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Multicountry clinical outcomes of a new nondiffractive presbyopia-correcting IOL

Chandra Bala, PhD, MBBS, FRANZCO, Francisco Poyales, MD, Mercè Guarro, MD, Ramón Ruiz Mesa, MD, Ali Mearza, MB, BS, FRCOphth, Devesh Kumar Varma, BEng, MD, FRCSC, Srichand Jasti, MS, Jessie Lemp-Hull, DrPH

Purpose: To evaluate the effectiveness and safety of a new presbyopia-correcting intraocular lens (IOL) with a nondiffractive design, DFT015, compared with an aspheric monofocal IOL, SN60WF.

Setting: 19 investigational sites in 4 countries: Australia, Canada, Spain, and the United Kingdom.

Design: Prospective, randomized, parallel-group, controlled, assessor- and patient-masked clinical study.

Methods: Participants aged ≥22 years with bilateral cataracts were randomized to DFT015 or SN60WF in a 5:4 ratio and masked until final postoperative follow-up at month 6. The primary effectiveness objective was superiority of DFT015 over SN60WF in mean monocular photopic distance-corrected intermediate visual acuity (DCIVA) at month 3. Secondary effectiveness objectives included noninferiority of DFT015 to SN60WF in mean monocular photopic corrected distance visual acuity (CDVA) and superiority in the mean monocular photopic distance-corrected near visual acuity (DCNVA) at month 3. Visual disturbances were assessed at month 6.

Results: 282 patients were randomized to DFT015 (n = 159) or SN60WF (n = 123). All effectiveness objectives were achieved at month 3 in first eyes. For monocular photopic results in first eyes, DFT015 demonstrated superior mean DCIVA (least squares means of −0.139 logMAR in favor of DFT015, $P < .001$), noninferior mean CDVA (97.5% upper confidence limit [UCL] of the difference was <0.1 logMAR) and superior mean DCNVA (95% UCL of the difference was <0.0 logMAR) compared with SN60WF at month 6. DFT015 exhibited a similar visual disturbance profile to that of SN60WF.

Conclusions: DFT015 provided superior intermediate and near vision and a similar visual disturbance profile compared with an aspheric monofocal IOL.

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Depth of focus is the amount of image displacement behind a lens that does not degrade the perceived image quality or the tolerance of the eye to retinal defocus; a large depth of focus allows sharp images of closer objects.[1] Intraocular lenses (IOLs) offer different depths of focus depending on the optical design.[1] Monofocal IOLs focus light on a single focal point, providing good distance vision; however, quality of vision at other distances is often insufficient to support activities of daily living without the use of spectacles.[2] Multifocal IOLs focus or split light into different foci, using either refractive or diffractive optics; bifocals have 2 primary focal points: distance and either intermediate or near, and trifocals offer 3 focal points: distance, intermediate, and near.[3–5] However, multifocal IOLs are associated with increased photic phenomena (such as glare and halo) and reduced contrast sensitivity compared with monofocal IOLs.[2] There is an unmet medical need for a presbyopia-correcting IOL that is easy to use and has a visual disturbance profile comparable with a monofocal IOL.

The American National Standards Institute (ANSI) has recently published clinical criteria to define extended depth-of-focus (EDoF) IOLs. According to these monocular criteria, an EDoF IOL must have the following: a depth of focus ≥0.5 diopters (D) greater than that of a monofocal IOL control at 0.2 logMAR; distance-corrected intermediate visual acuity (DCIVA) superior to that of a monofocal IOL; median DCIVA of 0.2 logMAR or better; and corrected distance visual acuity (CDVA) noninferior to that of a

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From PersonalEyes, Sydney, Australia (Bala); Miranza IOA Madrid Innova Ocular, Madrid, Spain (Poyales); OMIQ-Hospital General de Catalunya, Barcelona, Spain (Guarro); Hospital General de Granollers, Granollers, Spain (Guarro); Oftalvist CIO Jerez, Puerta del Sur Hospital, Cádiz, Spain (Mesa); Imperial College Healthcare NHS Trust & Ophthalmic Consultants of London, London, United Kingdom (Mearza); Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, Canada (Varma); Prism Eye Institute, Oakville, Ontario, Canada (Varma); Trillium Health Partners, Mississauga, Ontario, Canada (Varma); Alcon Laboratories, Inc., Fort Worth, Texas (Jasti, Lemp-Hull).

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Corresponding author: Chandra Bala, PhD, MBBS, FRANZCO, L 2, 30 York St, Sydney, NSW 2000, Australia. Email: bala@eyesmile.com.au.

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monofocal IOL.[6] The new standard has no clinical performance target that is analogous to intermediate vision, regarding near visual acuity or visual disturbances for EDoF IOLs; however, it does require that visual disturbances are assessed using a patient-reported outcome measure.

