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Title: Visual outcomes and safety of the TECNIS Symfony intraocular lens: results of a pivotal clinical trial

Running head: TECNIS Symfony IOL Visual Outcomes and Safety

Authors: Daniel H. Chang, MD,1 Devi Priya Janakiraman, OD, FAAO,2 Pamela J. Smith, MPH,2 Anne Buteyn, BS,2 Joy Domingo, MD,2 Jason J. Jones, MD,3 William C. Christie, MD4

Affiliations:

1Empire Eye and Laser Center, Bakersfield, CA
2Johnson & Johnson Surgical Vision, Inc., Santa Ana, CA
3Jones Eye Clinic, Sioux City, IA
4Scott & Christie and Associates, PC, Cranberry Township, PA
Corresponding author:

Devi Priya Janakiraman

Johnson & Johnson Vision

1700 East St. Andrew Place

Santa Ana, CA 92705

djanaki1@its.jnj.com

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**Key Words:** cataract, presbyopia, intraocular lens, range of vision, extended depth of focus

**Twitter text**

Randomized comparison of the TECNIS Symfony (ZXR00) and the TECNIS 1-piece monofocal (ZCB00) intraocular lenses in cataract surgery demonstrates improved intermediate and near vision with TECNIS Symfony.
Purpose: To compare the effectiveness and safety of the TECNIS Symfony® intraocular lens (IOL; ZXR00) with the TECNIS® 1-piece monofocal IOL (ZCB00).

Setting: Fifteen sites in the United States.

Design: Prospective, randomized, subject/evaluator-masked clinical trial.

Methods: Randomized participants received either the ZXR00 or ZCB00 IOL bilaterally. Six-month postoperative outcomes included monocular and binocular distance, intermediate, and near visual acuity (VA), spherical equivalent refraction and refractive cylinder, spectacle wear, and visual symptoms.

Results: Overall, 299 patients were implanted with a study lens (ZXR00, n = 148; ZCB00 control, n = 151). At 6-month follow-up, mean binocular uncorrected distance VA was comparable between ZXR00 and ZCB00 recipients (P = .1011). The ZXR00 group had significantly better mean binocular uncorrected intermediate VA and uncorrected near VA (both P < .0001) than the ZCB00 group. Mean binocular distance-corrected intermediate VA and distance-corrected near VA were also better in the ZXR00 group (both P < .0001). More ZXR00 recipients reported wearing spectacles “none of the time” or “a little of the time” for overall vision at 6 months compared with the ZCB00 group (85.0% vs 59.9%, P < .0001). In ZXR00-implanted patients, low incidence rates of night glare (mild to moderate, 2.7%), halo (mild to moderate, 13.6%; severe, 2.7%), and starbursts (mild to moderate, 7.5%; severe, 1.4%) were reported.

Conclusions: The TECNIS Symfony® IOL provided comparable distance vision and improved uncorrected and distance-corrected intermediate and near vision, along with decreased spectacle wear and low incidence rates of dysphotopsias, compared with the TECNIS® 1-piece monofocal IOL.
INTRODUCTION

Current clinical options for patients with cataracts desiring improved vision across a range of distances include a choice of monovision or multifocal lenses. Patients implanted with standard monofocal intraocular lenses (IOLs) often need spectacles for reading or performing other near tasks,\(^1\) even if a monovision option is selected.\(^2\) Common spectacle options, including bifocal and progressive addition lenses, can increase the risk for trips and falls in the elderly.\(^3\) Patients implanted with multifocal IOLs are able to read and perform other near tasks without spectacles, but they sometimes experience dysphotopsias (eg, halos and glare), particularly at night, and have limitations in intermediate vision.\(^4,5\) Accommodating IOLs are available, although their effect can depend upon fit within the capsular bag or capsular bag elasticity, and results have been less predictable.\(^6,7\)

The TECNIS Symfony extended depth of focus (EDOF) IOL (Johnson & Johnson Vision, Santa Ana, CA, USA) incorporates a diffractive echellette design that elongates the focus, creating a continuous range of vision. Unlike multifocal IOLs that split the light into distinct focal points, the elongated focal zone of EDOF IOLs reduces overlap of near and far images, thus generating a lower incidence of halos and glare.\(^8,9\) The use of achromatic technology to correct longitudinal chromatic aberrations improves visual performance of the EDOF IOL.\(^8,9\)

This pivotal clinical trial of the TECNIS Symfony IOL (model ZXR00) was designed to evaluate its effectiveness and safety compared with a monofocal lens, the TECNIS 1-piece IOL (model ZCB00).

METHODS

Study Design

This prospective, bilateral, randomized, comparative, subject/evaluator-masked, multicenter study was conducted at 15 sites throughout the United States (ClinicalTrials.gov; unique identifier: NCT02203721). The study was initiated in August 2014 and was
completed in June 2015. All patients provided written informed consent and US Food and Drug Administration and institutional review board approval was obtained. The study was conducted in accordance with the US Code of Federal Regulations, the Declaration of Helsinki, and all other applicable laws and regulations.

**Inclusion and Exclusion Criteria**

Patients were included in the study if they were 22 years or older with bilateral cataracts for which phacoemulsification extraction and posterior chamber IOL implantation were planned. Each eye had a preoperative corrected distance visual acuity (CDVA) of 20/40 Snellen or worse with or without a glare source, potential for postoperative best-corrected visual acuity of 20/30 Snellen or better, normal corneal topography, preoperative corneal astigmatism of 1.00 D or less, and clear intraocular media other than cataract. Patients were required to sign an informed consent and Health Insurance Portability and Accountability Act of 1996 (HIPAA) authorization and be able to understand and respond to a written questionnaire.

