4.7.2 Statistical Power and Sample Size Considerations

Sample size considerations were based on the primary outcome, distance-corrected visual acuity (BCDVA). The primary modelling strategy will be multiple linear regression, with post-op BCDVA (treated as a continuous variable) as the dependent or outcome variable in the regression model, and tilt and decentration as the independent variables of interest. Sample size justification based on simulations indicate that with a two-sided $\alpha < 0.05$, 200

eyes would provide $\geq 87\%$ power to detect a population effect size of 5 letters (0.1 in logMAR scale) per 1° change in tilt and 4 letters (0.08 in logMAR scale) per 0.1 mm variation in decentration.

4.8 Data Management

4.8.1 Data Collection and Storage

Data required by the protocol will be collected using a data collection form created by the investigative site. The investigator has ultimate responsibility for the collection and reporting of all clinical data entered on the data collection form. Excel worksheets will be used to create the data repository for the analysis data set which will be de-identified and employ range checking derived from the study data dictionary. Final data merges for analysis will be performed with statistical analysis system (SAS) software. Electronic data will be stored on encrypted drives and backed up routinely to a secure server. At the end of study completion, all electronic data will be stored on a password protected universal serial bus (USB) flash drive and archived with study documents.

Subject study eye images will also be included in the subject source documents.

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). All physical records will be kept in a locked file cabinet.

4.8.2 Records Retention

The investigator must agree to archive the study documentation (both electronic and paper-based records) in an archive after completion or discontinuation of the trial. The investigator should not destroy any documents without prior permission from Alcon. If the investigator cannot archive the documents at the trial site, they should notify Alcon. At the conclusion of this study, data from this study will be archived for 15 years for possible use in future research studies.

5 SAFETY MONITORING

5.1 Adverse Event Reporting

Clinical adverse events (AEs) and Serious Adverse Events (SAE) will be monitored from signing of the ICF until completion of all study procedures are completed (not including the retrospective chart review). All AEs and SAEs will be reported to an Investigator regardless of whether they are considered study-related. The date and time of onset and outcome, seriousness, intensity, action taken, and causality to study treatment will be assessed by a study investigator.

5.2 Definitions

An **adverse event** (AE) is any untoward, undesired, or unplanned event in the form of signs, symptoms, disease, or laboratory or physiologic observations occurring in a person given a test article or in a clinical study. This includes a clinically significant worsening of a concomitant illness and clinical laboratory abnormalities which are clinically significant, i.e. an abnormality that suggests a disease and is of a severity that requires active management. The event does not need to be causally related to the device or clinical study.

The following definitions are used when assessing the intensity of an AE:

- Mild: no or transient symptoms, no interference with the subject's daily activities.
- Moderate: marked symptoms, moderate interference with the subject's daily activities.
- Severe: considerable interference with the subject's daily activities; unacceptable.

The following definitions are used when assessing the causality (relationship) of an AE:

- Related: A causal relationship between the study treatment and the AE is a reasonable possibility. The Investigator must further qualify the degree of certainty as "possible" or "probable."
 - Possible: A causal relationship is conceivable and cannot be dismissed.
 - Probable: Good reason and sufficient documentation to assume a causal relationship.
- Not Related: A causal relationship between the study treatment and the AE is not a reasonable possibility.

Items to be considered when assessing the relationship of an AE to the study treatment are:

- Temporal relationship of the onset of the event to the initiation of the study treatment;
- The course of the event, considering especially the effect of the discontinuation of study treatment or the reintroduction of study treatment, as applicable;
- Whether the event is known to be associated with the study treatment or with other similar treatments;
- The presence of risk factors in the study subject known to increase the occurrence of the event; and,
- The presence of non-study treatment-related factors that are known to be associated with the occurrence of the event.

