Evaluating the new Synergy IOL - First 7 months data from Two US centers

Sponsor:	Center for Sight 2601 S Tamiami Trail Sarasota, FL 34239 (941) 925 2020 / (843) 881 3937
Principal Investigator:	Joaquin O. De Rojas, MD
Project Manager:	Helga P. Sandoval, MD, MSCR, Director of Research
Study Product:	JJV – Synergy IOL (DR00V or DFW150-375 – Synergy Toric II IOL) using TECNIS Simplicity Delivery System
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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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Presbyopia-correcting intraocular lenses (IOLs) have evolved rapidly in recent years. Such IOLs include extended depth of focus (EDOF) and multifocal (MF) IOLs. The ultimate goal of these lenses and their various iterations over time has been to provide an excellent range of focus at distance, intermediate, and near distances, good quality of vision and contrast sensitivity under different lighting conditions, good reading ability, and the minimization of photic phenomena.

The TECNIS Synergy IOL is a one-piece presbyopia-correcting IOL available in non-toric and toric versions that was introduced to the US market in June 2021. At our center, we were the first site in the US to implant the Synergy (June 7, 2021) and have been using the IOL ever since. This Synergy IOL is part of the TECNIS platform, which is composed of time-tested hydrophobic acrylic material with ultraviolet and violet light absorber, 6-mm aspheric optic, refractive index of 1.47, and continuous 360 ° posterior square edge design. The company boasts that the new Synergy IOL combines the benefits from the TECNIS Multifocal and TECNIS Symfony (EDOF) diffractive designs, and that it delivers a wider range of continuous vision and better near vision in day and night than a leading trifocal IOL.[1]

To date, there have been only a few investigator-initiated studies that have evaluated the clinical outcomes of the Synergy, but none of these studies have been US-based, nor have they featured a large number of subjects.[2-4]

We propose conducting a prospective evaluation of Synergy outcomes that will feature our first 7 months of data collected at our two high-volume, US-based cataract practices. We expect that this analysis will be the first of its kind and will be useful for US cataract surgeons who are considering implementing the Synergy lens in their practice.

1. OBJECTIVE:

To evaluate the visual outcomes in patients with and without astigmatism who underwent uneventful phacoemulsification and bilateral implantation of the TECNIS Synergy IOL.

2. STUDY DESIGN AND METHODS:

A. Test article: Tecnis Synergy Intraocular lens Toric (DFWXXX) and non-toric (DFR00V) using TECNIS Simplicity Delivery System

B. Study Design: Ambispective, multicenter (up to 2 sites in USA), non-therapeutic, single-visit study.

C. Subjects: All consecutive patients who underwent uneventful routine femtosecond assisted laser lens removal and implantation of the Synergy IOL between June 01, 2021 and December 31, 2021 (up to 100 patients) who meet the Inclusion/Exclusion criteria will be enrolled.

1. Inclusion Criteria:

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

1. Age: 18 years and older.
2. Gender: Males and Females.
3. Uneventful bilateral, femtosecond laser assisted lens extraction
4. Bilateral implantation of Synergy IOLs (toric and non-toric) by 5 anterior segment surgeons at Center For Sight (DWS, WJL, JWK, WLS, and JOD) and 1 surgeon at Carolina Eyecare Physicians (KDS) through the months of June to December 2021.
5. Willing and able to provide written informed consent for participation in the study.
6. Willing and able to comply with scheduled visit and study examination procedures.
7. Available Macular OCT, IOLMaster700, and Pentacam obtained preoperatively.
8. At least 3 months postoperative from second eye IOL implantation.
9. Postoperative best corrected 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. Established ocular pathology, including: glaucoma (except glaucoma suspects), uveitis, and clinically-significant retinal pathology affecting the macula (with visual acuity worse than 20/32) and/or any other ocular findings that may, in the opinion of the investigator, affect vision.
2. Uncontrolled diabetes.
3. Use of any systemic or topical drug known to interfere with visual performance.
4. Any concurrent infectious/non-infectious conjunctivitis, keratitis or uveitis.
5. Clinically significant corneal dystrophy.
6. Irregular astigmatism.
7. History of chronic intraocular inflammation.
8. Previous intraocular surgery.
9. Previous keratoplasty
10. Previous refractive surgery.
11. Severe dry eye
12. Pupil abnormalities
13. Any clinically significant, serious or severe medical or psychiatric condition that may interfere with the interpretation of study results.
14. 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.
15. Best-corrected distance visual acuity worse than 20/32 in each eye.
16. Inability to focus or fixate for prolonged periods of time (e.g., due to strabismus, nystagmus, etc.)
17. Abnormal iris
18. Patients who had a complication during cataract surgery, which could include ruptured zonules, torn capsule, or vitrectomy.