Key exclusion criteria precluded eligibility for the following reasons: any prior ocular trauma, ocular surgery, ocular or systemic condition or degenerative disorder that could affect visual outcomes or increase risk, previous corneal refractive surgery, use of systemic or ocular medications that could affect vision, inability to focus or fixate for prolonged periods of time, any condition associated with the fluctuation of hormones that could lead to refractive changes, or participation in any other clinical trial during or 30 days before the preoperative visit.

**Study IOL Description**

The two IOLs compared in this study were the investigational TECNIS Symfony IOL (model ZXR00) and the TECNIS 1-piece monofocal IOL (model ZCB00). The ZXR00 is a diffractive, aspheric, foldable, acrylic, 1-piece, posterior chamber IOL designed for placement in the capsular bag. Both are made of the same hydrophobic SENSAR® material,
with a refractive index of 1.47 and an Abbe number of 55. The IOLs have the same overall geometry/dimensions (13 mm overall length and 6 mm optic diameter) as the original parent, the SENSAR 1-Piece IOL (model AAB00). The ZXR00 has the same modified prolate (aspheric) design on the anterior optic surface as the ZCB00 to reduce spherical aberration. In addition, the ZXR00 includes a 9-ring diffractive profile on the posterior optic surface designed to extend the range of vision and to compensate for chromatic aberration of the eye.

Randomization

Patients were randomly assigned 1:1 to receive either the ZXR00 or the ZCB00; each patient was to receive the same lens model in both eyes. Randomization was undertaken by study personnel at each study site by opening sealed, sequentially numbered envelopes containing randomized lens group information. Study investigators were not masked, but all participants and study evaluators responsible for conducting vision testing remained masked to the type of IOL implanted in each eye during the 6-month study period.

Surgical Procedure

Before randomization, the investigator chose for each patient which eye to operate on first at his or her discretion based on his or her standard clinical practice (eg, the eye with the worse cataract, poorer corrected distance vision, more severe optical/visual complaints, or eye dominance). Emmetropia (±0.5 D) was targeted for all eyes in the study, with the targeted residual refractive error documented.

The investigator used his or her standard, small-incision, phacoemulsification cataract extraction surgical technique. The lenses were inserted into the capsular bag using the UNFOLDER Platinum 1 Series Implantation System (DK7796 handpiece with the UNFOLDER Platinum 1 Series cartridge, model 1MTEC30) or the ONE SERIES Ultra Implantation System (DK7786 or DK7791 handpiece with the One Series Ultra cartridge, model 1VPR30).
Clinical End Points

All patients were intended to have bilateral cataract surgery and were to be examined through 6 months postoperatively according to the visit schedule. Distance visual acuities were tested using 100% Early Treatment Diabetic Retinopathy Study (ETDRS) charts at a fixed test distance of 4.0 meters under photopic (85 cd/m$^2$) lighting conditions. Intermediate visual acuities were tested using 100% ETDRS intermediate charts at a fixed test distance of 66 cm, with and without distance correction, under photopic (85 cd/m$^2$) lighting conditions. Near visual acuities were tested using 100% ETDRS near charts at a fixed test distance of 40 cm, with and without distance correction, under photopic (85 cd/m$^2$) lighting conditions.

Defocus curve testing was performed on a subset of participants from each lens group at eight sites at the 6-month postoperative study examination. Binocular CDVA defocus curves were performed using the electronic Freiburg Visual Acuity and Contrast Test (FrACT).

Monocular corrected distance contrast sensitivity testing was performed using the Vector Vision ETDRS light box and contrast sensitivity charts under three lighting conditions: mesopic with glare, mesopic without glare, and photopic with glare.

Spectacle wear and other subjective spectacle independence items were assessed by directed, self-reported responses to a binocular subjective questionnaire: the Patient-Reported Spectacle Independence Questionnaire (PRSIQ). Optical/visual symptoms were collected through nondirected, spontaneously reported responses to the open-ended question “Are you having any difficulties with your eyes or vision?”

Safety was assessed by measuring the rate of medical complications or adverse events (AEs). An AE was considered serious if it was an untoward occurrence that may or may not have been related to use of the IOL and that was sight- or life-threatening, resulted in death, required inpatient hospitalization or prolongation of hospitalization, resulted in persistent or significant disability or incapability, or necessitated medical or surgical intervention to
prevent permanent impairment to a body structure or function. A Data Safety Monitoring Board reviewed and assessed all reports of serious AEs and, if necessary, discussed these with the reporting investigator without being specific about the lens type.

**Statistical Analysis**

Effectiveness and safety end points were compared for the ZXR00 and ZCB00 cohorts. Analyses were based on the safety population, defined as all first eyes or all patients implanted with either the ZXR00 or the ZCB00, and with data available at the time of analysis. One-sided, 2-sample *t* tests with an alpha level of 0.025 were used for the primary end points of monocular uncorrected intermediate visual acuity (UIVA) and distance-corrected intermediate visual acuity (DCIVA) and the secondary end point of monocular distance-corrected near visual acuity (DCNVA). Clinical significance for these end points was evaluated by examining whether the difference between the ZXR00 and ZCB00 control groups was greater than 25% for the proportion achieving 20/25 or better for intermediate and 20/40 or better for near. Fisher exact test with a 1-sided alpha of 0.025 was used for binocular overall spectacle wear. Nonparametric methods using the lower limit of a 90% confidence limit with a noninferiority margin of −0.15 log units were used for the contrast sensitivity end point. Hierarchical methods (Hodges-Lehman) were used to adjust for multiple statistical comparisons for primary and secondary end points.