Various optical principles can be applied to extend the range of vision for a patient.[7] The most common approach is by use of a diffractive optic that uses a step-structure design intended to split light into multiple focal points, to deliver vision at distance and at intermediate and/or near, but patients may experience reduced contrast sensitivity or increased photic phenomena in low-illumination conditions.[8,9] Other approaches may be nondiffractive. For example, a small aperture design blocks unfocused peripheral light rays while allowing central and paracentral light rays through a central aperture to extend the depth of focus.[9] The small aperture design has demonstrated reduced contrast sensitivity compared with a monofocal IOL.[10] In addition, patients with a naturally large pupil size may experience increased visual disturbances under mesopic conditions or a reduced defocus range because of the small diameter of the optic.[9] Some nondiffractive IOLs may use spherical aberration or a segmented refractive design to increase the depth of focus. For example, the optics of Miniwell IOL (Sifi Meditech Srl) consists of a central zone with positive spherical aberration, a middle zone with negative spherical aberration, and an outer monofocal zone.[9] However, this approach may be sensitive to corneal spherical aberration, which could potentially impact near visual acuities.[11] From an optical standpoint, it is expected that nondiffractive technologies, which do not split light, could be most capable of providing distance visual quality and a visual disturbance profile similar to that of an aspheric monofocal IOL and an increased range of vision.[8]

According to the information provided by the manufacturer, DFT015 IOL (AcrySof IQ Vivity Extended Vision IOL) is the first and only EDoF IOL with the nondiffractive X-WAVE technology.[12] The surface profile of DFT015 is relatively flat and smooth and, to the naked eye, looks similar to that of SN60WF IOL (AcrySof IQ monofocal IOL) (Figure 1, a). DFT015 IOL uses innovative wavefront-shaping technology (X-WAVE) that consists of 2 smooth surface transition elements that stretch and shift the wavefront (Figure 1, b and c). Surface transition element 1 is a slightly elevated smooth plateau (~1 μm) that delays a portion of the wavefront as it passes through the IOL, relative to the more advanced wavefront passing through the IOL outside of the central surface transition elements. As a result, the wavefront stretches as it collapses on the retina, with the delayed wavefront forming the image toward the near end of the extension and the advanced wavefront traveling further to form the image at the far end of the extension. Surface transition element 2 is a small change in curvature that shifts the wavefront to the anterior side of the retina to use all the available light. The simultaneous actions of the 2 surface transition elements deliver a naturally occurring extended focal range. The DFT015 IOL design is intended to provide a continuous extended range of vision; superior intermediate and near vision and comparable distance vision with that a monofocal IOL; good mesopic contrast sensitivity; and a visual disturbance profile similar to that of an SN60WF monofocal IOL.[12]

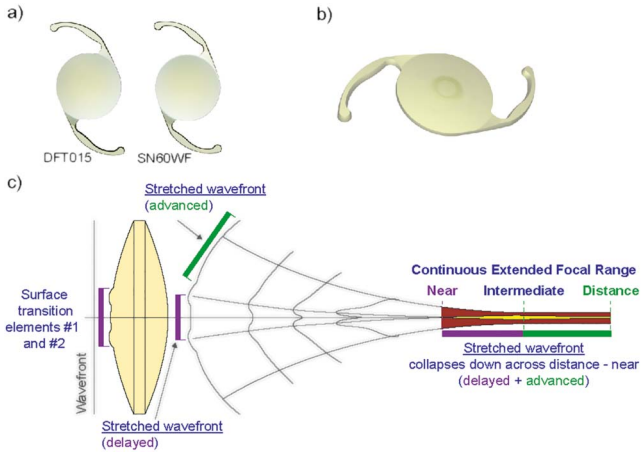

Figure 1. *a*: Surface profiles of the DFT015 and SN60WF IOLs, (*b*) 7× magnification of the central element of DFT015, and (*c*) mechanism of action of the DFT015 IOL.

The purpose of this international study was to evaluate the effectiveness and safety of a new presbyopia-correcting IOL with a nondiffractive design, DFT015, compared with an aspheric monofocal IOL control.

METHODS

Study Design

This was a prospective, multicenter, randomized, parallel-group, controlled, assessor- and patient-masked clinical study (ClinicalTrials.gov identifier NCT03010254) comparing DFT015 IOL with SN60WF, an aspheric monofocal IOL. Participants were randomized for bilateral implantation of either DFT015 or SN60WF IOL in a 5:4 ratio. Treatment groups remained masked until after the final database lock at 6 months. The study was conducted in accordance with the tenets of the Declaration of Helsinki and International Conference on Harmonization E6 GCP consolidated guidelines. The study also complied with the standards for IOLs set by the International Organization for Standardization (ISO) 11979-7:2014 and ISO 14155:2011 standards on good clinical practice (which were applicable at the time the study was conducted).[13,14] Standard operating procedures of the study sponsor and contract research organizations participating in the conduct of the clinical study and all other applicable regulations were also followed.

Study Population

Patients included in the study were aged ≥22 years and had to present with bilateral cataracts with planned removal by routine small-incision surgery and preoperative regular corneal astigmatism <1.0 D. The calculated IOL power for all eyes was within the clinical study supply range (18.0 to 25.0 D in 0.5 D steps) when targeted for emmetropia (0.0 ± 0.5 D).

Exclusion criteria included pregnancy, patients with previous intraocular or corneal surgery or requiring any other planned ocular surgical procedures, or those with a desire for monovision correction. In addition, patients were excluded if there was a history of, or current experience with, any anterior segment or posterior segment pathology, clinically significant corneal pathology that may adversely affect visual outcomes, clinically significant severe dry eye, or any other comorbidity that may confound the study results.

Effectiveness End Points and Safety Objectives

The primary effectiveness objective was to demonstrate superiority of DFT015 IOL over SN60WF IOL in mean monocular photopic DCIVA (logMAR) at 66 cm at month 3. Secondary effectiveness objectives, evaluated at month 3, for DFT015 IOL in comparison with SN60WF IOL included the following: demonstration of noninferiority in mean monocular photopic CDVA (logMAR) at 4 m; superiority in mean monocular photopic distance-corrected near visual acuity (DCNVA) (logMAR) at 40 cm; and mean monocular defocus curve with 0.5 D or greater negative range of defocus at 0.2 logMAR. Supportive effectiveness end points assessed at month 6 included the abovementioned end points and refractive outcomes and binocular distance-corrected and uncorrected visual acuity (VA) at each distance, binocular defocus curve, and reading speed at 66 cm.

