BAUSCH + LOMB

enVista ENVY™ TORIC

HYDROPHOBIC ACRYLIC IOL

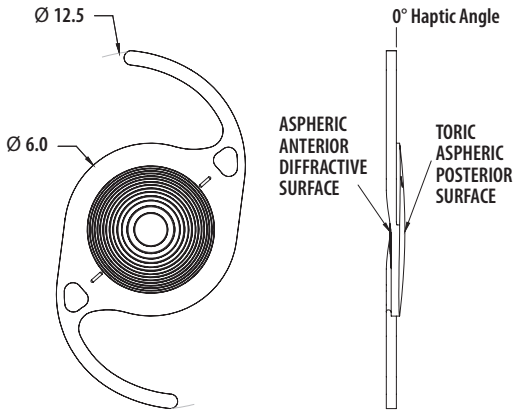
Device Description

The enVista Envy™ toric hydrophobic acrylic IOL (intraocular lens) (non-preloaded model: ETN / preloaded into shuttle model: ETPN) was developed to replace the natural crystalline lens in adult patients in whom the cataractous lens has been removed. The composition and characteristics of the IOL are specified in the table below.

The enVista Envy toric IOL has an aspheric apodized diffractive optic on the anterior lens surface, providing 1.60 D of intermediate and 3.1 D of near add powers. The posterior surface is designed to have -0.15 µm of spherical aberration to compensate for the positive spherical aberration of the average human cornea.

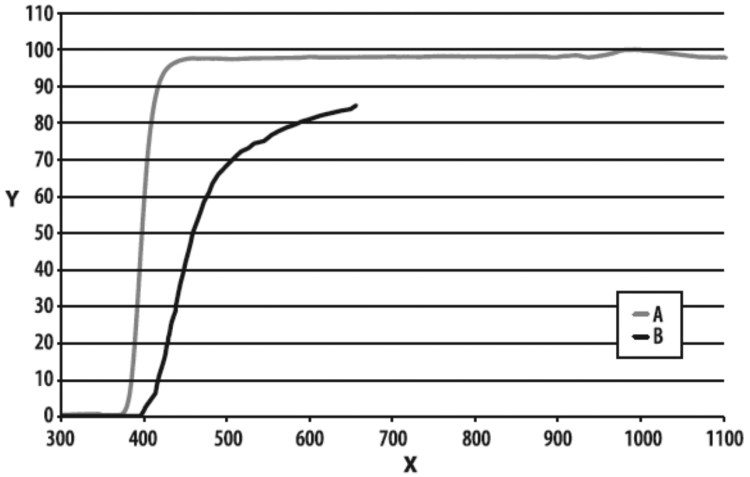
The optic is designed with the SureEdge™ posterior-squared step edge to provide a 360-degree PCO barrier. The IOL employs an Accuset™ haptic with a broad, modified C-loop design and optic-haptic offset to facilitate improved contact and stability within the capsular bag. The posterior-located cylinder axis marks denote the meridian with the lowest power. The enVista material that makes up the TruSight™ optic has been assessed for glistening-free capacity and scratch resistance. Glistenings are observed by ophthalmologists at the slit lamp as backscatter. There has been no established correlation between these backscatter observations and what patients observe. Incorporated StableFlex™ technology allows for enhanced IOL compliance for ease of loading, premium control through IOL delivery, and efficient optical recovery following implantation.

Physical Characteristics

Lens / Haptic Material	Hydrophobic acrylic (hydroxyethyl methacrylate (HEMA)-polyethylene glycol phenyl ether acrylate (poly(EG)PEA)-styrene copolymer, crosslinked with ethylene glycol dimethacrylate)										
Material Characteristics	Index Of Refraction: 1.53 @ 35°C; Specific Gravity: 1.19 g/ml										
Optic Type / Powers	Aspheric apodized diffractive / +6.0 to +34.0 Diopters in 0.5 Diopter increments (SE – Spherical Equivalent) / Intermediate 1.6 Diopters / Near 3.1 Diopters										
Cylinder Powers (CYL) – IOL Plane			1.25 D	1.50 D	2.00 D	2.50 D	3.00 D	3.50 D	4.25 D	5.00 D	5.75 D
Cylinder Powers (CYL) – Corneal Plane[1]			0.88 D	1.05 D	1.40 D	1.75 D	2.10 D	2.45 D	2.98 D	3.50 D	4.03 D
Dimensions	Body Diameter: 6.0 mm; Overall Diameter: 12.5 mm; Haptic Angle: 0°										
Image	 Dimensions are in mm										
Spectral Transmittance	**Ultraviolet:** UV (389) 10% transmittance for +20.0 Diopter IOL. See Figure **1** with chart's **X** value = Wavelength (nm) and **Y** value = % Transmittance; chart compares the transmittance curve of an enVista IOL to a 53-Year-Old Human Lens. **A** = +20 Diopter enVista IOL and **B** = 53-Year-Old Human Lens. **NOTE:** Light transmittance values for an IOL material may vary slightly depending on the method of measurement. **Reference:** 53-Year-Old Human Lens data from Boettner, E.A. and Wolter, J. R., "Transmission of the Ocular Media," Investigative Ophthalmology, 1:776-783, 1962.										

[1] Based on an average pseudophakic human eye

Figure 1



Indications

The enVista Envy toric hydrophobic acrylic IOL (non-preloaded model: ETN / preloaded into shuttle model: ETPN) is indicated for primary implantation in the capsular bag of the eye in adult patients for visual correction of aphakia and corneal astigmatism following removal of a cataractous lens to mitigate the effects of presbyopia by providing improved intermediate and near visual acuity, while maintaining comparable distance visual acuity to an aspheric monofocal IOL.

