VISUAL PERFORMANCE AND PATIENT SATISFACTION WITH A NEW MONOFOCAL INTRAOCULAR LENS

Sponsor:	Carolina Eyecare Physicians, LLC 1101 Clarity Rd., Suite 100 Mt. Pleasant, SC 29464 (843) 881 3937 Kerry D. Solomon, MD, Principal Investigator Helga P. Sandoval, MD, MSCR, Director of Research
Study Product:	JJV – Tecnis Eyhance Intraocular lens Toric (DIUxxx) and non-toric (DIB00)
Protocol Number:	CEP-21-001 Initial version date: 06Apr2021 Version 2.0 17May2021 Version 2.1 06Jul2021 Version 2.2 10Jan2022 Amendment #1
Investigator Agreement:	I have read the clinical study described herein, recognize its confidentiality and agree to conduct the described trial in compliance with Good Clinical Practices (GCP), the Declaration of Helsinki, this protocol and all applicable regulatory requirements. Additionally, I will comply with all procedures for obtaining informed consent, data recording and reporting, will permit monitoring, auditing, and inspection of my research center, and will retain all records until notified by the sponsor.
Name of the Investigator:	_____
Name of the Institution:	_____
Address:	_____ _____
Investigator:	_____ Signature Date

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INTRODUCTION

Current visual outcomes expectations of cataract in some patients are similar to those of refractive surgery patients. Their desire is to be spectacle independent for far, intermediate and near vision activities. Some may have already enjoyed freedom from glasses and would like to continue after the cataracts are removed. Different options are available. These options include: mono-vision and presbyopia correcting intraocular lenses (IOL).

Mono-vision can be achieved using monofocal IOLs by setting the non-dominant eye to -1.75 (range may vary according to patient's preference -1.25 to -2.50 D) and the dominant eye to plano at time of cataract surgery, or postoperatively using contact lenses, or undergoing LASIK.

Presbyopia correcting IOLs (PCIOLs) include accommodative, multifocal (MIOLs, bi and trifocals) and extended depth of focus (EDOF) IOLs. Patients' complaints of glare and halos are common with all MIOLs and EDOF. The severity of these symptoms varies according to the actual IOL design. These optical phenomena may prevent a large percentage of patients from choosing a PCIOL even though they still want to achieve spectacle independence postoperatively at all distances.

Monofocal lenses correct only at the target distance chosen (i.e., distance without intermediate or near vision improvement or near without distance improvement). Intermediate vision has become important for many daily activities such as reading a mobile phone or tablet. Tecnis Eyhance IOL, recently approved by the FDA,[A] is a new generation of monofocal lenses designed to improve and/or enhance intermediate vision without compromising the distance vision with low incidence of halo, glare or starburst. Auffarth et al[1] in a study that included 67 patients implanted bilaterally with the Eyhance IOL showed an improvement of 1 line of intermediate visual acuity compared to a standard monofocal IOL (ZCB00). Additionally, they reported no differences between the 2 groups in contrast sensitivity and visual disturbances complains.

The purpose of this study is to evaluate the visual outcomes of a monofocal IOL with an enhanced intermediate function, in patients with or without astigmatism, when both eyes are targeted for emmetropia and when the non-dominant eye is targeted for mini monovision (-0.75 D) in patients undergoing routine cataract surgery.

1. OBJECTIVE:

The main objective of this study is to evaluate the visual outcomes of a monofocal IOL with an enhanced intermediate function, in patients with or without astigmatism, when both eyes are targeted for emmetropia and when the non-dominant eye is targeted for mini monovision (-0.75 D) in patients undergoing routine cataract surgery.

2. STUDY DESIGN AND METHODS:

A. Test article: Tecnis Eyhance Intraocular lens Toric (DIUxxx) and non-toric (DIB00)

B. Study Design: Prospective, multicenter (up to 2 sites in USA), randomized, patient-masked bilateral eye study.

C. **Subjects:** A total of 74 subjects who met the Inclusion/Exclusion criteria will be enrolled.

1. Inclusion Criteria:

Subjects **MUST** fulfill the following conditions to qualify for enrollment into the trial

1. Subject is undergoing bilateral cataract extraction with intraocular lens implantation.
2. Gender: Males and Females.
3. Age: 50 years and older.
4. Willing and able to provide written informed consent for participation in the study
5. Willing and able to comply with scheduled visits and other study procedures.
6. Scheduled to undergo standard cataract surgery in both eyes within 6 - 30 days between surgeries.
7. Subjects who require an IOL power in the range of +5.0 D to +34.0 D only.
8. Potential postoperative visual acuity of 0.2 logMAR (20/32 Snellen) or better in both eyes.