The primary safety objective was to show that the rate of ocular adverse events (AEs) with DFT015 IOL was not worse than safety and performance end point rates as defined in ISO 11979-7:2014. Supportive safety end points included binocular mesopic contrast sensitivity (with and without glare), binocular photopic contrast sensitivity (without glare), AEs (including secondary surgical interventions [SSIs]), IOL position change (tilt/decentration), subjective posterior capsular opacification (PCO) assessment, posterior capsulotomy, and intraocular pressure.

A protocol amendment, implemented after initiation of enrollment, enabled formal statistical analyses of noninferiority in monocular mesopic contrast sensitivity and superiority of spectacle independence overall and at intermediate at month 6 to assess performance inherent in the optical design of DFT015 IOL. Furthermore, assessment of visual disturbances month 6 visit with the Quality of Vision (QoV) questionnaire was added as a supportive safety end point.[15]

Study Procedures

The first surgical eye was defined as the eye with the worse preoperative CDVA. If the CDVA was the same in both eyes, the right eye was the first surgical eye. The second-eye surgery was required to occur within 28 days of the first-eye surgery. A total of 10 scheduled visits were planned: screening, 2 operative visits, and postoperative days 1 to 2 and days 7 to 14 (after each surgery), days 30 to 60, days 70 to 100, and days 120 to 180 (after the second surgery).

Primary and secondary end point data were collected at the month 3 visit (postoperative days 70 to 100; with the exception of patient-reported spectacle use and visual disturbances) and repeated at the month 6 visit (postoperative days 120 to 180). Monocular and binocular uncorrected and distance-corrected VA tests were performed under photopic conditions at distance (4.0 m), intermediate (66 cm), and near (40 cm). Defocus curve testing was conducted at 4.0 m, under photopic conditions, using corrected distance refraction and added defocus. VA was measured between +1.50 D and −2.50 D in 0.50 D defocus steps, except in the region from +0.50 D to −0.50 D, which was assessed in 0.25 D steps. Contrast sensitivity was tested in mesopic conditions (with and without a glare) and in photopic conditions (without glare) using a CSV-1000 instrument (VectorVision, Inc.).

Patients who had not exited the study by the month 6 visit were asked to complete the spectacle use and QoV questionnaires. Because the questionnaires were added as a protocol amendment, some patients who had already exited the study were missed. The spectacle use questionnaire asked patients a series of questions, with the choice of answers being always, sometimes, or never. The following questions were asked: Q1, "How often do you wear eyeglasses for any purpose?"; Q2, "How often do you wear eyeglasses for near tasks (eg, reading print)?"; Q3, "How often do you wear eyeglasses for intermediate tasks (eg, computer)?"; and Q4, "How often do you wear eyeglasses for distance tasks (eg, driving)?" In addition, reading speed was assessed at intermediate distance (66 cm) using the MNREAD iPad application with 2.5 M, 2.0 M, 1.6 M, 1.25 M, and 1.0 M print sizes. The cutoff value for the test was 1.0 M because this provides 0 to 1 line of acuity reserve based on the anticipated binocular intermediate VA of 0.2 to 0.1 logMAR with DFT015. The QoV questionnaire proactively asked patients to report the frequency, severity, and bothersomeness of visual disturbances (halos, glare, and starbursts).

Statistical Analysis

Sample size calculations determined that a proposed sample size of 234 patients completing the study (DFT015 IOL, n = 130; SN60WF IOL, n = 104) would provide >99% power for the superiority hypotheses test on mean monocular DCIVA (66 cm) and mean monocular DCNVA (40 cm) when tested at the 0.025 level of significance (1-sided), assuming that the difference in means was −0.12 logMAR (SD = 0.18), and 74% power for the noninferiority hypothesis regarding mean monocular CDVA (4 m) when tested at the 0.025 level of significance (1-sided) with a noninferiority margin of 0.10 logMAR, assuming the difference in means was 0.04 logMAR (SD = 0.16). Thus, a total number of 260 patients were planned to be randomized to ensure achievement of the proposed sample size of 234 evaluable patients at the final visit.

The all-implanted analysis set, used as the primary analysis set for effectiveness analyses, included all randomized eyes with successful IOL implantation. The best-case analysis set, used as the primary analysis set for defocus curve testing, included all successfully implanted eyes that had at least 1 postoperative visit, no macular degeneration at any time, and no major protocol violations. The safety analysis set, used as the primary analysis set for all safety end points, included all eyes with attempted IOL implantation.

The mean monocular photopic DCIVA and DCNVA superiority hypotheses were tested based on a 2-sample *t* test, with a type I error rate of 2.5%, 1-sided. Superiority was demonstrated if the 2-sided *P* value was less than 0.05 from a 2-sample *t* test at month 3 or the upper confidence limit (UCL) of the 2-sided 95% CI was less than 0.0. The difference in means (DFT015 IOL − SN60WF IOL), the associated 2-sided 95% CI, and corresponding *P* value are presented. The mean monocular photopic CDVA noninferiority hypothesis was tested based on a 2-sample *t* test, with a type I error rate of 5%, 2-sided. Noninferior CDVA was demonstrated if the 1-sided 97.5% UCL was <0.1 logMAR. The difference in means (DFT015 IOL − SN60WF IOL) and the associated 1-sided 97.5% UCL are presented. For the assessment of mean monocular defocus curves at 0.2 logMAR, the outcome was met if DFT015 had a range of defocus ≥0.50 D greater negative range than SN60WF IOL, measured in the negative direction from zero D. For the assessment of mean mesopic contrast sensitivity, noninferiority was demonstrated if the 1-sided 97.5% lower confidence limit (LCL) was >0.15 log unit from a 2-sample *t* test, with a type I error rate of 5%, 2-sided. Finally, testing for superiority of DFT015 IOL over SN60WF IOL for independence from spectacle use was based on an LCL of >0% at month 6, with 2-sided 95% CI calculated using the Miettinen-Nurminen method.