Warnings

As with any surgical procedure, there is risk involved. Physicians considering IOL implantation under any of the following circumstances should weigh the potential risk/benefit ratio:

1. Recurrent severe anterior or posterior segment inflammation or uveitis.
2. Patients in whom the IOL may affect the ability to observe, diagnose, or treat posterior segment diseases.
3. Surgical difficulties at the time of cataract extraction, which might increase the potential for complications (e.g., persistent bleeding, significant iris damage, uncontrolled positive pressure, or significant vitreous prolapse or loss).
4. A distorted eye due to previous trauma or developmental defect in which appropriate support of the IOL is not possible.
5. Circumstances that would result in damage to the endothelium during implantation.
6. Suspected microbial infection.
7. Patients in whom neither the posterior capsule nor zonules are intact enough to provide support.
8. Some visual disturbances may be expected due to the superposition of focused and unfocused multiple images. These may include some perceptions of halos or radial lines around point sources of light (starbursts) under nighttime conditions, glare, double vision, haziness and blurred vision. It is expected that, in a small percentage of patients, the observation of such phenomena will be annoying and may be perceived as a hindrance, particularly in low illumination conditions such as nighttime driving. As with other trifocal IOLs, there is a possibility that visual disturbances may be significant enough that the patient will request explant of the IOL.
9. A reduction in contrast sensitivity as compared to a monofocal IOL may be experienced by some patients, therefore, patients implanted with trifocal IOLs should exercise caution when driving at night or in low light or poor visibility conditions.
10. Patients with predicted postoperative astigmatism greater than 1.0 D may not fully benefit from a trifocal IOL in terms of spectacle independence or improved intermediate and near vision seen in patients with lower astigmatism.
11. Care should be taken to achieve IOL centration as IOL decentration may result in patients experiencing visual disturbances or suboptimal vision under certain lighting conditions.
12. The surgeon must target emmetropia to achieve optimal visual performance.
13. Patients should be advised that unexpected outcomes could lead to continued spectacle dependence or the need for secondary surgical intervention (e.g., intraocular lens replacement or repositioning).
14. The lens should not be implanted if the posterior capsule is ruptured, if the zonules are damaged, or if a primary posterior capsulotomy is planned.
15. Carefully remove all viscoelastic from both the anterior and posterior sides of the lens. Residual viscoelastic may cause complications including lens rotation resulting in misalignment of the enVista Envy Toric Trifocal IOL with the intended axis of placement.
16. Rotation of the IOL away from the intended axis can reduce its astigmatic correction. Misalignment greater than 30° may increase postoperative refractive cylinder. If necessary, IOL positioning should occur prior to capsule fibrosis and IOL encapsulation.
17. Do not attempt to resterilize the IOL as this can produce undesirable side effects.
18. Prior to opening, inspect vial pouch and vial for signs of damage that may affect integrity of device sterility. If damaged, do not use. The IOL should be used immediately after opening.
19. Do not use if product sterility or quality is thought to be compromised due to damaged packaging or signs of leakage (such as the loss of saline storage solution, or the presence of salt crystallization).
20. Store at room temperature. Do not freeze. Avoid high temperatures (>43°C / >109°F). Keep dry. Keep away from sunlight. Do not use if the packaging is exposed to environmental conditions outside of those specified.

21. Do not soak or rinse the IOL with any solution other than sterile balanced salt solution or sterile normal saline.
22. Do not place the IOL in contact with surfaces where such contamination can occur.
23. Do not autoclave the IOL.
24. Do not re-use the IOL. It is intended for permanent implantation. If explanted, sterility and proper function cannot be ensured.

Precautions

1. Prior to surgery, prospective patients should be informed of the possible risks and benefits associated with the enVista Envy Trifocal IOLs. A Patient Information Brochure can be found at www.bausch.com/IFU. Please provide a copy of the Patient Information Brochure to the patient.
2. As with other multifocal IOLs, patients may need glasses when reading small print or looking at small objects.
3. Posterior capsule opacification (PCO) may significantly affect the vision of patients with multifocal IOLs earlier in its progression than patients with monofocal IOLs. This may be due to the reduced contrast sensitivity observed with multifocal IOLs.
4. The safety and effectiveness of the IOL have not been substantiated in patients with pre-existing ocular conditions and intraoperative complications (see below). Careful preoperative evaluation and sound clinical judgment should be used by the surgeon to decide the benefit/risk ratio before implanting an IOL in a patient with one or more of these conditions. Physicians considering IOL implantation in such patients should explore the use of alternative methods of aphakic correction and consider IOL implantation only if alternatives are deemed unsatisfactory in meeting the needs of the patient.

   Before Surgery

   - Irregular corneal astigmatism
   - Significant irregular corneal aberration
   - Corneal irregularity (including irregularity due to dry eye syndrome)
   - Retinal conditions or predisposition to retinal conditions, previous history of, or a predisposition to retinal detachment, or proliferative diabetic retinopathy in which future treatment may be compromised by implanting this IOL
   - Amblyopia
   - Clinically severe corneal dystrophy (e.g., Fuchs', epithelial, stromal, or endothelial dystrophy), keratitis, keratoconjunctivitis, keratouveitis, keratopathy, or kerectasia
   - Any Inflammation or edema (swelling) of the cornea
   - Rubella, congenital, traumatic or complicated cataracts
   - Extremely shallow anterior chamber, not due to swollen cataract
   - Recurrent anterior or posterior segment inflammation of unknown etiology, or any disease producing an inflammatory reaction in the eye (e.g., iritis or uveitis)
   - Aniridia
   - Iris neovascularization
   - Glaucoma (uncontrolled or controlled with medication)
   - Microphthalmos or macrophthalmos
   - Optic nerve atrophy
   - Previous corneal transplant
   - Pre-existing ocular conditions which may negatively impact stability of the implant
   - Previous refractive surgery
   - Cervical dystonia or spasmodic torticollis may interfere with the pre-operative surgical plan or IOL axis orientation during surgery
   - Pregnancy