Medical complications and AEs were compared with International Organization for Standardization (ISO) safety and performance endpoint (SPE) rates for the ZXR00 lens group using a one-sided Fisher’s exact test based on the binomial distribution. Monocular, first-eye, mean CDVA was compared with the ZCB00 lens group using a noninferiority margin of .1 logMAR (1 line). Comparisons between lens groups for binocular uncorrected distance visual acuity (UDVA) were performed using 2-sided, 2-sample *t* tests with alpha set to 0.05.

The sample size was justified based on the primary study end points of monocular UIVA and DCIVA and the requirements for contrast sensitivity testing. With at least 135
evaluable patients in each lens group, this study had >90% power to detect a difference of ≥0.7 lines in mean visual acuity between the ZXR00 and ZCB00 lens groups for UIVA and DCIVA.

RESULTS

Patient Disposition

A total of 299 patients were enrolled and implanted with a study lens across 15 US clinical study sites. Of the patients enrolled, 49.5% (148/299) were implanted with the ZXR00 (148 bilaterally implanted) and 50.5% (151/299) were implanted with the ZCB00 (150 bilaterally implanted). All patients were bilaterally implanted except for 1 ZCB00-implanted patient who was implanted unilaterally due to illness and subsequent death. Of the implanted participants, almost all with ZXR00 (99.3% [147/148]) and ZCB00 (98.0% [148/151]) IOLs completed the 6-month follow-up visit.

Patient demographics were similar between the ZXR00 and ZCB00 control groups (Table 1). The average age of study participants in both groups was 68 years and more than half of both IOL groups were female. Most patients were White (ZXR00: 96.6% [143/148]; ZCB00: 86.1% [130/151]). The remaining patients were Black (ZXR00: 2.7% [4/148]; ZCB00: 10.6% [16/151]), Asian (ZXR00: 0.7% [1/148]; ZCB00: 2.0% [3/151]), or American Indian/Alaska Native (ZCB00: 1.3% [2/151]).

Monocular Uncorrected and Corrected Visual Aucities

At 6-month follow-up, the ZXR00 and ZCB00 groups demonstrated similar mean monocular UDVA (Snellen equivalent 20/25 vs 20/25; difference −0.3 lines; 90% confidence interval [CI], −0.054 to 0.001) and CDVA (20/20 vs 20/20; difference −0.2 lines; 90% CI, −0.036 to −0.003) (Figure 1A). The difference in monocular mean CDVA between the ZXR00 and ZCB00 groups was −0.2 lines (1 letter), which was within the noninferiority margin of 1 line. A postoperative UDVA of 20/20 or better was observed in 39% (57/147) of ZXR00 eyes and 47% (70/148) of ZCB00 eyes, whereas a UDVA of 20/25 or better was
observed in 65% (96/147) of ZXR00 eyes and 72% (106/148) of ZCB00 eyes. Most ZXR00 (84% [123/147]) and ZCB00 (89% [131/148]) eyes achieved postoperative CDVA of 20/20 or better, and almost all ZXR00 (98% [144/147]) and ZCB00 (97% [143/148]) eyes achieved postoperative CDVA of 20/25 or better.

Figure 1A also shows mean monocular UIVA, uncorrected near visual acuity (UNVA), DCIVA, and DCNVA for ZXR00- and ZCB00-implanted patients, presented as LogMAR values. At 6-month follow-up, the ZXR00 was associated with significantly better monocular UIVA (Snellen equivalent 20/25 vs 20/36; difference 1.7 lines; \( P < .0001 \)), UNVA (20/35 vs 20/58; difference 2.2 lines; \( P < .0001 \)), DCIVA (20/25 vs 20/44; difference 2.4 lines; \( P < .0001 \)), and DCNVA (20/42 vs 20/69; difference 2.2 lines; \( P < .0001 \)) compared with the ZCB00. Differences between ZXR00 and ZCB00 groups were statistically and clinically significant, with a larger proportion (>40%) of ZXR00- versus ZCB00-implanted patients achieving predefined targets of 20/25 or better for UIVA and DCIVA and 20/40 or better for DCNVA (Table 2).

**Binocular Uncorrected and Corrected Visual Acuities**

At 6-month follow-up, the ZXR00 and ZCB00 groups had similar mean binocular UDVA (Snellen equivalent 20/21 vs 20/20; difference −0.2 lines; 90% CI, −0.043 to 0.000; \( P = .1011 \)) and CDVA (20/20 vs 20/16; difference −0.3 lines; 90% CI, −0.046 to −0.015), which was within the noninferiority margin of 1 line (Figure 1B). More ZXR00-implanted patients achieved a binocular UDVA of 20/25 or better (91.2% [134/147]) or 20/32 or better (97.3% [143/147]) compared with ZCB00-implanted patients (84.5% [125/148] and 95.9% [142/148], respectively) (Figure 2). Six-month postoperative mean binocular UNVA and UIVA were significantly better for ZXR00 compared with ZCB00 (\( P < .0001 \)) (Table 3). More ZXR00-implanted patients achieved binocular UNVA of 20/25 or better compared with ZCB00-implanted patients (55.1% [81/147] vs 12.8% [19/148]; \( P < .0001 \)) (Figure 2). The results were more dramatic for intermediate visual acuity, with almost all ZXR00-implanted
patients having UIVA of 20/25 or better compared with ZCB00-implanted patients (96.6% [142/147] vs 60.1% [89/148]; \( P < .0001 \)) (Figure 2).