Overall, type I error was maintained at the 0.05 level for month 3 analyses using a sequential testing approach of the superiority test for DCIVA (primary outcome), followed by the noninferiority test for CDVA and the superiority test for DCNVA (secondary outcomes). If the primary and both secondary null hypotheses were rejected, a sequential testing approach was also used to analyze month 6 outcomes in the following order: the superiority test for DCIVA (primary outcome), followed by the noninferiority test for CDVA and the superiority test for DCNVA, and then the noninferiority test for mesopic contrast sensitivity and the superiority test for spectacle use (all secondary outcomes).

After study completion, a post hoc exploratory descriptive analysis was performed in DFT015 IOL recipients to evaluate the visual outcomes of patients that achieved minimonovision compared with nonmonovision. Stratification of DFT015 IOL recipients was based on manifest refraction spherical equivalent (MRSE) at month 6. The minimonovision subgroup (n = 19) was defined as ≥0.50 D absolute difference in MRSE between eyes and MRSE of −0.25 D, or more myopic, in at least 1 eye. The nonmonovision subgroup (n = 132)

was defined as remaining patients who did not meet minimonovision criteria. Because of the small patient numbers in the minimonovision subgroup and post hoc nature of this analysis, inferential statistics were not performed on the resulting data.

RESULTS

Patient Disposition and Demographics

A total of 322 participants were enrolled across 19 investigational sites in 4 countries (Australia, Canada, Spain, and the United Kingdom), of which 40 patients discontinued prior to randomization, mostly because of screening failure (n = 39) (Supplemental Figure 1, http://links.lww.com/JRS/A399). The remaining 282 patients were randomized to the DFT015 (n = 159) or SN60WF (n = 123) study groups. Of these, 3 patients were excluded prior to implantation in each of the DFT015 IOL group (IOL power calculation was not within the clinical study supply range for 2 patients; 1 patient withdrew voluntarily) and the SN60WF IOL group (IOL power calculation was not within the clinical study supply range for 1 patient; 2 patients had surgical complications). Of the 276 patients who were implanted, 270 completed the study (DFT015, n = 152; SN60WF, n = 118); 4 patients in the DFT015 IOO group were lost to follow-up and 1 patient in the SN60WF IOL group withdrew because of an AE (Supplemental Figure 1, http://links.lww.com/JRS/A399).

Patient demographics and baseline characteristics were generally similar between the 2 groups (Table 1). The overall mean age was 69.7 ± 7.4 years and 57.6% of patients were women; the DFT015 IOL group had a slightly higher proportion of women than the SN60WF IOL group (60.3% and 54.2%, respectively). For the first eyes, the mean baseline monocular CDVA was worse than 0.2 logMAR in both groups and the mean baseline corneal astigmatism was low (~0.5 D). At month 6 postoperatively, 11 (7.2%), 55 (36.2%), and 86 (56.6%) DFT015 IOL patients and 9 (7.6%), 40 (33.9%), and 69 (58.5%) SN60WF IOL patients had small (<3.0 mm), medium (3.0 to 4.0 mm), and large (>4.0 mm) photopic pupil sizes, respectively.

Table 1. Patient Demographics and Baseline Characteristics.

Characteristic	DFT015 IOL (n = 156)	SN60WF IOL (n = 120)
Median age, y (range)	70.5 (46, 84)	70.0 (51, 87)
Age, y, n (%)		
Younger than 65	34 (21.8)	25 (20.8)
65 or older	122 (78.2)	95 (79.2)
Sex, n (%)		
Women	94 (60.3)	65 (54.2)
Men	62 (39.7)	55 (45.8)
Race, n (%)		
White	129 (82.7)	101 (84.2)
Black or African American	4 (2.6)	1 (0.8)
Asian	12 (7.7)	8 (6.7)
Other	11 (7.0)	10 (8.3)
Mean (SD) CDVA, logMAR	0.27 (0.22)	0.25 (0.16)
Mean (SD) axial length, mm	23.41 (0.70)	23.42 (0.80)
Axial length, n (%)		
Short (<21 mm)	0	0
Medium (21, 26 mm)	156 (100.0)	119 (99.2)
Long (>26 mm)	0	1 (0.8)
Mean (SD) corneal astigmatism[a], D	0.51 (0.25)	0.56 (0.25)

First eye (all-implanted analysis set)
[a]Absolute (K1 − K2)

Refractive and Visual Outcomes

Refractive Outcomes At month 6, 138 (90.8%) of patients in the DFT015 IOL group and 100 (84.7%) of patients in the SN60WF IOL group achieved an absolute MRSE ≤0.50 D in the first eyes (Supplemental Table 1, http://links.lww.com/JRS/A399). One eye in each group presented with MRSE of >1.0 D at month 6. The mean target residual refractive errors for the DFT015 and SN60WF IOL groups at month 6 were −0.15 ± 0.32 D and −0.09 ± 0.38 D, respectively.