The following definitions are used when assessing the outcome of an AE:

- Recovered/resolved: The subject has fully recovered, or by medical or surgical treatment the condition has returned to the level observed at the first trial-related activity after the subject signed the ICF.
- Recovering/resolving: The condition is improving, and the subject is expected to recover from the event. This term is only applicable if the subject has completed the trial or has died from another AE.
- Recovered/resolved with sequelae: The subject has recovered from the condition, but with lasting effect due to a disease, injury, treatment or procedure. If a sequela meets an SAE criterion, the AE must be reported as an SAE.
- Not recovered/not resolved: The condition of the subject has not improved, and the symptoms are unchanged, or the outcome is not known.
- Unknown: This term is only applicable if the subject is lost to follow-up.

A **serious adverse event** (SAE) is any untoward medical occurrence that at any dose:

- Results in death;
- Is life-threatening (i.e., the subject was at immediate risk of death from the AE as it occurred; this does not include an event that, had it occurred in a more severe form or was allowed to continue, might have caused death);
- Requires inpatient hospitalization or prolongation of existing hospitalization;
- Results in persistent or significant disability/incapacity;
- Is a congenital anomaly/birth defect;

- Is a medically important event.

5.3 Recording and Reporting

A subject's AEs and SAEs will be recorded and reported from the signing of the informed consent form until the subject's final study procedures are completed (not including the retrospective chart review). All SAEs must be reported to the PI.

6 ADMINISTRATIVE PROCEDURES

6.1.1 Changes to the Protocol

There are to be no changes to the protocol without written approval from the Investigators and sponsors. Protocols will be followed as written.

Any change to the protocol requires a written protocol amendment or administrative change that must be approved before implementation by the sponsor and IRB. Amendments specifically affecting the safety of subjects, the scope of the investigation, or the scientific quality of the study require additional approval by the applicable IRBs of all investigational sites. These requirements should in no way prevent any immediate action from being taken by the Investigator or by the Sponsor in the interest of preserving the safety of all subjects included in the study. If an immediate change to the protocol is felt by the Investigator to be necessary for safety reasons, the sponsor and IRB must be notified promptly.

Changes affecting only the administrative aspects of the study do not require formal protocol amendments or IRB approval, but the IRB must be kept informed of such changes. In these cases, the Principal Investigator will send a letter to the IRB detailing such changes.

6.1.2 Adherence to the Protocol

The Investigators will conduct the study in strict accordance with the protocol, which has been written to enable the Investigator's compliance with Good Clinical Practices.

6.1.3 Monitoring Procedures

6.1.3.1 Responsibilities of the Principal Investigator

The principal investigator is required to ensure compliance with all procedures required by the clinical trial protocol and agrees to provide reliable data requested by the clinical trial

protocol in an accurate and legible manner. The principal investigator may delegate other individuals as they deem appropriate as sub-investigators to assist in the conduct of the clinical trial. The sub-investigators will work under the responsibility of the principal investigator. The principal investigator will provide them with a copy of the clinical trial protocol and all necessary information.

6.1.3.2 Responsibilities of the Monitor

The monitor of this clinical trial is responsible for taking all reasonable steps to ensure the proper conduct of the clinical trial regarding ethics, protocol compliance, and integrity and validity of the data recorded. Thus, the main duty of the monitor is to help the principal investigator maintain a high level of ethical, scientific, technical and regulatory quality in all aspects of the clinical trial.

Throughout the clinical trial, the monitor will contact the site through monitoring visits or phone calls to review study progress, investigator and patient compliance with the protocol, and any study-related issues. The monitoring visits will include, but not be limited to, review of the following aspects: patient ICFs, patient recruitment and follow-up, SAE documentation and reporting, AE documentation, compliance with the study protocol, and quality of data. The monitor must check the data collected against the source documents.

7 PUBLICATION PLAN

Results from this research (without any subject identifiers) will be submitted for journal publication and presentation at national meetings. Important findings may be submitted to conferences and for publication in peer-reviewed scientific journals. The identity of the subjects may not be disclosed, unless required by law, to any persons not immediately involved in the study or the study procedures.

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