2. Exclusion Criteria:

Subjects with **ANY** of the following conditions on the eligibility exam may **NOT** be enrolled into the trial.

1. Severe preoperative ocular pathology: amblyopia, rubella cataract, proliferative diabetic retinopathy, shallow anterior chamber, macular edema, retinal detachment, aniridia or iris atrophy, uveitis, history of iritis, iris neovascularization, medically uncontrolled glaucoma, microphthalmos or macrophthalmos, optic nerve atrophy, macular degeneration (with anticipated best postoperative visual acuity less than 20/30), advanced glaucomatous damage, etc.
2. Uncontrolled diabetes.
3. Use of any systemic or topical drug known to interfere with visual performance.
4. Contact lens use during the active treatment portion of the trial.
5. Any concurrent infectious/non-infectious conjunctivitis, keratitis or uveitis.
6. Clinically significant corneal dystrophy.
7. Irregular astigmatism.
8. History of chronic intraocular inflammation.
9. History of retinal detachment.
10. Pseudoexfoliation syndrome or any other condition that has the potential to weaken the zonules.
11. Previous intraocular surgery.
12. Previous refractive surgery.
13. Previous keratoplasty
14. Severe dry eye
15. Pupil abnormalities

16. Subject who may reasonably be expected to require a secondary surgical intervention at any time during the study (other than YAG capsulotomy, i.e. LASIK)
17. Anesthesia other than topical anesthesia (i.e. retrobulbar, general, etc).
18. Any clinically significant, serious or severe medical or psychiatric condition that may increase the risk associated with study participation or may interfere with the interpretation of study results.
19. Participation in (or current participation) any ophthalmic investigational drug or ophthalmic device trial within the previous 30 days prior to the start date of this trial.

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

3. Exclusion Criteria during surgery

If any of the following exclusion criteria are applicable to the study eye, the subject should not continue in the study.

1. Other planned ocular surgery procedures, i.e iStent.
2. Significant vitreous loss.
3. Significant anterior chamber hyphema.
4. Uncontrollable intraocular pressure.
5. Zonular or capsular rupture.
6. Bag-sulcus, sulcus-sulcus or unknown placement of the haptics.
7. Suturing of incision required at time of surgery.
8. Intraocular lens tilt or decentration
9. Significant sedation or retrobulbar block during surgery.
10. Other procedure, such as pupil stretch, expanders, iris hooks during surgery.

Note: Any subject in which surgery has been aborted for either eye should immediately be discontinued from the study and an exit form completed for that subject. These subjects will be followed up as per the clinic standard of care, monitored for safety, and their data will be excluded from the study efficacy analysis (obtained from FDA Database Research Results Feb, 05, 2009). All adverse events will be appropriately documented and reported.

Additionally, participants who are considered to be a vulnerable subject population are not to be enrolled into the study without prior written authorization from both the Sponsor and the IRB to ensure that a description of additional safeguards are in place during the consenting and enrollment processes. Vulnerable populations include, but are not limited to, the following:

1. Prisoners
2. Nursing home residents /institutionalized individuals
3. Mentally disabled /cognitively impaired individuals
4. Sponsor employees and their family members
5. Site employees and their family members that are directly and indirectly involved with the study
6. Students of the university or the principal investigator participating in the study

7. Economically and/or educationally disadvantaged individuals
8. Comatose individuals / traumatized individuals
9. Adults who do not read and/or write
10. Hearing impaired individuals
11. Terminally ill individuals / individuals with life-threatening conditions

3. Study Procedures

A. Informed Consent / Subject enrollment

Potential subjects will be identified from the patients presenting at the clinic. Additionally, an ad will be placed in social media and in the practice website, if deemed necessary. Once identified as a study candidate, the patient will be asked if he/she would like to participate. The sub-investigator, study coordinator or an appropriately trained staff member will answer any and all questions and will obtain informed consent. A copy of the signed informed consent document will be given to the subject. The principal investigator will be available if the subject wants to discuss further details with him. Any testing that is part of the investigative site's standard preoperative cataract evaluation may be performed prior to the informed consent being signed, provided these tests are conducted within 90 days of surgery. The patient will understand that participation in the study, or declining to participate, will not affect his/her quality of care.

No subject will be enrolled into the study that 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 research records.