   During Surgery

   - Other planned ocular surgery procedures, including but not limited to, LASIK, astigmatic keratotomy, and limbal relaxing incisions
   - Excessive iris mobility
   - Mechanical or surgical manipulation required to enlarge the pupil
   - Vitreous loss (significant)
   - Anterior chamber bleeding (significant)
   - Uncontrollable positive intraocular pressure
   - Complications in which the IOL stability could be compromised, including, but not limited to:
     - Zonular damage, separation, or rupture
     - Capsulotomy by any technique other than a circular tear or femtosecond laser
     - The presence of radial tears known or suspected at the time of surgery
     - Situations in which the integrity of the circular tear cannot be confirmed by direct visualization
     - Cataract extraction by techniques other than phacoemulsification or liquefaction
     - Situations where the need for a large capsulotomy can be anticipated (e.g., diabetics, retinal detachment in the fellow eye, peripheral retinal pathology, etc.)
     - Capsular rupture or capsulorhexis tear
     - Bag-sulcus, sulcus-sulcus or unknown placement of the haptics
5. Patients with preoperative problems such as corneal endothelial disease, abnormal cornea, macular degeneration, retinal degeneration, glaucoma, and chronic drug miosis may not achieve the visual acuity of patients without such problems. The physician must determine the benefits to be derived from IOL implantation when such conditions exist.
6. When binocular implantation of the enVista Envy Trifocal IOLs is planned, both eyes of a patient are not intended to be operated on the same day. Simultaneous binocular implantation has not been studied.
7. A high level of surgical skill is required for IOL implantation. The surgeon should have observed and/or assisted in numerous implantations and successfully completed one or more courses on IOL implantation before attempting to implant the IOL.
8. As with any surgical procedure, there is risk involved. Potential complications accompanying cataract or implant surgery may include, but are not limited to, the following: corneal endothelial damage, infection (endophthalmitis), retinal detachment, vitritis, cystoid macular edema, corneal edema, pupillary block, cyclitic membrane, iris prolapse, hypopyon, transient or persistent glaucoma, acute corneal decompensation, toxic anterior segment syndrome (TASS), and secondary surgical intervention. Secondary surgical interventions include, but are not limited to: IOL repositioning, IOL replacement, vitreous aspiration or iridectomy for pupillary block, wound leak repair, and retinal detachment repair.
9. Care should be taken to remove all viscoelastic from the anterior and posterior surfaces of the lens to minimize the possibility of lens rotation causing misalignment of the IOL from the intended axis placement.
10. The clinical study of the enVista Envy Trifocal IOL was conducted with the lens intended for implantation in the capsular bag only. There are no clinical data to demonstrate its safety and effectiveness for placement in the ciliary sulcus.
11. Effectiveness of implanting a toric IOL in reducing postoperative astigmatism is affected by many factors, including the following:
    - The degree of mismatch between the postoperative magnitude of corneal astigmatism and effective IOL power in the corneal plane.
    - Misalignment between the intended axial position and final IOL axial orientation.
    - Error in prediction of the postoperative corneal cylinder axis and power. Error in prediction of cylinder axis is greatest for lower levels of preoperative corneal astigmatism.
    - Manufacturing variation in power and axis markings can influence intended correction.
12. The enVista Envy Toric IOL has not been evaluated in a clinical study. In general, astigmatism that is corrected with a higher cylinder power IOL can result in clinically significant residual astigmatism. The effect of residual astigmatism at distance, intermediate, and near was evaluated in a clinical study of patients who had been implanted with non-toric enVista Envy IOLs and were induced with cylinder power to simulate various levels of residual astigmatism. Visual acuity results with simulated residual astigmatism are shown in the clinical study results section.
13. Anatomic and/or surgical factors may be related to the likelihood that a toric IOL could be placed incorrectly or rotate away from the intended position after placement. Some of these factors can be identified before or during the surgery, but others cannot. If a secondary surgical intervention is necessary to reposition the IOL, explanation should be considered as some patients may have recurrent or persistent issues related to rotational instability and misalignment.
14. All preoperative surgical parameters are important when choosing a toric lens for implantation, including preoperative keratometric cylinder (magnitude and axis), incision location, surgeons estimated surgically induced astigmatism (SIA) and biometry. Variability in any of the preoperative measurements can influence patient outcomes, and the effectiveness of treating eyes with lower amounts of preoperative corneal astigmatism.

Medical Device Re-Use Statement

If this product is reprocessed and/or re-used, Bausch + Lomb cannot guarantee the functionality, material structure, or cleanliness or sterility of the product. Re-use could lead to illness, infection and/or injury to the patient or user and, in extreme incidents, death. This product is labeled as 'single-use' which is defined as a device intended to be used once only for a single patient.

Calculation Of Lens Power

Suggested A-Constant: 119.5 (OPTICAL BIOMETRY)

The recommended A-Constant is intended for use with axial length measurements obtained by optical biometry. Use of axial length measurements by other techniques (e.g., Applanation A-scan) will normally require a different lens constant. This number is a guideline only and is based on an evaluation of clinical data obtained using the IOL Master. The physician should determine preoperatively the power of the lens to be implanted.

The astigmatism to be corrected should be determined from keratometry and biometry data rather than refractive data since the presence of lenticular astigmatism in the crystalline lens to be removed may influence results. The size and location of the surgical incision may affect the amount and axis of corneal astigmatism. Pre-operative keratometry and biometry data, incision location (temporal was used in the clinical study of the parent toric multifocal IOL), and the surgeon's estimated surgically induced corneal astigmatism are used to determine the appropriate enVista Envy Toric Trifocal IOL model, spherical equivalent lens power, and axis of placement in the eye.

Selection And Placement Of enVista Toric IOL

Keratometry and biometry data should be used in place of refractive data to determine targeted amount of astigmatism correction. Incision size and location influence amount of postoperative corneal astigmatism and its respective axis. It is recommended that surgeons customize their surgically-induced corneal astigmatism values based upon individual surgical technique and past results. To facilitate IOL selection and axis placement, Bausch + Lomb provides a web-based proprietary tool, the enVista toric Calculator (https://envista.toriccalculator.com), for the surgeon. Preoperative keratometry and biometry data are used as inputs for the enVista toric Calculator. These inputs are used to determine the axis of placement in the eye and the predicted residual refractive astigmatism for up to three different enVista toric IOL models. In eyes with low levels of corneal astigmatism, the predicted residual refractive astigmatism for implantation of the enVista toric IOL will be displayed for evaluation by the surgeon to determine the clinically meaningful benefit of implanting a toric IOL. Prior to surgery, the operative eye should be marked in the following manner: With the patient sitting upright, precisely mark the twelve o'clock and/or the six o'clock position with a T marker, a surgical skin marker, or a marking pencil indicated for ophthalmic use. Using these