Monocular Distance-Corrected Visual Acuity All effectiveness objectives were achieved at month 3 in the first eyes and were similar to month 6 outcomes; therefore, the focus was on month 6 outcomes. Superiority of DFT015 IOL over SN60WF IOL in the primary effectiveness end point of mean monocular photopic DCIVA (66 cm) was demonstrated in the first eyes at month 6, based on the observed UCL of the 2-sided 95% CI of −0.099 logMAR for the difference in least squares means (LSMeans) between the 2 groups, which was less than the UCL reference value of 0.0 logMAR (Table 2). The statistically significant differences in LSMeans of −0.139 logMAR (>1 line), in favor of DFT015, were observed at month 6 ($P < .001$). Overall, 62.7% of DFT015 IOL and 33.1% of SN60WF IOL first eyes achieved a monocular DCIVA of 0.2 logMAR or better at month 6.

For secondary effectiveness outcomes, DFT015 was noninferior to SN60WF in the mean monocular photopic CDVA (4 m) in first eyes at month 6, based on the observed 97.5% UCL of 0.063 logMAR for the statistically significant difference in LSMeans between the 2 groups, which was less than the noninferiority margin of 0.1 logMAR (Table 2). In addition, DFT015 IOL was superior to SN60WF IOL in the mean monocular photopic DCNVA (40 cm) in the first eyes at 6 months, based on the observed 95% UCL of −0.048 logMAR for the statistically significant difference in LSMeans between the 2 groups, which was less than the UCL reference value of 0.0 logMAR (Table 2).

Binocular Distance-Corrected and Uncorrected Visual Acuity Both DFT015 and SN60WF IOL groups achieved a mean binocular CDVA of <0.0 logMAR at month 6 (−0.063 ± 0.092 and −0.104 ± 0.076 logMAR, respectively) (Table 2). A >1-line difference in favor of DFT015 IOL compared with SN60WF IOL was observed for mean (±SD) binocular DCIVA at month 6 (0.075 ± 0.126 and 0.196 ± 0.160 logMAR, respectively). An approximately 1-line difference in favor of DFT015 IOL vs SN60WF IOL was demonstrated in the mean binocular DCNVA at month 6 (0.306 ± 0.157 and 0.404 ± 0.175 logMAR, respectively).

Similar results were achieved for binocular uncorrected VA at month 6. Both groups achieved a mean binocular uncorrected distance visual acuity of approximately 0.0 logMAR (20/20) with <1-line difference between DFT015 and SN60WF IOL groups (0.013 ± 0.125 and −0.016 ± 0.113 logMAR, respectively). DFT015 IOL recipients achieved better than

Table 2. Photopic Visual Acuity Outcomes at Month 6 (All-Implanted Analysis Set).				
Monocular				
LSMean ± SE, logMAR	**DFT015 IOL (n = 150)**	**SN60WF IOL (n = 118)**	**Between-group difference**	***P* value**
CDVA (97.5% UCL)	−0.008 ± 0.0076	−0.048 ± 0.0086	0.041 ± 0.0115 (0.063)	
DCIVA (95% CI)	0.161 ± 0.0136 (0.134, 0.188)	0.300 ± 0.0153 (0.270, 0.330)	−0.139 ± 0.0204 (−0.179, −0.099)	< .001
DCNVA (95% CI)	0.414 ± 0.0138 (0.387, 0.441)	0.513 ± 0.0156 (0.482, 0.543)	−0.098 ± 0.0208 (−0.139, −0.057)	< .001
Binocular				
Mean ± SD, logMAR	**DFT015 IOL (n = 149)**	**SN60WF IOL (n = 117)**	**—**	**—**
DCIVA	0.075 ± 0.126	0.196 ± 0.160	—	—
CDVA	−0.063 ± 0.092	−0.104 ± 0.076	—	—
DCNVA	0.306 ± 0.157	0.404 ± 0.175	—	—
UIVA	0.060 ± 0.115	0.112 ± 0.163	—	—
UDVA	0.013 ± 0.125	−0.016 ± 0.113	—	—
UNVA	0.232 ± 0.164	0.345 ± 0.188	—	—

LSMean = least squares mean; UCL = upper confidence limit
In the DFT015 and SN60WF monocular IOL groups, the numbers of evaluable patients were 150 and 118 for CDVA and DCVIVA and 153 and 115 for DCNVA, respectively

20/25 binocular uncorrected intermediate visual acuity (UIVA) and approximately 20/32 binocular uncorrected near visual acuity (UNVA), with 0.052-line and >1-line differences in favor of DFT015 IOL vs SN60WF IOL observed for mean (±SD) binocular UIVA (0.060 ± 0.115 and 0.112 ± 0.163 logMAR) and UNVA (0.232 ± 0.164 and 0.345 ± 0.188 logMAR), respectively.

Defocus Curve DFT015 IOL exhibited a greater monocular depth of focus than SN60WF IOL, which was sustained at month 6 in the first eyes (Supplemental Figure 2, http://links.lww.com/JRS/A399); the difference in depth of focus between the 2 IOLs was 0.52 D at 0.2 logMAR in favor of DFT015 IOL, meeting the secondary effectiveness objective. This outcome was supported by second operative eyes at month 6. The binocular defocus curve indicated that patients with DFT015 IOL achieved ≤0.0 logMAR VA from +0.50 D to −0.50 D, <0.1 logMAR out to −1.50 D, and <0.2 logMAR VA out to −2.00 D (50 cm) (Figure 2). The difference in binocular depth of focus between the 2 IOLs was 0.62 D at 0.2 logMAR, in favor of DFT015 IOL.