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.

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 presenting at the clinic. Additionally, surgery scheduled will be queried to identify patients implanted with the Synergy lens. Once identified as a study candidate, the patient will be asked if he/she would like to participate. The 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 investigators will be available if the subject wants to discuss further details with him. 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. Study Visit Schedule and Assessments (Table 1).

1. **Visit Schedule:**

All subjects enrolled in the study are intended to have undergone uneventful bilateral femtosecond laser assisted cataract surgery with Synergy IOL implantation at least 3 months prior to study visit. Subjects will complete one study visit that can be divided to be completed over two days to accommodate subject fatigue, if necessary.

C. Measurements and evaluations:

Data from routine examination performed prior to the informed consent process may be used to identify potential eligible subjects (e.g., subject chart notes from previous examination documented presence of IOL, and Snellen BCDVA recorded as 20/30 or better in both eyes). However, subject eligibility must be confirmed by collection of new data during the screening and study procedures.

1. Informed consent process will be conducted at this visit. Assessments (Table 1) include:
    a. Slit lamp examination
    b. Manifest refraction
    c. Monocular and binocular uncorrected (UC) and best-corrected distance visual acuity (VA) at 4 m.
    d. Binocular low contrast (10%) photopic and mesopic BCDVA.
    e. Binocular UCIVA (at 66 cm), DCIVA (at 66 cm), UCNVA (at 33 and 40 cm), and DCNVA (at 33 and 40 cm) under photopic and mesopic conditions.
    f. Binocular DC reading speed under photopic and mesopic conditions at 40 cm.
    g. Pupil size under photopic and mesopic conditions
    h. Posterior capsule opacification (PCO) evaluation.
    i. Patient satisfaction, spectacle independence, visual symptoms, and functional vision questionnaires.

All adverse events and complaints will be monitored and recorded at the study visit.

Table 1. Visits and Study Assessments

	Visit 1 Study visit
Informed Consent	X
Inclusion/Exclusion	X
Demographics	X
Manifest refraction – Max Plus	X
UCVA ETDRS (4m)	X*
BCVA ETDRS (4m)	X*
BCVA Photopic low contrast (10%) at 4 m	X**
BCVA Mesopic low contrast (10%) at 4 m	X**
UCIVA ETDRS (66 cm) under photopic conditions	X**
DCIVA ETDRS (66 cm) under photopic conditions	X**
UCNVA ETDRS (40 cm) under photopic conditions	X**
DCNVA ETDRS (40 cm) under photopic conditions	X**
UCNVA ETDRS (33 cm) under photopic conditions	X**
DCNVA ETDRS (33 cm) under photopic conditions	X**
UCIVA ETDRS (66 cm) under mesopic conditions	X**

DCIVA ETDRS (66 cm) under mesopic conditions	X**
UCNVA ETDRS (40 cm) under mesopic conditions	X**
DCNVA ETDRS (40 cm) under mesopic conditions	X**
UCNVA ETDRS (33 cm) under mesopic conditions	X**
DCNVA ETDRS (33 cm) under mesopic conditions	X**
Reading speed at 40 cm under photopic conditions	X**
Reading speed at 40 cm under mesopic conditions	X**
Pupil size under photopic conditions	X
Pupil size under mesopic conditions	X
SLE	X
Dilated fundus exam	X‡
Preoperative data (Macular OCT, IOL Master700 and Pentacam)	X¥
Intraoperative data (IOL type, IOL power, target refraction, formula used to calculate IOL power, if toric IOL, final axis placement, estimated residual astigmatism and axis)	X
PCO evaluation	X
Toric IOL position	X‡
Questionnaires and non-directed complaints	X
AE/Device deficiencies	X