**Spherical Equivalent Refraction and Refractive Cylinder**

No statistically significant difference was found between IOL groups for mean target spherical equivalent (SE), mean SE at 6 months, and mean refractive cylinder at 6 months (all \( P > .05 \)). Postoperative mean SE was slightly myopic for both IOL groups, with a mean of −0.42 (±0.41) for the ZXR00 and −0.36 (±0.41) for the ZCB00 group; mean target SEs were −0.20 (±0.15) and −0.19 (±0.15), respectively. Mean refractive cylinder was 0.39 (±0.38) for the ZXR00 group and 0.42 (±0.39) for the ZCB00 group.

Six-month postoperative absolute manifest SE relative to the intended emmetropic target was within ±0.50 D of emmetropia in 103/147 of ZXR00-implanted first eyes (70.1%) and 105/148 of ZCB00-implanted first eyes (70.9%); absolute manifest SE was within ±1.00 D of emmetropia in 141/147 of ZXR00-implanted first eyes (95.9%) and 141/148 of ZCB00-implanted first eyes (95.3%) (Figure 3). Six-month postoperative refractive cylinder was within ±0.50 D of emmetropia in 111/147 of ZXR00-implanted first eyes (75.5%) and 111/148 of ZCB00-implanted first eyes (75.0%); refractive cylinder was within ±1.00 D of emmetropia in 140/147 of ZXR00-implanted first eyes (95.2%) and 145/148 of ZCB00-implanted first eyes (98.0%) (Figure 4). No significant differences were observed between IOL groups for the proportions of eyes within 0.5 D and 1.0 D for SE (\( P = .8989 \) and \( P = 1.0000 \)) or for refractive cylinder (\( P = 1.0000 \) and \( P = .2177 \), respectively).

**Defocus Curves**

Binocular defocus curves revealed an approximately 1.0 D greater range of defocus by ZXR00 versus ZCB00 (Figure 5). Mean binocular acuities were 20/32 or better for the ZXR00 group through −2.0 D (50 cm). The ZXR00 group binocular defocus curves showed a 1- to 2-line acuity improvement over the ZCB00 group through 4.0 D of defocus. When visual acuity means from standard ETDRS acuity testing are plotted on the defocus chart at
far, intermediate, and near distances, a similar difference of 1 to 2 lines of acuity is seen in favor of the ZXR00 group from −1.0 to −4.0 D of focus over the ZCB00 group.

**Patient-Reported Outcomes**

*Spectacle Wear*

Spectacle wear was significantly lower for patients receiving the ZXR00 IOL compared with the ZCB00. At the 6-month postoperative visit, 85% (125/147) of patients with bilateral ZXR00 versus 59.9% (88/147) with ZCB00 reported wearing glasses or contact lenses “none of the time” or “a little of the time” for overall vision within the last 7 days ($P < .0001$). A significantly higher proportion of ZXR00-implanted patients reported wearing glasses or contacts “none of the time” at the 6-month postoperative visit, compared with the ZCB00 group (62.6% [92/147] vs 32.0% [47/147]; $P < .0001$) (Figure 6).

*Visual Symptoms*

Spontaneous nondirected reports of image quality were excellent in both ZXR00- and ZCB00-implanted patients, with only 4.1% (6/147) and 5.4% (8/148) reporting blurred vision overall. Visual symptoms typically associated with presbyopia-correcting IOLs were low for patients implanted with the ZXR00 and were only slightly higher than reports from patients implanted with the ZCB00 (Table 4). At 6 months, the most common spontaneously reported optical/visual symptoms were halos and starbursts for the ZXR00. Night glare difficulty was uncommon with both the ZXR00 and ZCB00 (2.7% [4/147] and 0% [0/148]).

*Quality of Nighttime Vision*

At 6-month follow-up, most patients implanted with the ZXR00 or ZCB00 reported having “good vision” quality for far (78.8% [115/146] and 83.6% [122/146], respectively), intermediate (76.0% [111/146] and 78.1% [114/146]), and near (67.8% [99/146] and 75.3% [110/146]) distances under nighttime outdoor lighting conditions.
Contrast Sensitivity

The median values for monocular best-corrected contrast sensitivity for ZXR00 and ZCB00 were not statistically different at 1.5 and 3.0 cpd under either mesopic or mesopic with glare lighting conditions (Table 5; Figure 7A and 7B). At 6.0 and 12.0 cpd, the median difference between IOL groups exceeded −0.15 log units for mesopic with glare and the lower limit of the 90% CI was below the noninferiority margin of −0.15 log units for with and without glare; however, the median difference and lower limit of the 90% CI were within −0.30 log units (the difference typically considered clinically significant loss when occurring at 2 or more spatial frequencies).