marks as reference points, an axis marker can be used immediately prior to or during surgery to mark the axis of IOL placement. Input from the enVista toric Calculator can be used to determine optimal axis of placement. Toric axis markings at the haptic-optic junction identify the flat meridian of the enVista toric IOL and represent an imaginary line of the plus cylinder axis. After the IOL is inserted in the capsular bag, precisely align the axis markings on the enVista toric IOL with the marked axis of IOL placement. Be sure to remove all viscoelastic from the capsular bag. Reconfirm proper alignment of the enVista toric IOL following viscoelastic removal and/or inflation of the capsular bag at the end of the surgical case. Residual viscoelastic and/or over-inflation of the bag may cause lens rotation away from the intended axis of placement. Deviation from the intended axis of placement may compromise effectiveness of astigmatic correction. Inaccurate astigmatism measurements, errors in corneal markings, inaccurate placement of the enVista toric IOL axis during surgery, unanticipated surgically-induced changes in the cornea, or physical rotation of the lens after implantation may also limit the desired effect of the toric IOL on correction of corneal astigmatism.

Directions For Use

1. Inspect vial pouch and vial for signs of damage that may affect integrity of device sterility. If damaged, do not use.
2. Examine the label on the unopened package for model, powers (base power, add powers, and cylinder power as appropriate), proper configuration, and expiration date.
3. After opening the cardboard storage container, verify lens case information (e.g., model, power, serial number) is consistent with information on outer package labeling.
4. Open the peel pouch and remove the vial in a sterile environment.
5. Remove the lid from the vial.
6. Follow steps below.
   a) Non-preloaded IOL (model: ETN)
      1. With a pair of smooth forceps, remove the IOL from the vial by gently grasping the IOL haptic.
      2. Rinse the entire IOL with sterile balanced salt solution or sterile normal saline.
      3. Examine the IOL thoroughly to ensure particles have not become attached to it, and examine the lens optical surfaces for other defects.
      4. The IOL may be soaked in sterile balanced salt solution until ready for implantation.
      5. It is recommended to use an approved inserter per the Validated Inserters table below.
   b) Preloaded IOL (model: ETPN)
      1. Remove the SnapSet™ IOL shuttle from the vial by grasping the tab on the top.
      2. The SnapSet IOL shuttle may be flushed with sterile balanced salt solution during preparation for delivery.
      3. The SnapSet IOL shuttle preloaded with the enVista IOL (model: ETPN) is designed for use with the EyeGility™ inserter for enVista preloaded.
7. It is recommended to use an approved viscoelastic for lubrication of the IOL during implantation. See table below.
8. There are various surgical procedures that can be utilized, and the surgeon should select a procedure that is appropriate for the patient. Surgeons should verify that appropriate instrumentation is available prior to surgery.
9. The IOL and insertion device should be discarded if the IOL has been held in the folded state within the insertion device for more than 20 minutes. Not doing so may result in damage to the IOL.

Validated Inserters

Model	Inserter	Viscoelastic
ETN	BLIS INJ100	Amvisc™ Plus, Amvisc™, OcuCoat™
ETPN (IOL only)	EyeGility (2.0 mm or 2.4 mm)	

Overview Of Clinical Studies

Clinical studies have been conducted on the enVista Envy IOL and on the enVista toric (model MX60T). The trifocal IOL showed statistical non-inferiority to the monofocal IOL parent in photopic monocular UDVA and statistical superiority in photopic monocular UNVA and UIVA. No unexpected safety findings were observed. The enVista Envy Toric IOL is a combination of the optical design of the trifocal IOL and MX60T parents. The results of a clinical study to evaluate the safety and effectiveness of the enVista toric (model MX60T) IOL provide reasonable assurance that the MX60T IOL is safe and effective for the visual correction of aphakia and corneal astigmatism following cataract extraction. The data support a significant dioptric reduction in refractive cylinder and reduction in absolute cylinder, rotational stability of the lens, and uncorrected visual acuity at distance following implantation of the MX60T IOL.

enVista MX60T Clinical Trial

The US clinical trial of the enVista toric intraocular lens was conducted in 191 participants (191 eyes). The dioptric power range was 16.0 to 27.0 D with cylindrical powers at the lens plane of 1.25 D, 2.00 D, and 2.75 D for the MX60T.

Study Description

The study was a prospective, multicenter, parallel-group, partially randomized, partially controlled, double-masked, monocular clinical trial to evaluate the safety and effectiveness of the enVista toric IOL, Model MX60T, in reducing postoperative refractive astigmatism in participants undergoing cataract extraction. Participants in the lowest astigmatic IOL power (1.25 D) cohort were randomized to undergo implantation of either the toric test lens (enVista one-piece hydrophobic acrylic toric IOL, Model MX60T) or the non-toric spherical control lens (enVista one-piece hydrophobic acrylic IOL, Model MX60) in one eye. Participants in the higher astigmatic power cohorts (2.00 D, 2.75 D) were implanted with a test lens only in one eye. Postoperatively, participants underwent complete ophthalmic evaluations at regularly scheduled intervals through Form 4 (Postoperative Days 120-180).

The test lens was the enVista toric IOL (Model MX60T). The effective corneal powers for each of the test lens plane cylindrical powers of the test IOLs are shown in Table 1.

Table 1: enVista Toric IOL Cylinder Power

Cylinder Power at IOL Plane (D)	Cylinder Power at Corneal Plane (D)	Range of Predicted Postoperative Corneal Cylinder[1] (D)
1.25	0.90	0.90 - 1.39
2.00	1.40	1.40 - 1.92
2.75	1.93	1.93 - 2.40

[1]Each Surgeon's individual surgically-induced astigmatism (SIA) was added to the recommended preoperative correction range to determine eligibility based on preoperative corneal cylinder. Once the SIA was estimated, this value stayed constant during the study for each investigator.

In order to facilitate toric IOL selection and axis placement, the B+L proprietary enVista toric Calculator was used to determine the appropriate enVista toric IOL model and axis of placement for each eye. The calculator accounted for surgically induced astigmatism (SIA), incision location, and the participant's preoperative corneal astigmatism. In this trial all cataract incisions were to be placed on the preoperative keratometric steep axis.