Spectacle Independence At month 6, 106 patients with DFT015 and 80 patients with SN60WF who had not exited the study completed a spectacle use questionnaire. A greater number of patients with DFT015 than patients with SN60WF reported never requiring spectacles for any purpose at month 6 (30.2% and 10.0%, respectively), for intermediate tasks at month 6 (75.5% and 53.8%, respectively), and for near tasks (29.2% and 8.8%, respectively). For any purpose and intermediate tasks, the observed 95% LCLs of 8.77% and 7.92%, respectively, for the difference in proportions between the 2 groups were greater than the reference value of 0%. Both DFT015 and SN60WF IOL groups demonstrated similar frequencies of patients reporting never requiring spectacles for distance tasks (91.5% and 90.0%, respectively). Inferential statistics were not preplanned for distance or near spectacle independence.

Reading Speed Test at 66 cm Patients in the DFT015 IOL group showed functional reading speeds (>80 words per minute) at uncorrected and distance-corrected intermediate distance for every print size tested down to 1.0 M.[16] By contrast, patients in the SN60WF IOL group only demonstrated functional reading at uncorrected and distance-corrected intermediate distance up to 1.25 M print size.

Safety Outcomes

Adverse Events The rates of ocular serious AEs, including SSIs, for the first and second eyes in the DFT015 group were below ISO 11979-7:2014 thresholds. One SSI (IOL repositioning required due to YAG posterior capsulotomy) was reported in DFT015 first eyes and 1 SSI (laser-assisted in situ keratomileusis) was reported in DFT015 IOL second eyes (Supplemental Table 2, http://links.lww.com/JRS/A399). No SSIs relating to the optical properties of the IOL were reported in the DFT015 or SN60WF IOL groups. Among DFT015 IOL recipients, no first eyes had ≥1-degree tilt and 1 second eye had ≥1-degree tilt. Two first eyes with DFT015 IOL and 1 first eye with SN60WF IOL had IOLs decentered by ≥0.5 mm. Rates of clinically nonsignificant subjective PCO, clinically significant PCO, and those requiring YAG were similar between groups. The incidence rate of posterior capsulotomy was low and similar between groups. There were no reported deaths during the study.

Contrast Sensitivity Reductions in contrast sensitivity for DFT015 IOL compared with SN60WF IOL were generally observed at higher spatial frequencies, although no differences >0.3 log units between DFT015 and SN60WF IOLs were observed for mean monocular or binocular photopic (without glare) or mesopic contrast sensitivity (with and without glare) at any spatial frequency tested.[14,17]

At month 6, noninferiority of DFT015 IOL in mean monocular mesopic contrast sensitivity at 12 cycles per degree (cpd) compared with SN60WF IOL in the first eyes was not achieved based on observed 97.5% LCLs of −0.287 log units in both groups, with and without glare conditions, because the difference in LSMeans between the 2 groups and was greater than the margin of −0.15 log units.

At month 6, differences in binocular mean mesopic contrast sensitivity (with and without glare) and photopic contrast

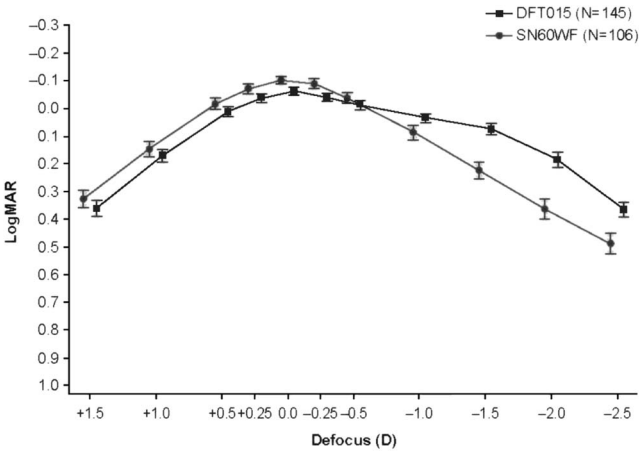

Figure 2. The mean binocular defocus curves (logMAR) at month 6. Best-case analysis set; 95% CIs.

sensitivity (without glare) between DFT015 and SN60WF IOL recipients were ≤0.23 and ≤0.16 log units, respectively, at each of the spatial frequencies tested (Figure 3, a–c).

Quality of Vision Questionnaire At month 6, 106 DFT015 IOL patients and 80 SN60WF IOL patients who had not exited the study reported on the frequency severity, and bothersomeness of visual disturbances using the QoV questionnaire (Figure 4, a–c). The frequency of severe visual disturbances was low and similar between groups at month 6; frequencies of severe glare, halos, and starbursts were 3.8% (n = 4), 0.9% (n = 1), and 3.8% (n = 4) with DFT015 IOL and 2.5% (n = 2), 0%, and 2.5% (n = 2), respectively, with SN60WF IOL. In addition, the frequency of patients experiencing very bothersome visual disturbances was low (≤5.0%) and similar between groups at month 6; frequencies of very bothersome glare, halos, and starbursts were 3.8% (n = 4), 0.9% (n = 1), and 1.9% (n = 2) with DFT015 IOL and 5.0% (n = 4), 0%, and 2.5% (n = 2) with SN60WF IOL, respectively. The frequency of patients responding not at all bothered by glare, halos, and starbursts were 73.6% (n = 78), 75.5% (n = 80), and 72.6% (n = 77) for DFT015 IOL and 57.5% (n = 46), 77.5% (n = 62), and 63.8% (n = 51) with SN60WF IOL, respectively.