Safety

The most frequently reported medical complications/AEs 1 day postoperatively for both lens groups for first eyes were cells (ZXR00: 79.7% [118/148]; ZCB00: 78.8% [119/151]), flare (ZXR00: 16.9% [25/148]; ZCB00: 19.2% [29/151]), and corneal edema (ZXR00: 27% [40/148]; ZCB00: 26.5% [40/151]), which diminished over time to minimal levels by the 1-month visit in both lens groups. Similar results were found for second eyes for both groups. Nd:YAG capsulotomy rates were low in both groups at 6 months, with 4.7% (14/296) ZXR00 and 1.7% (5/301) ZCB00 control eyes requiring the procedure during the study.

Overall, 2.7% (4/148) of ZXR00-implanted patients experienced serious AEs during the study and none (0%; 0/148) experienced device-related or unanticipated events. Serious ZXR00 IOL adverse events were as follows: cystoid macular edema (2 eyes), hypopyon/endophthalmitis (1 eye), pupillary capture (1 eye), and secondary surgical intervention (antibiotic injections [2 eyes]). Serious AEs were more common in the ZCB00 group (6.0%, 9/151), comprising cystoid macular edema (5 eyes), anterior ischemic optic neuropathy (1 eye), and secondary surgical intervention (6 eyes; fragment removals [2 eyes], treatment injections for medical complications [2 eyes], epiretinal membrane peel [1 eye], and stromal puncture for anterior basement membrane dystrophy [1 eye]).
DISCUSSION

This clinical investigation evaluated the effectiveness and safety of an extended depth of focus lens, the TECNIS Symfony EDOF IOL, model ZXR00, compared with the monofocal control lens, the aspheric TECNIS 1-piece IOL, model ZCB00. The IOL delivers well-focused vision over an enhanced range, thus providing good distance vision and improved intermediate and near vision compared with monofocal IOls.\textsuperscript{10-12} In addition, the ZXR00 IOL maintained high-contrast visual acuity and patient satisfaction following cataract surgery or refractive lens exchange. The clinical study results achieved at 6 months after surgery demonstrated improved uncorrected and distance-corrected intermediate and near vision, an increased depth of focus, and decreased spectacle wear in participants who received the ZXR00 compared with the monofocal control IOL. End points for distance visual acuity showed comparable performance for the ZXR00 IOL and the monofocal control lens. Safety measures showed good contrast sensitivity, typical optical/visual symptoms, and low rates of AEs.

Theoretical attributes\textsuperscript{11} and clinical outcomes\textsuperscript{10,12-14} of the ZXR00 IOL have been previously published. An analysis comparing the ZXR00 and ZCB00 monofocal IOls in 80 eyes reported significantly better uncorrected monocular and binocular distance, intermediate, and near visual acuities ($P \leq .013$) for the ZXR00 versus the monofocal group, and no significant between-group differences in contrast sensitivity or optical quality parameters ($P > .05$).\textsuperscript{10} Similarly, in a multicenter study of 411 patients who received bilateral implantations with the ZXR00 IOL and assigned to a micro-monovision arm ($n = 112$; residual myopia was targeted in the nondominant eye between 0.50 D and 0.75 D) or a group targeted for emmetropia, mean binocular UDVA ($0.03 \pm 0.10$ logMAR), UIVA ($0.12 \pm 0.16$ logMAR), and UNVA ($0.19 \pm 0.17$ logMAR) were similar to those reported in the present study, with the UNVA approximately 1 line better for the micro-monovision group.
versus the group targeted for emmetropia. In a prospective non-comparative case series of 52 eyes, bilateral implantation of the TECNIS Symfony IOL was also associated with excellent UDVA and UIVA (< 0.1 logMAR) and acceptable UNVA (< 0.3 logMAR). Furthermore, comparison of two EDOF IOLs, TECNIS Symfony and IC-8, in 6-month prospective randomized trial of 36 patients, also reported excellent UDVA, good UNVA and UIVA, and high patient satisfaction regarding visual acuity without spectacles/contact lenses for both EDOF IOLs. Studies evaluating multifocal IOLs (TECNIS ZM900 and TECNIS ZKB00 [Johnson & Johnson Vision, Santa Ana, CA, USA]) have also reported positive distance, intermediate, and near visual acuities, which were comparable to visual acuity outcomes observed with the ZXR00 IOL in the present study. Furthermore, visual symptoms of halo and glare reported with the ZXR00 IOL were substantially lower than those reported for the ZM900 and ZKB00 multifocal lenses, meeting the intended design concept of reduced visual symptoms with the ZXR00 IOL.

The PRSIQ is a new tool primarily developed for assessing spectacle independence in patients following cataract surgery. It is the only validated questionnaire for posterior chamber IOLs, and it aims to determine the need, wear, and frequency of spectacle or contact lens use during the 7 days immediately prior to the survey. The PRSIQ was effectively used in the present study to determine spectacle use following surgery and showed that a significantly higher proportion of patients implanted with ZXR00 reported not wearing glasses or contact lens 6 months after surgery (P < .0001).