Results

The results of the clinical study provide reasonable assurance that the Model MX60T IOL is safe and effective for the visual correction of aphakia and corneal astigmatism following cataract extraction.

The data support a significant dioptric reduction in cylinder and reduction in absolute cylinder, rotational stability of the lens, and improvement of both best corrected and uncorrected visual acuity at distance following implantation of the enVista toric IOL.

The primary effectiveness endpoints were mean toric IOL axial stability from Form 3 to Form 4, dioptric reduction in cylinder at Form 4, lens axis misalignment from surgical target markings at Form 4, and best corrected distance visual acuity at Form 4. All participants in the toric IOL treatment groups demonstrated ≤ 5 degrees rotation from Form 3 (Table 2). Mean cylinder reduction from preoperative keratometric cylinder measurements in the randomized ITT population at Form 4 was 0.479 ± 0.665 D among those participants with control IOLs and 0.865 ± 0.487 D among those participants with 1.25 D toric IOLs (Table 3), showing a statistically significant improvement favoring the 1.25 D toric IOLs ($P < 0.001$). The mean percent reduction in absolute cylinder at Form 4 was 69.4% for all toric IOL Cohort and 36.8% for the control IOL Cohort (Table 4). The percent of eyes within 0.50 D and 1.00 D of intended correction for All toric Cohort at Form 4 was 57.3% and 90.9%, respectively (Table 5). At Form 4, > 90% of eyes in each toric IOL arm had misalignments of ≤ 10 degrees of intended markings, including 93.3% of all toric IOL eyes (Table 6). Preservation of best-corrected distance visual acuity showed 99.1% of eyes in the ITT population implanted with a toric IOL reported a VA of 20/40 or better at Form 4. Best-corrected distance visual acuity (BCDVA) results for all toric IOL treatment group are presented in Table 7 and Table 8. At Form 4, 109 participants (99.1%) in the All toric IOL Cohort achieved BCDVA of 20/40 or better. At Form 4, the mean ± SD UCDVA was 0.19 ± 0.16 logMAR in the control IOL treatment group and 0.11 ± 0.14 logMAR in the 1.25 D toric IOL treatment group (Table 9), which was a significant difference favoring the 1.25 D toric IOL arm ($P < 0.001$). At Form 4, 94.5% of all toric IOL eyes and 83.3% of control eyes had UCDVA of 20/40 or better.

The analysis of safety was based on the Safety cohort of 191 participant eyes for the implantation of a study lens (either test or control). The key safety outcomes are presented in Table 10. The rates of FDA defined potentially sight-threatening adverse events that occurred in the clinical trial at Form 4 were found to be less than the "FDA Grid" of historical controls. No serious adverse events occurred in the study eye.

Table 2: Mean Toric IOL Axial Stability From Form 3 To Form 4 (ITT Population)

Absolute rotation (degrees)	Toric IOL			All Toric IOL (N=112)
	1.25 D (N=80)	2.00 D (N=20)	2.75 D (N=12)	
Absolute rotation from Form 3 to Form 4				
n	74	15	12	101
Mean ± SD	1.15 ± 1.08	0.92 ± 1.09	1.08 ± 0.73	1.11 ± 1.04
≤ 5 degrees rotation	74 (100.0%)	15 (100.0%)	12 (100.0%)	101 (100.0%)
95% exact Confidence Interval	95.1% to 100.0%	78.2% to 100.0%	73.5% to 100.0%	96.4% to 100.0%

Table 3: Mean Dioptric Cylinder Reduction From Preoperative Measurements (ITT Population)

Cylinder reduction (D)	Control IOL (N=79)	Toric IOL			All Toric IOL (N=112)
		1.25 D (N=80)	2.00 D (N=20)	2.75 D (N=12)	
Form 2					
n	77	80	20	12	112
Mean reduction ± SD	0.640 ± 0.591	0.966 ± 0.466	1.486 ± 0.498	2.115 ± 0.328	1.182 ± 0.594
Form 3					
n	79	79	18	12	109
Mean reduction ± SD	0.532 ± 0.627	0.864 ± 0.455	1.446 ± 0.519	1.926 ± 0.364	1.077 ± 0.584

Cylinder reduction (D)	Control IOL (N=79)	Toric IOL			All Toric IOL (N=112)
		1.25 D (N=80)	2.00 D (N=20)	2.75 D (N=12)	
Form 4					
n	78	80	18	12	110
Mean reduction ± SD	0.479 ± 0.665	0.865 ± 0.487	1.413 ± 0.532	1.944 ± 0.327	1.072 ± 0.601
Treatment effect at Form 4		0.39			
95% Confidence Interval of effect		0.228 to 0.545			
Multiple imputation p-value[2]		< 0.001			

[2]P-values and treatment effects are from a linear model Type II analysis, which include an effect for investigator and compare the control and 1.25 D toric IOLs at Form 4.

Note: Dioptric change in cylinder = |preoperative keratometric cylinder| - |postoperative manifest cylinder|

Table 4: Mean Percent Reduction In Absolute Cylinder At Form 4

	Control IOL Mean ± SD	Toric IOL 1.25 D	Toric IOL 2.00 D	Toric IOL 2.75 D	All Toric IOL Mean ± SD
	N=79 n=78	N=80 n=80	N=20 n=18	N=12 n=12	N=112 n=110
Mean[3] % Reduction in Absolute Cylinder (± SD)	36.8% ± 50.49%	64.8% ± 36.8%	81.0% ± 31.3%	82.8% ± 13.0%	69.4% ± 34.8%

[3]Mean of all participant (N) results at Form 4 - n (%)

Table 5: Mean Percent Of Eyes With Reduction In Cylinder Within 0.50 D And 1.00 D Of Intended At Form 4 (ITT Population)

	Control IOL (N=79)	Toric IOL 1.25 D (N=80)	Toric IOL 2.00 D (N=20)	Toric IOL 2.75 D (N=12)	All Toric IOL (N=112)
Total Non-Missing, n	78	80	18	12	110
Within 0.50 D of Intended, n (%)	27 (34.6%)	43 (53.8%)	12 (66.7%)	8 (66.7%)	63 (57.3%)
Within 1.00 D of Intended, n (%)	45 (57.7%)	71 (88.8%)	17 (94.4%)	12 (100.0%)	100 (90.9%)