Minimonovision The median binocular UIVA and UNVA were better by nearly 1 line in the DFT015 IOL minimonovision subgroup compared with the nonmonovision subgroup (Supplemental Figure 3, http://links.lww.com/JRS/A399). The mean MRSE in the minimonovision subgroup for the distance and myopic eyes were 0.026 ± 0.311 D and −0.586 ± 0.240 D, respectively. The mean MRSE in the nonmonovision subgroup for the first and second eyes were −0.137 ± 0.293 D and −0.148 ± 0.282 D, respectively. Both groups exhibited similar levels of spectacle independence for distance tasks (minimonovision, 93.3%; nonmonovision, 91.2%) at month 6. However, a higher number of patients with minimonovision compared with patients with nonmonovision reported spectacle independence for intermediate tasks (93.3% and 72.5%, respectively) and near tasks (46.7% and 26.4%, respectively) at month 6.

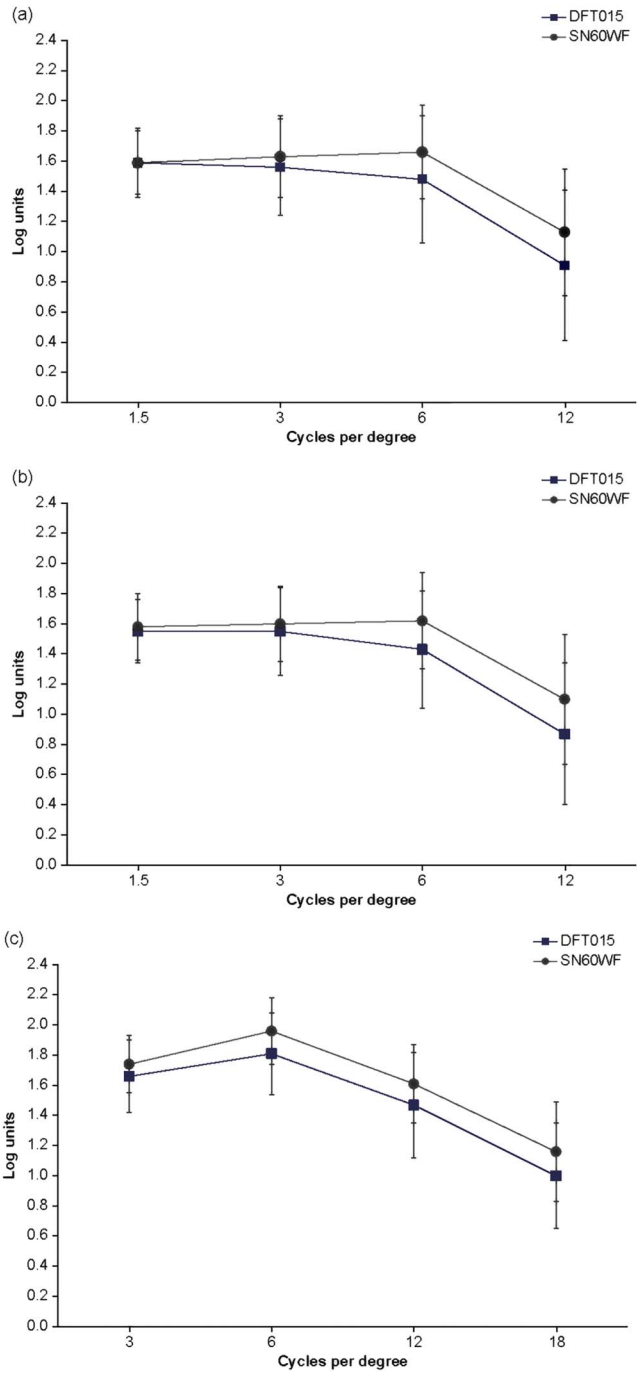

Figure 3. The mean binocular contrast sensitivity at month 6 (safety analysis set): (*a*) mean mesopic without glare; (*b*) mean mesopic with glare; and (*c*) mean photopic without glare.

The QoV questionnaire-assessed halo profile of patients in the DFT015 IOL minimonovision subgroup was similar to that in the nonmonovision subgroup at month 6; 93.3% of patients in the minimonovision subgroup and 87.9% in the nonmonovision subgroup rated halo severity as not at all/mild, and 100% of patients in the minimonovision subgroup and 94.5% in the nonmonovision subgroup rated halo bothersomeness as not at all/a little.