Positive visual outcomes with trifocal IOLs, which combine two diffractive profiles to improve vision across all spectrums, have been previously reported for the AT LISA tri 839MP (Carl Zeiss Meditec, Jena, Germany), FineVision Micro F (PhysIOL S.A., Liege, Belgium), and AcrySof IQ PanOptix (Alcon Laboratories, Inc., Fort Worth, TX, USA) IOLs. These smaller, uncontrolled studies reported binocular uncorrected visual acuities 3 to 6 months after surgery that ranged from −0.06 to 0.02 LogMAR for distance (4 m), 0.00 to 0.32 LogMAR for intermediate (70–80 cm), and 0.02 to 0.15 LogMAR for near (40
Defocus curves for the FineVision Micro F trifocal IOL showed two peaks that corresponded with distance and near acuities, with a smaller drop between these peaks when compared with defocus curves for a bifocal IOL. Photic phenomena reports were evaluated by different methods in each of the studies, with the highest complaints being glare and halo, at similar or lower levels than are seen in other multifocal lenses. Compared with the findings of these trifocal studies, the ZXR00 IOL shows similar binocular uncorrected visual acuities and the unique extended range of vision feature, shown in the monotonically decreasing defocus curve. Indeed, a small 6-month, prospective, randomized study comparing two trifocal IOLs (AcrySof IQ PanOptix and FineVision Micro F) and the TECNIS Symfony IOL also reported similar binocular UDVA and UIVA outcomes, low incidence rates of photic phenomena (<1%), and a high level of spectacle independence (90% overall). Furthermore, a 6-month study of 411 patients bilaterally implanted with the TECNIS Symfony IOL demonstrated that loss of binocular UDVA, UIVA, or UNVA did not exceed 1 line and was not clinically relevant in eyes with residual cylinders up to 0.75 D. These findings highlight that the TECNIS Symfony IOL may provide better tolerance to postoperative refractive errors (ie, residual astigmatism), which is an important factor for ensuring patient satisfaction.

Binocular UDVA was similar between the ZXR00 and ZCB00 IOL control groups, demonstrating the ability of ZXR00 to provide good distance visual acuity. Pedrotti et al. found similar positive distance visual acuity results with the Symfony IOL. In their study, the authors reported significantly improved mean monocular UDVA in the Symfony group (0.08 ± 0.12 logMAR) compared with monofocal IOLs (0.14 ± 0.14 logMAR, *P* = .013) at 3-month follow-up. Binocular UDVA of 0.20 logMAR or better (Snellen 20/30) was observed with both Symfony (0.00 ± 0.09 logMAR) and monofocal (0.03 ± 0.11 logMAR) IOLs. In another study comparing the Symfony IOL with trifocal IOLs, the Symfony IOL was associated with significantly better mean UDVA compared with the AT LISA tri 839 and PhysIOL FineVision IOLs (1.01 [−0.004 logMAR] vs .96 [0.018 logMAR] and 0.95
These findings indicate that the Symfony IOL provides good-quality distance vision.

Some noteworthy findings of the study were those observed for the contrast sensitivity testing and defocus curves. A slight but not clinically significant reduction in monocular contrast sensitivity at higher frequencies was found for the ZXR00 IOL compared with the aspheric control IOL, a lens known to have contrast superior to nonaspheric monofocal IOLs. The optical design of the ZXR00 IOL includes a diffractive profile on the posterior optic surface designed to reduce the chromatic aberrations of the eye. Preclinical data predict that the correction of spherical and chromatic aberration is expected to counteract the change in contrast that accompanies an extension of depth of focus such that overall contrast is maintained comparable to that of a low-dispersion monofocal lens that corrects spherical aberration only.

Although there were differences in contrast sensitivity between the ZXR00 IOL and the aspheric monofocal control, it should be noted that the control lens in this study is a monofocal lens that fully corrects spherical aberration and minimizes chromatic aberration, yielding higher contrast than standard spherical IOLs, particularly ones with higher levels of chromatic dispersion. In addition, contrast sensitivity tests in this study were conducted monocularly, and it is possible that differences in contrast outcomes between IOL groups may be reduced when testing binocularly, because binocular summation helps patients achieve contrast values closer to the retinal threshold limits.

Another finding of interest in this study concerns the methods used to evaluate defocus curves, which illustrate the extended depth of focus of the Symfony optic design. In this study, distance, intermediate, and near visual acuities were measured with the ETDRS chart, and defocus testing was performed using FrACT. The FrACT test uses Landolt C optotype and a thresholding method to measure visual acuity, whereas the ETDRS test is a standard method that has been optimized for efficient clinical visual acuity testing. Both ETDRS and FrACT are valid visual acuity measurement systems that showed generally good
correlation for visual acuity testing. However, ETDRS visual acuity results tested at a specific distance may not be directly comparable to FrACT defocus results obtained through minus lenses because of the difference in measurement methods. In the current clinical study, fatigue due to the order of testing and the long duration of FrACT defocus testing may have further contributed to lower visual acuities in the FrACT defocus test compared with the ETDRS real distance test. Nonetheless, the differences seen between ETDRS and FrACT were similar for both Symfony and monofocal control groups and across all sites. As lower acuities were found with the FrACT defocus method compared with ETDRS direct testing, the use of the FrACT system for the defocus testing may provide a more conservative estimate of defocus diopter range with visual acuity of 20/32 or better compared with using ETDRS for defocus testing. In this study, the defocus curve for ZXR00 IOL showed that near vision fell below the 20/40 level at 2.5 D (40 cm), after which the near vision continued to decline monotonically. Because this reduction in visual acuity with the FrACT test was observed with both Symfony and monofocal control IOLs, the difference in depth of focus between lenses is robust.

Patient-reported outcomes indicated that “good vision” under nighttime outdoor lighting conditions was reported by most patients receiving the ZXR00 IOL. Although halo and starburst effects were more common with ZXR00 than monofocal IOLs, most cases were mild or moderate. These findings highlight that the ZXR00 IOL provides good quality nighttime vision with a low incidence of night vision symptoms.