Table 6: Mean Toric Lens Axis Misalignment From Surgical Markings At Form 4 (ITT Population)

Axis Misalignment	Toric IOL			All Toric IOL (N=112)
	1.25 D (N=80)	2.00 D (N=20)	2.75 D (N=12)	
Form 4 signed axis misalignment, degrees				
n	77	16	11	104
Mean ± SD	1.11 ± 8.69	3.08 ± 10.51	2.52 ± 3.03	1.56 ± 8.57
95% tolerance interval for 90% of the population	-15.51 to 17.73	-22.54 to 28.70	-5.78 to 10.82	-14.45 to 17.57
Form 4 absolute axis misalignment, degrees				
n	77	16	11	104
Mean ± SD	4.77 ± 7.33	5.15 ± 9.61	3.32 ± 2.01	4.68 ± 7.33
95% tolerance interval for 90% of the population	-9.25 to 18.79	-18.28 to 28.58	-2.19 to 8.83	-9.02 to 18.38
Form 4 absolute axis misalignment category, n (%)				
≤ 5 degrees	56 (72.7%)	13 (81.3%)	9 (81.8%)	78 (75.0%)
≤ 10 degrees	71 (92.2%)	15 (93.8%)	11 (100.0%)	97 (93.3%)
Form 4 signed axis misalignment category, n (%)				
-10.00 to -5.01 degrees	4 (5.2%)	2 (12.5%)	0 (0.0%)	6 (5.8%)
-5.00 to -0.01 degrees	31 (40.3%)	3 (18.8%)	2 (18.2%)	36 (34.6%)
0.00 degrees	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
+0.01 to +5.00 degrees	25 (32.5%)	10 (62.5%)	7 (63.6%)	42 (40.4%)
+5.01 to +10.00 degrees	11 (14.3%)	0 (0.0%)	2 (18.2%)	13 (12.5%)

Table 7: Preservation Of BCDVA At Each Examination (All Toric IOLs, ITT Population)

BCDVA	Preoperative	Form 2	Form 3	Form 4
	N=112	N=112	N=109	N=110
20/40 or Better, n (%)	27 (24.1%)	108 (96.4%)	109 (100%)	109 (99.1%)
Worse than 20/40, n (%)	85 (75.9%)	4 (3.6%)	0 (0.0%)	1 (0.9%)

Table 8: BCDVA Without Glare At Form 4 (ITT Population)

	Control IOL (N=79)	Toric IOL 1.25 D (N=80)	Toric IOL 2.00 D (N=20)	Toric IOL 2.75 D (N=12)	All Toric IOL (N=112)
BCDVA (LogMAR)					
Total Non-Missing, n	78	80	18	12	110
Mean (± SD)	0.01 (± 0.09)	0.00 (± 0.09)	0.05 (± 0.10)	-0.01 (± 0.09)	0.01 (± 0.09)
BCDVA (Snellen)					
20/40 or Better, n (%)	78 (100.0%)	79 (98.8%)	18 (100.0%)	12 (100%)	109 (99.1%)
Worse than 20/40, n (%)	0	1 (1.3%)	0	0	1 (0.9%)

Table 9: UCDVA At Form 4 (ITT Population)

	Control IOL (N=79)	Toric IOL 1.25 D (N=80)	Toric IOL 2.00 D (N=20)	Toric IOL 2.75 D (N=12)	All Toric IOL (N=112)
UCDVA (LogMAR)					
Total Non-Missing, n	78	80	18	12	110
Mean (± SD)	0.19 (± 0.16)	0.11 (± 0.14)	0.12 (± 0.11)	0.13 (± 0.18)	0.11 (± 0.14)
UCDVA (Snellen)					
20/40 or Better, n (%)	65 (83.3%)	76 (95.0%)	18 (100.0%)	10 (83.3%)	104 (94.5%)
Worse than 20/40, n (%)	13 (16.7%)	4 (5.0%)	0	2 (16.7%)	6 (5.5%)

Table 10: ISO 11979-7 Safety And Performance Endpoints (SPE) Adverse Events Reported At Each Postoperative Visit, Implanted Participants (Safety, All Toric IOL)

	Form 1 n/N (%)	Form 2 n/N (%)	Form 3 n/N (%)	Form 4 n/N (%)	Cumulative n/N (%)	ISO 11979-7 SPE rate (%)	p-value
Endophthalmitis	0/112	0/112	0/112	0/112	0/112	0.1	>0.999
Hypopyon	0/112	0/112	0/112	0/112	0/112	0.3	>0.999
Lens Dislocated From Posterior Chamber	0/112	0/112	0/112	0/112	0/112	0.1	>0.999
Cystoid Macular Edema	0/112	1/112 (0.9)	1/112 (0.9)	0/112	2/112 (1.8)	3.0	0.853
Pupillary Block	0/112	0/112	0/112	0/112	0/112	0.1	>0.999
Retinal Detachment	0/112	0/112	0/112	0/112	0/112	0.3	>0.999
Secondary Surgical Intervention	0/112	0/112	0/112	0/112	0/112	0.8	>0.999
Persistent Adverse Events: Noted at Form 4[4]							
Corneal Stromal Edema				0/112		0.3	>0.999
Iritis				0/112		0.3	>0.999
Cystoid Macular Edema				0/112		0.5	>0.999
Raised IOP Requiring Treatment				0/112		0.4	>0.999

[4]Cumulative versus persistent AEs are defined by the FDA SPE Grid and ISO 11979-7 as those occurring at Form 4 in this clinical study.

enVista ENVY (Trifocal In The US) Clinical Study Summary

This was a prospective, multicenter, randomized, active-controlled binocularly implanted study of the enVista one-piece hydrophobic acrylic trifocal IOL in participants undergoing cataract extraction compared to the enVista one-piece hydrophobic acrylic monofocal IOL.