X To be performed as scheduled
* Monocular and binocular testing
** Binocular testing only
‡ To be performed as deem necessary by the investigator.
¥ If available

4. Study endpoint criteria

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

B. Study Completion: The study will be complete when all subjects are enrolled and have completed the study visit.

5. STATISTICAL CONSIDERATIONS

A. **Sample size**
As a single-arm study designed to provide normative results for the lens, there is no relevant sample size calculation. Some subgroup analysis is desirable (e.g., toric vs. non-toric, photopic vs. mesopic results, differences by surgeon and/or site). It is expected that 100 subjects (200 eyes) will be sufficient to allow this type of subgroup analysis.

B. Statistical Analysis

All data will be collected by each 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. Data analysis will be conducted by a third-party consultant.

C. Study Endpoints:

1. Primary Endpoints:

1. Binocular distance corrected near visual acuity at 40 cm under photopic conditions
2. Binocular distance corrected near visual acuity at 40 cm mesopic conditions

2. Secondary Endpoints:

1. Binocular low contrast distance visual acuity under photopic and mesopic conditions
2. Uncorrected and distance-corrected near (40 cm) visual acuity
3. Uncorrected and distance-corrected intermediate (66 cm) visual acuity
4. Uncorrected and best-corrected distance (4 m) visual acuity
5. Distance-corrected near visual acuity at best distance
6. Non-directed complaints
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. To evaluate the functional vision questionnaire
11. Residual mean spherical equivalent refraction
12. Residual refractive sphere
13. Residual refractive cylinder
14. Percentage of eyes with postoperative MRSE accuracy to target ≤ 0.5D

D. 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. 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, sub-investigator(s) 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 years 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 project manager.

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. Databases will be saved on the site's server. The project manager has access to such server for remote monitoring. Additionally, on-site monitoring visits will be made by the project 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. It may 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, access to the server requires a user specific password. The database will be password protected when sending to statistician.

8. INVESTIGATIONAL PRODUCT

A. Description

The Synergy IOL (DR00V or DFW150-375 – Synergy Toric II IOL) using TECNIS Simplicity Delivery System is a presbyopia correcting IOL designed to improve intermediate and near vision, while maintaining distance visual acuity. The lens provides a full range of vision and increased spectacle independence.

B. Treatment/Dosing Regimen

The Tecnis Synergy IOL is intended for primary implantation for the visual correction of aphakia secondary to removal of a cataractous lens in adult patients. The IOL was already implanted at time of the 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

N/A

D. Subject Compliance Monitoring

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

E. Packaging, Receiving, Storage, Dispensing and Return

N/A

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 eye exam. However, there is always the risk that uncommon or previously unknown side effects may occur.

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. TECNIS Synergy Value Brief, Johnson & Johnson Surgical Vision. 2021.
2. Ferreira TB, Ribeiro FJ, Silva D, Matos AC, Gaspar S, Almeida S. Comparison of Refractive and Visual Outcomes of Three Presbyopia-Correcting Intraocular Lenses. *J Cataract Refract Surg.* 2021.
3. Gabric N, Gabric I, Gabric K, Biscevic A, Pinero DP, Bohac M. Clinical Outcomes With a New Continuous Range of Vision Presbyopia-Correcting Intraocular Lens. *J Refract Surg.* 2021;37(4):256-262.
4. Palomino-Bautista C, Sanchez-Jean R, Carmona-Gonzalez D, Pinero DP, Molina-Martin A. Depth of field measures in pseudophakic eyes implanted with different type of presbyopia-correcting IOLS. *Sci Rep.* 2021;11(1):12081.