Chromophores that selectively reduce high-energy, short-wavelength light have the potential to reduce night vision symptoms. IOLs with violet filtering have been developed to further reduce these symptoms. In a randomized study of 240 patients comparing a violet light-filtering monofocal IOL with a colorless IOL, comparable CDVA was observed between the violet light-filtering and colorless IOLs, with similar proportions of patients achieving 20/20 or better and 20/40 or better in both first (82.4% and 100% vs 86.6% and 100%) and second (84.9% and 99.2% vs 92.5% and 100%) eyes. Compared with
the colorless IOL group, significantly greater proportions of patients in the violet light-filtering IOL group reported no difficulty driving during daytime (98.1% vs 91.7%; \( P = .033 \)) or at nighttime (52.8% vs 44.4%; \( P = .017 \)) and no frustration with vision (89.8% vs 79.8%; \( P = .0325 \)). Taken together, these findings indicate that the use of violet-filtering IOLs can improve visual functioning while maintaining visual acuity and contrast sensitivity. In particular, improvements in visual function related to daily activities (eg, nighttime driving) support the use of violet-filtering technology in presbyopia-correcting IOLs to provide patients receiving these lenses with potentially greater benefits in terms of activities associated with scotopic vision.

Findings from this randomized, controlled, masked clinical study provide practitioners and patients with information about the safety and effectiveness of this unique IOL technology. The ability of EDOF IOLs, such as the ZXR00 IOL, to provide a more natural range of vision provides the opportunity for a personalized approach to IOL selection in which EDOF and multifocal IOLs can be used in tandem to achieve a range of vision and nighttime vision symptom profile suitable for each individual patient. Recently, “blended” implantation of the ZXR00 in the dominant eye and +3.25 “low-add” multifocal IOL (Tecnis ZLB00 [Johnson & Johnson Vision, Santa Ana, CA, USA]) in the nondominant eye provided excellent uncorrected visual acuity at near, intermediate, and far distances with minimal ocular symptoms. Blended implantation of the ZXR00 and a diffractive multifocal IOL (TECNIS ZMB00 [Johnson & Johnson Vision, Santa Ana, CA, USA]) also exhibited better performance with regards to quality of vision for long, intermediate, and short distances, compared with a trifocal IOL (Acrysof IQ Panoptix TFNT00 [Alcon Laboratories, Inc., Fort Worth, TX, USA]).

Results for defocus testing in this study were conservative because of the aforementioned testing differences but provide a basis for potential functional performance that can be expected with this IOL design. Understanding the differences inherent to clinical testing can also help with future study designs and interpretation of results. To expand the
knowledge base for this IOL technology, future studies are needed in both real-world and clinical settings.

In conclusion, clinical results from this study at 6 months after surgery demonstrated that the TECNIS Symfony IOL provided patients with improved uncorrected intermediate and near visual acuity, comparable distance visual acuity, an increased depth of focus, and decreased use of spectacles when compared with the monofocal control IOL. Review of safety outcomes with the new IOL design revealed no significant safety concerns, acceptable contrast sensitivity and optical/visual symptoms, and low rates of AEs.
What Was Known

- Cataract surgery with monofocal lenses often requires patients to wear spectacles for reading or performing other near tasks, even if a monovision option is selected.

- Patients with multifocal lenses are able to read and perform other near tasks without spectacles, but they sometimes experience dysphotopsias (eg, halos), particularly at night, and have limited intermediate ability (eg, they may need spectacles to work on a computer).

What This Paper Adds

- The TECNIS Symfony IOL, model ZXR00, is a safe and effective option in patients undergoing cataract surgery, providing improved uncorrected and distance-corrected intermediate and near vision, an increased depth of focus, and decreased spectacle wear when compared with the TECNIS 1-piece IOL.
References


36–38.
Figure Legends

Figure 1. Mean monocular (A) and binocular (B) visual acuities at 6-month follow-up (CDVA = corrected distance visual acuity; DCIVA = distance-corrected intermediate visual acuity; DCNVA = distance-corrected near visual acuity; UDVA = uncorrected distance visual acuity; UIVA = uncorrected intermediate visual acuity; UNVA = uncorrected near visual acuity).

Figure 2. Cumulative binocular uncorrected visual acuity at distance, intermediate, and near distances.

Figure 3. Postoperative absolute manifest refraction spherical equivalent relative to the intended emmetropic target at 6-month follow-up.

Figure 4. Absolute refractive cylinder at 6-month follow-up.

Figure 5. Binocular best-corrected distance visual acuity defocus curves and visual acuity means (IOL = intraocular lens).

Figure 6. Frequency of glasses/contacts wear for overall, distance, intermediate, and near vision during the last 7 days as reported 6 months after surgery.

Figure 7. Median monocular contrast sensitivity at 6 months under mesopic conditions with (A) and without (B) glare.
### Table 1. Sex, mean age, and mean postoperative spherical equivalent refractive error (safety population).

<table>
<thead>
<tr>
<th>Lens Group</th>
<th>Treated (N)</th>
<th>Males n (%)</th>
<th>Females n (%)</th>
<th>Age (mean years ± SD)</th>
<th>6-Month Postoperative Spherical Equivalent (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TECNIS Symfony</td>
<td>148</td>
<td>57 (38.5)</td>
<td>91 (61.5)</td>
<td>68.0 ± 7.5</td>
<td>-0.42 ± 0.41</td>
</tr>
<tr>
<td>TECNIS Monofocal</td>
<td>151</td>
<td>65 (43.0)</td>
<td>86 (57.0)</td>
<td>67.9 ± 7.9</td>
<td>-0.36 ± 0.41</td>
</tr>
</tbody>
</table>

SD = standard deviation
Table 2. Percentage of subjects achieving targeted level of postoperative monocular visual acuity.