The study was conducted between 2018 and 2023 with 501 participants from 23 sites in the United States. Participants scheduled to undergo cataract surgery by phacoemulsification and implantation of bilateral IOLs were screened for eligibility through extensive inclusion exclusion criteria, and with extensive preoperative assessments with both eyes of each participant included in the study after having met eligibility criteria at the Preoperative Visit. At the time of the first surgery, participants were enrolled and randomly assigned by an Interactive Response Technology system in a 2:1 ratio to either the test - enVista trifocal IOL or the control - enVista monofocal IOL, respectively. All participants underwent bilateral implantation of the enVista trifocal IOL or the enVista monofocal IOL and were followed up through post-operative scheduled visits through Postoperative Visit #5 (11-14 Months) with ophthalmic examinations and standardized pre-, peri-, and postoperative care under the supervision of the Physician/Investigator.

Study enrollment occurred in 3 phases covering Phase 1/pilot, Phase II and Phase III. Enrolled participants who met eligibility criteria were seen at 11 or 12 visits, including a preoperative visit, 2 operative visits (1 for each eye), and 8 mandatory postoperative visits (3 for each eye and 2 for both eyes), as well as an additional 1 postoperative visit only for those participants who consented at participating sites (Day 2 to 30 after otherwise last visit/Postoperative Visit 5) for the Trial Frame Astigmatism Sub-Study.

The participant was considered enrolled in the study at the time of randomization at the first Operative Visit (Visit 00A). Randomization followed the completion of uncomplicated cataract extraction in the first eye. Only participants who were randomized but did not have the lens inserted into the eye could be replaced. For those eligible participants who consented to participate in the Trial Frame Astigmatism Simulation Sub-Study, a Postoperative Visit 6 (Day 2 to 30 after otherwise last visit/Postoperative Visit 5) was conducted as the final visit to complete the study.

Outcome Endpoints:

Primary Safety Analyses

The proportion of first Modified Safety Set eyes with at least one ocular treatment-emergent Serious Adverse Event (SAE) was summarized using categorical summary statistics by treatment received with each eye counted only once in the calculation of the rate.

Secondary Surgical Interventions (SSIs) related to the optical properties of the IOL were summarized categorically by treatment received for first Modified Safety Set eyes. Noninferiority of the test lens compared to the control lens was evaluated.

Adverse events (AEs) in first Modified Safety Set eyes were compared to the International Organization for Standardization (ISO) Safety and Performance Endpoint (SPE) rates as defined in ISO 11979-7, through study exit.

Primary Effectiveness Analyses

The statistical success of the trial depended on the statistical success of all three co-primary effectiveness endpoints.

Photopic monocular logMAR Best Corrected Distance Visual Acuity (BCDVA) in first eyes at Postoperative Visit 4 (4-6 Months after second eye implant) was summarized using continuous summary statistics by treatment group for the modified Intent-to-Treat (mITT) Set.

BCDVA at Postoperative Visit 4 (4-6 Months) for the test group was summarized categorically for the mITT and Best Case Sets.

For the analyses of the mITT and Best Case Sets, 1-sided exact binomial tests comparing the proportion of multifocal IOL eyes with BCDVA 20/40 or better to the relevant control rate were performed and p-values presented. If the p-value was ≤ 0.05, then the null hypothesis was rejected. If the null hypothesis was not rejected for the mITT and Best Case Sets in the primary analyses, then it was concluded that the multifocal IOL was statistically successful in this outcome.

Photopic monocular Distance Corrected Near Visual Acuity (DCNVA) at 40 cm and Distance Corrected Intermediate Visual Acuity (DCIVA) at 66 cm in first eyes at Postoperative Visit 4 (4-6 Months) were summarized using continuous summary statistics in logMAR units by treatment assignment for the mITT Set.

For each endpoint, an overall p-value resulting from the MI method was estimated. The treatment effect in logMAR units was summarized using continuous summary statistics and a 2-sided 95% CI. If the p-value from the MI analysis of treatment effect was ≤ 0.05 and the treatment effect was ≤ -0.10 logMAR units for DCIVA or DCNVA, then it was concluded that the test IOL is statistically and clinically successful in the corresponding outcome.

Accountability And Demographics Of The PMA Cohort

All 501 participants randomized were implanted (enVista trifocal IOL group, n=332; enVista monofocal IOL group, n=169). Of 1002 eyes randomized, 996 were implanted (enVista trifocal IOL group, n=659; enVista monofocal IOL group, n=337); 2 participants each had 1 eye (OS-Left eye and OD-Right eye, respectively) that was touched by an IOL that was not implanted.

The Modified Safety Set population was primarily White (92.0% [461/501]), not Hispanic/Latino (88.0% [441/501]), and female (63.9% [320/501]; Table 11). The mean ± SD age of the population was 68.0 ± 7.76 years. Similar demographics were observed across treatment groups.

Table 11: Demographics (Modified Safety Set)

Variable	enVista Trifocal IOL (N=332)	enVista Monofocal IOL (N=169)	All Participants (N=501)
Age, years			
n	332	169	501
Mean (SD)	67.6 (7.89)	68.8 (7.46)	68.0 (7.76)
Median	68.0	70.0	69.0
Minimum, maximum	32, 85	41, 85	32, 85
Age categories, n (%)			
18–64 years	95 (28.6)	35 (20.7)	130 (25.9)
65–84 years	235 (70.8)	133 (78.7)	368 (73.5)
≥ 85 years	2 (0.6)	1 (0.6)	3 (0.6)
Gender, n (%)			
Male	120 (36.1)	61 (36.1)	181 (36.1)
Female	212 (63.9)	108 (63.9)	320 (63.9)
Race, n (%)			
American Indian/Alaska Native	0	0	0
Asian	11 (3.3)	4 (2.4)	15 (3.0)
Chinese	1 (0.3)	1 (0.6)	2 (0.4)
Non-Chinese	10 (3.0)	3 (1.8)	13 (2.6)
Black/African American	14 (4.2)	9 (5.3)	23 (4.6)
Native Hawaiian/Pacific Islander	1 (0.3)	0	1 (0.2)
White	305 (91.9)	156 (92.3)	461 (92.0)
Multiple[a]	1 (0.3)	0	1 (0.2)
Other	0	0	0
Ethnicity, n (%)			
Hispanic/Latino	40 (12.0)	20 (11.8)	60 (12.0)
Not Hispanic/Latino	292 (88.0)	149 (88.2)	441 (88.0)
First eye, n (%)			
OD	218 (65.7)	95 (56.2)	313 (62.5)
OS	114 (34.3)	74 (43.8)	188 (37.5)
Study phase under which participant enrolled, n (%)			
Phase I/Pilot	29 (8.7)	13 (7.7)	42 (8.4)
Phase II	49 (14.8)	24 (14.2)	73 (14.6)
Phase III	254 (76.5)	132 (78.1)	386 (77.0)

eCRF = electronic Case Report Form; IOL = intraocular lens; OD = right eye; OS = left eye; SD = standard deviation.

