Evaluating A Novel Strategy: The Synergy IOL Mixed and Matched with the Symfony with Intelilight

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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: _____
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Investigator: _____
Signature Date

EVALUATING A NOVEL STRATEGY: THE SYNERGY IOL MIXED AND MATCHED WITH THE SYMFONY WITH INTELILIGHT

Presbyopia-correcting intraocular lenses (IOLs) have evolved rapidly in recent years. Such IOLs include extended depth of focus (EDOF) and multifocal (MF) IOLs. The 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]

Early reports from many centers across the country and other countries appear to indicate that the Synergy IOL implanted bilaterally is yielding very good results at all ranges, particularly at near.[2-4] Anecdotally, some surgeons have reported excellent near vision with good but not great distance vision.

Prior to utilizing the Synergy IOL, our center along with many high-volume centers across the country, employed a mix and match strategy utilizing the TECNIS Symfony in the dominant eye and the TECNIS Multifocal in the non-dominant eye with good results and high patient satisfaction.[5]

We propose conducting a prospective evaluation of a mix and match strategy incorporating Symfony with InteliLight in the dominant eye and Synergy IOL in the non-dominant eye. The Symfony lens, an Extended Depth of Focus (EDOF) lens, known for its superior distance and intermediate vision, has been upgraded to the OptiBlue version (InteliLight). The Symfony with InteliLight has an enhanced echelette design and a violet light filter. The upgraded echelette design utilizes a high-resolution lathing process that helps reduce light scatter and halo intensity. The violet light filter is designed to mitigate halo, glare, and starbursts.

1. OBJECTIVE:

The purpose of this study is to evaluate the visual outcomes, visual disturbances, patient satisfaction and spectacle independence of the Symfony with InteliLight when implanted in

the dominant eye and a Synergy is implanted in the non-dominant eye in patients with or without astigmatism after routine cataract surgery.

2. STUDY ENDPOINTS:

1. Primary Endpoints:

Binocular defocus curve at 3 months

2. Secondary Endpoints:

a. Monocular and binocular uncorrected and distance-corrected near at 40 cm visual acuity at 3 months.
b. Monocular and binocular uncorrected and distance-corrected near at 33 cm visual acuity at 3 months
c. Monocular and binocular uncorrected and distance-corrected intermediate (66 cm) visual acuity at 3 months
d. Monocular and binocular uncorrected and best-corrected distance (4 m) visual acuity at 3 months
e. To evaluate patient's vision satisfaction at 3 months
f. To evaluate patient's spectacle independence at 3 months
g. To evaluate visual symptoms using a questionnaire at 3 months
h. To evaluate functional vision using a questionnaire at 3 months

3. STUDY DESIGN:

Prospective, multicenter (up to 2 site in US), non-randomized, bilateral eye study.

4. INCLUSION/EXCLUSION CRITERIA

4.1. Inclusion Criteria:

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

1. Subject is undergoing bilateral lens extraction with intraocular lens implantation of the Symfony with InteliLight in the dominant eye and a Synergy in the non-dominant eye.
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 with topical anesthesia in both eyes within 2 to 30 days between surgeries
7. Subjects who require an IOL power in the range of +5.00 D to +34.0 D only.
8. Subjects who require a toric IOL up to +3.75 D at the IOL plane (2.57 D corneal plane).
9. Potential postoperative visual acuity of 0.2 logMAR (20/32 Snellen) or better in both eyes.

4.2. 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. History of chronic intraocular inflammation.
8. History of retinal detachment.
9. Pseudoexfoliation syndrome or any other condition that has the potential to weaken the zonules.
10. Previous intraocular surgery.
11. Previous corneal refractive surgery (i.e. LASIK, PRK, RK).
12. Previous keratoplasty
13. Severe dry eye
14. Pupil abnormalities
15. Anesthesia other than topical or peribulbar anesthesia (i.e. retrobulbar, general, etc).
16. 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.
17. 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.

4.3. Exclusion Criteria at time of surgery:

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

1. Other ocular surgery procedures, i.e. iStent, anterior vitrectomy
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

5. STUDY PROCEDURES

5.1. Subject enrollment

Potential subjects will be identified from the patients presenting at the clinic. Additionally, a flyer will be placed in the check-in area and/or the in-house TV's of the different locations, on the practices website and social media as deem necessary. Once identified as a study candidate, the patient will be asked if he/she would like to participate. The sub-investigator(s), study coordinator or an appropriately trained staff member will answer any and all questions and will obtain informed consent. A copy of the 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 patient given consent, 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 consent to be enrolled in the study. Informed consent will be obtained prior to collecting any data for the study. The original documents will be maintained by the investigator as a permanent part of the subject's research records and a copy will be provided to the patient.

5.2. Informed consent:

Subjects will be consented either in person in the office or verbally over the phone.

- In person consent process: Patients being considered for enrollment who are consented in the office will be required to sign the ICF agreeing to participate in the study. A copy of the signed consent form will be given to the subject.
- Over the phone consent process: Site staff delegated to perform the informed consent process along with a witness will sign the ICF. Subject will be asked to sign the consent during visit 2. A copy of the signed consent form will be given to the subject.

5.3. Surgery Procedures:

Subjects will be implanted with the Symfony with IntelliLight in the dominant eye and a Synergy lens in the non-dominant eye. Patients will receive either a non-toric or toric IOL based on the amount of astigmatism. The target refraction for both eyes will be closest to plano.