B. Surgery Procedures:

Patients will be randomized to one of two groups:

- Group A, plano OU. The target refraction for both eyes will be emmetropia (± 0.25 D).
- Group B, mini monovision. The target refraction for the dominant eye will be plano (± 0.25 D) and for the non-dominant eye between -0.75D ±0.15.

C. Study Visit Schedule and Assessments (Table 1).

1. Visit Schedule: Subjects will be examined at the following intervals:

1. Visit 1: Screening and enrollment: Preoperative evaluation completed not more than eight weeks before surgery
2. Visit 2: Day of Surgery
3. Visit 3: Day 1: (12 to 48 hours) after surgery
4. Visit 4: Month 1: 30 ±7 days postoperative after second eye surgery
4. Visit 5: Month 3: 90 ±15 days postoperative after second eye surgery

D. Measurements and evaluations

1. Visit 1: Informed consent process will be conducted at this visit. Assessments include best-corrected distance visual acuity (BCDVA, Snellen chart), manifest refraction, intraocular pressure (IOP), corneal topography (if astigmatism correction), eye dominance, slit lamp examination including dilated fundus exam, cataract density and type. Any testing that is part of the site's standard of care preoperative cataract surgery evaluation may be performed prior to the informed consent being signed provided these tests are conducted within 90 days of the surgery and notation of the date performed is entered onto the CRF. The surgeon's standard pre cataract surgery treatment will be used in all his patients

   Each subject will be randomized to Group A (emmetropia OU) or B (mini monovision). Randomization will ensure that an equal number of subjects are enrolled in each group.

2. Visit 2: The surgeon may use his preferred small incision cataract extraction technique (manual phacoemulsification or laser assisted). The assigned lens will be implanted in the bag. The following information will be captured the day of surgery: phaco technique (manual or laser), lens implanted and power, target refraction for IOL power implanted, additional surgical procedures, intraoperative complications, and any device deficiencies. The surgeon's standard post cataract surgery treatment will be used in all his patients. IOL power changes based on intraoperative aberrometry (i.e., ORA) are not allowed.

3. Visit 3: monocular UCVA (Snellen), slit lamp examination, IOP, and lens orientation (if toric lens and deem necessary by the investigator) and any device deficiencies.

4. Visit 4: Slit lamp examination, manifest refraction, monocular and binocular UCDVA, BCDVA, UCIVA (at 66 cm), DCIVA (at 66 cm), UCNVA (at 40 cm), and DCNVA (at 40), IOP, IOL orientation (if toric lens) and dilated fundus exam as deemed necessary by the investigator, patient satisfaction, visual symptoms and spectacle independence questionnaires, and any device deficiencies.

5. Visit 5: Slit lamp examination, manifest refraction, binocular UCDVA, BCDVA, UCIVA (at 66 cm), DCIVA (at 66 cm), UCNVA (at 40 cm), DCNVA (at 40), and DCNVA at best distance, binocular low contrast (10%) photopic and mesopic BCDVA, DC binocular defocus curve, IOL orientation (if toric lens) and dilated fundus exam as deemed necessary by the investigator, patient satisfaction, visual symptoms and spectacle independence questionnaires, and any device deficiencies.

DC: distance corrected. DC, for the purpose of this study, is defined as corrected for the target refraction (i.e. emmetropia OU corrected for plano. Mini monovison dominant eye corrected for plano and the non-dominant eye for -0.75).

All adverse events and complaints will be monitored and recorded at all study visits.

Table 1. Visits and Study Assessments

	Visit 1 Screening	Visit 2/2A DOS	Visit 3/3A POD #1	Visit 4 1-Month	Visit 5 3-Month
Informed Consent	X				
Inclusion/Exclusion	X				
Demographics/PMH/Ocular history	X				
Eye dominance	X				
BCVA (Standard of care, Snellen)	X				
UCVA (Standard of care, Snellen)			X		
UCVA ETDRS (4m)				X*	X**
Manifest refraction – Max Plus				X	X
BCVA ETDRS (4m)				X*	X**
UCIVA ETDRS (66 cm)				X*	X**
DCIVA ETDRS (66 cm)				X*	X**
UCNVA ETDRS (40 cm)				X*	X**
DCNVA ETDRS (40 cm)				X*	X**
DCNVA at best distance					X**
DCVA Photopic low contrast (10%)					X**
DCVA Mesopic low contrast (10%)					X**
Defocus curve					X**
Intraocular Pressure (Standard of care)	X		X	X	
SLE	X		X	X	X
Dilated fundus exam	X			X‡	X‡
Cataract density / type	X				
Corneal topography¥	X				
Intraoperative data		X			
Toric IOL position		X†	X†‡	X†‡	X‡
Questionnaires	X			X	X
AE/Device deficiencies		X	X	X	X