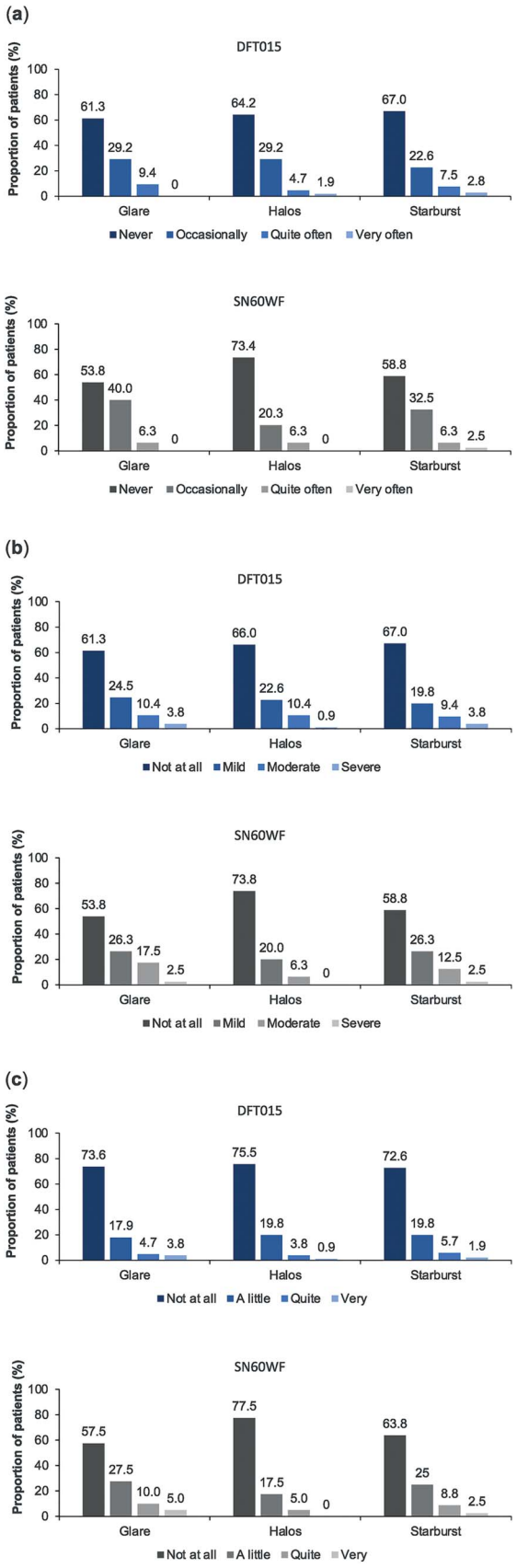

Figure 4. Frequency (*a*), severity (*b*), and bothersomeness (*c*) of visual disturbances at month 6. Overall percentages may not equate to 100% because of rounding. *Only 79 SN60WF recipients responded to the question regarding the frequency of halos.

DISCUSSION

Compared with an aspheric monofocal IOL, DFT015 IOL provides superior intermediate (66 cm) and near (40 cm) vision and noninferior distance vision, while maintaining a visual disturbance profile similar to that of the SN60WF monofocal IOL. Criteria for monocular photopic distance-corrected depth of focus were met at month 3 and maintained at month 6. DFT015 IOL demonstrated continuous extended vision, with at least a 0.5 D greater monocular depth of focus over the monofocal comparator at 0.2 logMAR. These effectiveness results exceed the ANSI criteria for EDoF IOLs.[6,18]

DFT015 IOL demonstrated a mean binocular CDVA of 0.0 logMAR or better, a mean DCIVA of 0.1 logMAR or better, and DCNVA of 0.3 logMAR. The distance VA outcomes the DFT015 IOL group were supported by binocular defocus curve results that demonstrated ≤0.0 logMAR (20/20) in the defocus range of +0.5 D to −0.5 D, suggesting that this IOL to be tolerant to low amounts of residual refractive error.

Enhanced near and intermediate vision were reflected in patient-reported outcomes, which indicated that DFT015 IOL recipients were able to engage in activities that require a range of vision with reduced use of spectacles compared with monofocal IOL recipients, including functional reading at print sizes as low as 1.0 M (8 pt. font). Targeting minimonovision in DFT015 IOL recipients may further improve uncorrected near and intermediate vision and increase spectacle independence for intermediate and near tasks without increasing the risk for halos.

Diminished contrast sensitivity has long been a limitation of some multifocal and EDoF IOLs, particularly in mesopic conditions or with glare.[19,20] Differences in binocular and monocular mean mesopic (with and without glare) and photopic (without glare) contrast sensitivity observed between DFT015 and SN60WF IOL recipients in this study were less than 0.3 log units at all spatial frequencies tested.[14,17] Monocularly, a 1-sided noninferiority test using a noninferiority margin of 0.15 log units was conducted at the highest spatial frequency (12 cpd) because this spatial frequency seems to be the most sensitive to optical designs that extend focus.[14,17] DFT015 IOL demonstrated lower mesopic contrast sensitivity with and without glare at the highest spatial frequency tested.

Although diffractive IOLs that provide a similar range of vision to DFT015 IOL, such as ZXR00 IOL (TECNIS Symfony), have been associated with higher rates of photic phenomena compared with a monofocal IOL, the results of this study using a validated patient-reported outcome questionnaire clearly showed that the new, nondiffractive design of DFT015 IOL results in a visual disturbance profile comparable with that of an aspheric monofocal IOL.[21] In fact, DFT015 IOL demonstrated a numerically higher proportion of patients never experiencing glare or starburst compared with SN60WF IOL at month 6. DFT015 IOL demonstrated a good safety profile, with the rate of cumulative and persistent serious AEs, including SSIs, in the first and second eyes

among DFT015 IOL recipients being below the threshold established in ISO 11979-7:2014.[14] Furthermore, no SSIs reported among DFT015 IOL recipients were related to the optical properties of the IOL.

For patients whose daily priorities include activities in the distance to functional near range and who have a need for monofocal quality of distance vision, DFT015 IOL would be the right choice and recommendation.[8] This clinical study showed that this first, to our knowledge, and the only nondiffractive presbyopia-correcting IOL with X-WAVE technology, DFT015 IOL, clearly exceeds ANSI-defined EDoF criteria, providing patients with a continuous extended range of vision that results in both superior intermediate and near vision and decreased spectacle wear compared with a monofocal IOL control and distance vision and a visual disturbance profile similar to that of a SN60WF monofocal IOL.

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WHAT WAS KNOWN

- Diffractive multifocal IOLs can provide an enhanced depth of focus but at the cost of an increased prevalence of visual disturbances.

WHAT THIS PAPER ADDS

- The new, nondiffractive presbyopia-correcting IOL, DFT015, provided a continuous extended range of vision, resulting in superior intermediate and near vision and noninferior distance vision compared with an aspheric monofocal IOL, SN60WF.
- DFT015 IOL demonstrated a visual disturbance profile similar to that of an aspheric monofocal IOL, SN60WF.

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First author:
Chandra Bala, PhD, MBBS, FRANZCO

PersonalEyes, Sydney, Australia