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

5.4.1. 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 for each eye
3. Visit 3: Month 3: 90 ±15 days postoperative after second eye surgery

5.4.2. Measurements and evaluations

1. Visit 1: Informed consent process will be conducted at this visit. Assessments include best-corrected Snellen visual acuity, intraocular pressure (IOP), slit lamp examination including dilated fundus exam, cataract density and type, and visual symptoms, patient satisfaction, spectacle independence and visual function

questionnaires. Any testing that is part of the site's preoperative cataract surgery standard of care evaluation may be performed prior to signing the informed consent 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 patients

2. Visit 2: The surgeon may use his preferred cataract extraction technique (manual or laser). The 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, residual astigmatism and axis for Toric Calculator (if applicable), additional surgical procedures, intraoperative complications, and any device deficiencies. The surgeon's standard post cataract surgery treatment will be used in all patients.

Visit 3: Slit lamp examination, manifest refraction, monocular and binocular uncorrected as well as distance corrected visual acuities will be evaluated at 4 m, 66 cm, 40 cm, 33 cm and best distance, and defocus curve. Additionally, dilated fundus exam (as deem necessary by the investigator), visual symptoms, patient satisfaction, spectacle independence and visual function questionnaires, adverse events and any device deficiencies will be evaluated.

Table 1. Study Visit Schedule and Assessments

	Visit 1 Screening	Visit 2 and 2A DOS	Visit 3 3-Month 90 ±15 days
Informed Consent	X		
Inclusion/Exclusion	X	X	
Demographics/Ocular history	X		
BCVA Snellen	X		
Eye dominance	X		
UCVA ETDRS (4m)			X*
UCIVA ETDRS (66 cm)			X*
UCNVA ETDRS (40 cm)			X*
UCNVA ETDRS (33 cm)			X*
UCNVA ETDRS (at best distance)			X*
Manifest refraction – Max Plus			X
BCVA ETDRS (4m)			X*
DCIVA ETDRS (66 cm)			X*

DCNVA ETDRS (40 cm)			X*
DCNVA ETDRS (33 cm)			X*
DCNVA ETDRS (at best distance)			X*
Defocus curve			X**
SLE	X		X
Intraocular pressure	X		
Dilated fundus exam	X		X†
Cataract density / type	X		
Intraoperative data		X	
Toric IOL position		X	X†
Questionnaires	X		X
AE/Device deficiencies		X	X

X To be performed as scheduled
* Monocular and binocular testing
** Binocular testing only
†To be performed as deem necessary by the investigator.
DC: distance corrected.

5.5. Study endpoint criteria

5.5.1. Patient Completion of Study: If a study patient has completed the final visit (Visit 3) of the study, he/she is considered to have completed the study.

5.5.2. 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. Subjects who are discontinued after first eye surgery before second eye surgery will also be replaced.

5.5.3. 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.

5.5.4. 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.

5.5.5. Study Completion: The study will be complete when all enrolled patients have completed Visit 3 or have been terminated from the study.

6. STATISTICAL CONSIDERATIONS

6.1. Sample size

A total of 40 subjects will be enrolled. In order to calculate the sample size, we need to know an accurate estimate of the standard deviation of the outcome measure which we do not know; therefore, we consider this study a pilot trial. When estimating the sample size for a pilot study, the simplest method is to apply a sample size rule of thumb. Browne suggests a general flat rule to 'use at least 30 subjects or greater to estimate a parameter'.

6.2. 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. Vision satisfaction, spectacle independence and visual symptoms will be compared to a historical control of patients implanted bilaterally with Synergy OU. Data analysis will be conducted by a third-party consultant.

6.3. 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.

7. DATA HANDLING AND RECORD KEEPING

7.1. 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. Any statistical analysis and publication will not include any subject identifiers. Medical records will be made available only for review by the investigators, 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.

7.2. 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 2 years after the date on which the investigation is terminated or completed then records will be scanned and kept electronically in a secured server.

8. 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. If electronic source records are maintained, these records must be 21 CFR Part 11 compliant and will be printed and certified for verification as needed.

Required examination must be recorded on the CRFs. CRFs will 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. Upon completion of the CRFs, the data will be reviewed by study designated personnel and statistician for accuracy and completeness. If corrections and/or any additions to the data are deemed necessary, queries will be generated. Designated research staff 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.

9. INVESTIGATIONAL PRODUCT

9.1. Description

The Symfony InteliLight IOL (DXR00V or DXW150 – 375 – Toric II IOL) combines an echelette design (to create an extended depth of focus) with an achromatic technology (to correct chromatic aberrations) and a violet-light filter that diminishes the perception of visual disturbances such as halo, glare and starburst. The lens has been designed to provide high quality vision up to 26 inches so patients may still need to wear glasses for some activities mainly at near.

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. This continuous range of focus lens provides a full range of vision and increased spectacle independence.

9.2. Treatment/Dosing Regimen

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.

9.3. Method for Assigning Subjects to Treatment/Dosing Groups

N/A

9.4. Subject Compliance Monitoring

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

9.5. Packaging, Receiving, Storage, Dispensing and Return

N/A

10. ETHICAL CONSIDERATIONS

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 follow the applicable regulatory laws and conditions of approval imposed by the IRB.

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.

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