X To be performed as scheduled
* Monocular and binocular testing
** Binocular testing only
‡ To be performed as deem necessary by the investigator.
† If toric lens
¥ If astigmatism correction (toric or corneal arcuates)

DC: distance corrected. DC, for the purpose of this study, is defined as corrected for the target refraction (i.e. emmetropia OU corrected for plano. Mini monovison dominant eye corrected for plano and the non-dominant eye for -0.75).

4. Study endpoint criteria

A. Patient Completion of Study: If a study patient has completed the final visit (Visit 5) of the study, he/she is considered to have completed the study.

B. 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.

C. 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.

D. 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.

E. Study Completion: The study will be complete when all enrolled patients have completed Visit 5 or have been terminated from the study.

5. STATISTICAL CONSIDERATIONS

A. Sample size

The sample size estimates depend in large part on the standard deviation (SD) for logMAR UCIVA. Assuming a SD of 0.12 (from a previous Eyhance study), for the two-sided t-test (alpha =0.05) for the intermediate visual acuity endpoint, we will need 31 subjects in each group (emmetropia / mini monovision) to detect differences of 0.1 logMAR (1 line difference) with 90% power. Total sample size = 62. Allowing 10 % for the potential confounding factor of having 2 sites, and 10% assumed dropout rate, 74 subjects will be enrolled (37 in each group). Table 2 summarizes the sample size estimate.

Table 2. Sample size estimate.

	TOTAL	Mini monovision	Emmetropia
Sample size	62	31	31
10% multiple sites	6	3	3

10% dropout rate	6	3	3
Total sample size	**74**	**37**	**37**

B. Statistical Analysis

All data will be collected by the site and entered into a database. Subjects will be assigned an ID number. Data analysis will be performed without patient identification. Statistical analysis will be performed using standard descriptive statistics and other tests as deemed appropriate based on the characteristics of the data to be analyzed. All statistical tests will be two-sided and interpreted at a 5% significance level. Comparisons between the groups will be made. Data analysis will be conducted by a third-party consultant.

C. Study Endpoints:

Comparisons between the groups:

1. Primary Endpoints:

Binocular distance-corrected intermediate (66 cm) visual acuity at 3 months. Distance corrected. DC, for the purpose of this study, is defined as corrected for the target refraction (i.e. emmetropia OU corrected for plano. Mini monovison dominant eye corrected for plano and the non-dominant eye for -0.75).

2. Secondary Endpoints:

1. Binocular defocus curve at 3 months
2. Binocular low contrast distance visual acuity at 3 months
3. Uncorrected and distance-corrected near (40 cm) visual acuity at 1 and 3 months
4. Uncorrected and distance-corrected intermediate (66 cm) visual acuity at 1 and 3 months
5. Uncorrected and best-corrected distance (4 m) visual acuity at 1 and 3 months
6. Distance-corrected near visual acuity at best distance at 3 months
7. To evaluate patient's overall satisfaction of their vision
8. To evaluate patient's spectacle independence
9. To evaluate visual symptoms using a questionnaire.
10. Residual mean spherical equivalent refraction at 3 months
11. Residual refractive sphere at 3 months
12. Residual refractive cylinder at 3 months
13. Percentage of eyes with postoperative MRSE accuracy to target ≤ 0.5D at 3 months

D. Safety Analyses

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

treatment-related. Comparison of treatment groups with respect to the proportion of study patients reporting adverse events will be made using Fisher's Exact Test.

6. DATA HANDLING AND RECORD KEEPING

A. Confidentiality

To ensure confidentiality in this study, records of the participants will be examined only by the principal investigator and research staff involved in the study. Study records will be kept on file at each site. Any statistical analysis and publication will not include any subject identifiers. Medical records will be made available only for review by the investigators, study Monitor or Auditor, Sponsor Company or Research Institution, the IRB, and other State or Federal Regulatory Agencies, if necessary. All information in these records will be kept confidential.

B. Records Retention

The PI is accountable for the integrity, retention and security of all study related data. The investigator must maintain accurate, complete and current records relating to the clinical study. The investigator must maintain the required records during the investigation and for a period of 3 year after the date on which the investigation is terminated or completed.