<table>
<thead>
<tr>
<th>End Point</th>
<th>TECNIS Symfony (N=147)</th>
<th>TECNIS Monofocal (N=148)</th>
<th>Difference (percentage points)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UIVA 20/25 or better</td>
<td>76.9%</td>
<td>33.8%</td>
<td>43.1%</td>
</tr>
<tr>
<td>DCIVA 20/25 or better</td>
<td>70.1%</td>
<td>13.5%</td>
<td>56.6%</td>
</tr>
<tr>
<td>DCNVA 20/40 or better</td>
<td>61.9%</td>
<td>16.2%</td>
<td>45.7%</td>
</tr>
</tbody>
</table>

UIVA= uncorrected intermediate visual acuity; DCIVA= distance-corrected intermediate visual acuity; DCNVA= distance-corrected near visual acuity
Table 3. Binocular uncorrected visual acuity at distance, intermediate, and near.

<table>
<thead>
<tr>
<th>Testing Distance</th>
<th>TECNIS Symfony (N=147)</th>
<th>TECNIS Monofocal (N=148)</th>
<th>LogMAR Difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Snellen Equivalent</td>
<td>Mean ± SD</td>
<td>Snellen Equivalent</td>
</tr>
<tr>
<td>UDVA (4 m)</td>
<td>0.03 ± 0.11</td>
<td>20/21</td>
<td>0.01 ± 0.12</td>
<td>20/20</td>
</tr>
<tr>
<td>UIVA (66 cm)</td>
<td>0.00 ± 0.09</td>
<td>20/20</td>
<td>0.13 ± 0.14</td>
<td>20/27</td>
</tr>
<tr>
<td>UNVA (40 cm)</td>
<td>0.15 ± 0.11</td>
<td>20/28</td>
<td>0.33 ± 0.17</td>
<td>20/43</td>
</tr>
</tbody>
</table>

NS = not significant; SD = standard deviation; UDVA = uncorrected distance visual acuity; UIVA = uncorrected intermediate visual acuity; UNVA = uncorrected near visual acuity
Table 4. Optical/visual symptoms at 6 months postoperatively (non-directed).

<table>
<thead>
<tr>
<th>Symptom</th>
<th>TECNIS Symfony (N = 147)</th>
<th>TECNIS Monofocal (N = 148)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None % (n)</td>
<td>None % (n)</td>
</tr>
<tr>
<td>Night glare</td>
<td>97.3 (143)</td>
<td>100 (148)</td>
</tr>
<tr>
<td>Halos</td>
<td>83.7 (123)</td>
<td>98.6 (146)</td>
</tr>
<tr>
<td>Starburst</td>
<td>91.2 (134)</td>
<td>98.6 (146)</td>
</tr>
</tbody>
</table>
Table 5. Median monocular best-corrected contrast sensitivity (in log units) at 6 months, under mesopic lighting conditions, with glare and without glare.

<table>
<thead>
<tr>
<th>Spatial Frequency</th>
<th>IOL</th>
<th>N</th>
<th>Mesopic Without Glare</th>
<th>Mesopic With Glare</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Median</td>
<td>Lower 90% CI</td>
</tr>
<tr>
<td>1.5 cpd</td>
<td>Symfony</td>
<td>146</td>
<td>1.520</td>
<td>1.445</td>
</tr>
<tr>
<td></td>
<td>Monofocal</td>
<td>147</td>
<td>1.595</td>
<td>1.520</td>
</tr>
<tr>
<td></td>
<td>Difference</td>
<td></td>
<td>-0.075</td>
<td>-0.075</td>
</tr>
<tr>
<td>3.0 cpd</td>
<td>Symfony</td>
<td>146</td>
<td>1.415</td>
<td>1.340</td>
</tr>
<tr>
<td></td>
<td>Monofocal</td>
<td>147</td>
<td>1.490</td>
<td>1.475</td>
</tr>
<tr>
<td></td>
<td>Difference</td>
<td></td>
<td>-0.075</td>
<td>-0.145</td>
</tr>
<tr>
<td>6.0 cpd</td>
<td>Symfony</td>
<td>146</td>
<td>1.380</td>
<td>1.380</td>
</tr>
<tr>
<td></td>
<td>Monofocal</td>
<td>147</td>
<td>1.540</td>
<td>1.465</td>
</tr>
<tr>
<td></td>
<td>Difference</td>
<td></td>
<td>-0.145</td>
<td>-0.170</td>
</tr>
<tr>
<td>12.0 cpd</td>
<td>Symfony</td>
<td>146</td>
<td>0.910</td>
<td>0.845</td>
</tr>
<tr>
<td></td>
<td>Monofocal</td>
<td>147</td>
<td>1.080</td>
<td>0.995</td>
</tr>
<tr>
<td></td>
<td>Difference</td>
<td></td>
<td>-0.085</td>
<td>-0.170</td>
</tr>
</tbody>
</table>

CI = confidence interval; IOL = intraocular lens
A

Log Contrast Sensitivity

Cycles Per Degree

B

Log Contrast Sensitivity

Cycles Per Degree