7. STUDY MONITORING, AUDITING, AND INSPECTING

The nature and location of all source documents will be identified to ensure that original data required to complete the case report forms (CRFs) exist and are accessible for verification by the monitor. If electronic source records are maintained, these records must be 21 CFR Part 11 compliant and will be printed and certified for verification by the monitor as needed.

Required examination must be recorded on the CRFs. Provided CRFs can be used as source document. All data reported must have corresponding entries in the source documents. The principal investigator or sub-investigator must review the reported data and certify that the CRFs are accurate and complete. No subject identifiers should be recorded on the CRFs beyond subject number, subject initials and study specific identifiers.

Data from CRFs will be entered into a database provided to each site, site will email the password protected file to the study manager with the CRFs for remote monitoring. Additionally, monitoring site visits will be made by the study manager throughout the study.

Upon completion of the CRFs, the data will be reviewed by study manager and statistician for accuracy and completeness. If corrections and/or any additions to the data are deemed

necessary, queries will be generated and forwarded to the investigative site. Designated research staff is expected to respond to data queries in a timely manner and ensure that the corrections and changes made to the data in the database are reflected in the subjects' source documentation. Any changes will need to be initialed and dated by the authorized personnel making such changes.
Data will not be sold to third parties nor will it be used for future research.
Electronic data will be stored and accessed on a portable device. The laptop is password protected and only the study manager has access to it. Additionally, database will be password protected.

8. INVESTIGATIONAL PRODUCT

A. Description

The Eyhance IOLs (DIB00 and DIUxxx) are monofocal refractive IOLs designed to enhance intermediate distance vision without compromising distance vision. The lens power continuously increases from its edge to the center extending the range of vision when compared to a standard monofocal IOL.

B. Treatment/Dosing Regimen

The Tecnis Eyhance IOL is intended for primary implantation for the visual correction of aphakia secondary to removal of a cataractous lens in adult patients. The IOL will be implanted at time of uncomplicated routine cataract surgery. Intraocular lenses are implantable medical devices and are intended for long term use over the lifetime of the patient.

C. Method for Assigning Subjects to Treatment/Dosing Groups

Each site will be provided with randomization envelopes. The envelopes will be sequentially numbered.

D. Subject Compliance Monitoring

Since the IOL is implanted at time of cataract surgery, subject compliance will not be an issue in this particular study.

E. Packaging, Receiving, Storage, Dispensing and Return

An account will be set up with the manufacturer of the lens (Johnson and Johnson Vision) that will provide the lens at no cost to the participants. IOLs will be ordered once the subject's qualification for the study has been confirmed. IOLs will be shipped to the site and will be stored and dispensed following the routine standard of care for cataract surgery. Unused IOLs will be returned to Johnson and Johnson Vision following their instructions.

Or, Johnson and Johnson Vision will provide a consignment of lenses that will be stored at the site and unused IOLs will be returned to Johnson and Johnson Vision following their instructions at the

end of the study.

In both instances, an implantation log will be kept.

9. ETHICAL CONSIDERATION

This clinical trial will be conducted in accordance with the principles of the Declaration of Helsinki, and Good clinical practice. The Investigator and all clinical trial staff will conduct the clinical trial in compliance with this protocol. The Investigator will ensure that all personnel involved in the conduct of the clinical trial are qualified to perform their assigned duties through relevant education, training, and experience. Deviations from the clinical protocol must be documented in each subject's study records including the dates and reasons for each deviation. The PI must ensure that all aspects of the trial are in compliance with the applicable regulatory laws and conditions of approval imposed by the IRB.

10. RISKS AND BENEFITS

The risk of being in the study is not greater than the risk of undergoing routine cataract surgery with implantation of monofocal intraocular lenses. However, there is always the risk that uncommon or previously unknown side effects may occur. The study includes additional postoperative examinations at no cost.

11. IN CASE OF AN INJURY RELATED TO THIS RESEARCH STUDY

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 instructions and requirements, the patient will be instructed to immediately contact the principal investigator and/or study staff. Treatment will be provided as needed for those injuries caused directly by this research study. In the event of injury or illness caused by or occurring during the participation in this study, all charges for medical care provided will be billed to the patient's insurance company. The medical care costs for injuries or illnesses that are not caused directly by the research study will not be covered.

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.

13. REFERENCES

1. Auffarth GU, Gerl M, Tsai L et l. Clinical evaluation of a new monofocal intraocular lens with enhanced intermediate function in cataract patients. J Cataract Refract Surg. 2021; 47:184 – 191

A. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P980040S117