[a]Participants who selected more than 1 race on the eCRF are grouped into the "Multiple" category.

The ITT Set, mITT Set, and the Modified Safety Set all included all 501 randomized participants and 998 of the 1002 randomized eyes (Table 12).

Table 12: Participant Accountability By Visit Up To Visit 5 (11-14 Months)

Modified Intent-to-Treat Set Treatment: All Subjects

	Total Number	Visit 0A/B (Pre-Op) n (%)	Operative Visit 00A n (%)	Visit 1A n (%)	Visit 2A n (%)	Visit 3A n (%)
All Subjects	501	–	–	–	–	–
Subjects with an Eye Touched with Study IOL	501	–	–	–	–	–
Implanted Subjects	501	–	–	–	–	–
Available for Analysis[a]	–	501 (100.0)	501 (100.0)	501 (100.0)	493 (98.4)	480 (95.8)
Discontinued[b]	–	0	0	0	0	1 (0.2)
Missing at Scheduled Visit but Seen Later[c]	–	0	0	0	8 (1.6)	19 (3.8)
Not Seen but Accounted for[d]	–	0	0	0	0	0
Lost to Follow-up	–	0	0	0	0	1 (0.2)
% Accountability		100.0	100.0	100.0	98.4	96.0

	Operative Visit 00B n (%)	Visit 1B n (%)	Visit 2B n (%)	Visit 3B n (%)	Visit 4 n (%)	Visit 5 n (%)
Available for Analysis[a]	499 (99.6)	495 (98.8)	486 (97.0)	481 (96.0)	470 (93.8)	460 (91.8)
Discontinued[b]	1 (0.2)	1 (0.2)	2 (0.4)	3 (0.6)	10 (2.0)	20 (4.0)
Missing at Scheduled Visit but Seen Later[c]	0	3 (0.6)	10 (2.0)	14 (2.8)	17 (3.4)	16 (3.2)
Not Seen but Accounted for[d]	0	0	0	0	0	0
Lost to Follow-up	1 (0.2)	2 (0.4)	3 (0.6)	3 (0.6)	4 (0.8)	5 (1.0)
% Accountability	99.8	99.0	97.4	96.6	95.7	95.6

Abbreviations: IOL = intraocular lens; Op = operative.

Note: Percentages are based on the total number of subjects in the analysis population.

% Accountability = 100 *(Available for Analysis) / (All Modified Intent-to-Treat Subjects – Discontinued)

[a]Represents the total number of subjects for whom data are available at the visit.

[b]Represents the total number of subjects that have discontinued treatment prior to the visit for any reason (e.g., death or device replacement), but does not include subjects that are lost to follow-up.

[c]Represents the total number of subjects that were seen outside the time window associated with the visit.

[d]Represents the total number of subjects that were missing at the scheduled visit but were accounted for by being contacted (e.g., by phone).

Effectiveness And Safety Results:

A. Primary Effectiveness Variables

All of the co-primary effectiveness endpoints on this study were met, with the trifocal IOL showing statistical noninferiority to the monofocal IOL in photopic monocular BCDVA, satisfactory BCDVA performance compared to the International Organization for Standardization (ISO) grid performance standards, and statistical superiority to the monofocal IOL in photopic monocular DCNVA and DCIVA (both $P < 0.0001$).

Mean ± SD/SE photopic monocular BCDVA at Visit 4 (4-6 Months) in first eyes of the mITT Set was 0.022 ± 0.0950/0.0054 logMAR in the trifocal IOL group and -0.017 ± 0.0897/0.0072 logMAR in the monofocal IOL group (Table 13).

The LS mean ± SE difference between treatment groups was 0.040 ± 0.0085 logMAR, for a 2-sided 90% CI of 0.026 to 0.054 logMAR. Since the upper confidence limit was less than 0.1 logMAR, the trifocal IOL is statistically noninferior to the control IOL. Similar results were observed for the PP Set.

Table 13: Photopic Monocular (First Eyes) BCDVA (4 m) At Visit 4 (4-6 Months) (mITT Set)

BCDVA, LogMAR	enVista Trifocal IOL (N=332)	enVista Monofocal IOL (N=169)
n	312	156
Mean (SD/SE)	0.022 (0.0950/0.0054)	-0.017 (0.0897/0.0072)
Median	0.000	0.000
Minimum, maximum	-0.18, 0.58	-0.30, 0.40
LS mean (SE)[a]	0.032 (0.0058)	-0.008 (0.0076)
LS mean difference (SE)[a]	0.040 (0.0085)	
2-sided 90% CI[a]	0.026, 0.054	

ANCOVA = analysis of covariance; BCDVA = best-corrected distance visual acuity; CI = confidence interval; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; LS = least-squares; SD = standard deviation; SE = standard error.

[a]Statistics are based on an ANCOVA model with BCDVA as the dependent variable and treatment and site as fixed factors.

In the mITT Set at Visit 4 (4-6 Months), photopic monocular BCDVA of 20/40 or better was achieved by 98.7% of first eyes in the trifocal IOL group versus 92.5%, which is the ISO standard SPE rate for the mITT Set; the observed proportion was not statistically significantly worse than the SPE rate ($P > 0.9999$; Table 14).

Table 14: Proportion Of First Eyes That Achieved 0.30 LogMAR (20/40) Or Better In Photopic Monocular BCDVA (4 m) At Visit 4 (4-6 Months) (mITT Set And Best Case Set)

Population	enVista Trifocal IOL
mITT Set	N=312
n (%)	308 (98.7)
90% CI	97.1, 99.6
1-sided p-value[a]	>0.9999
Best Case Set	N=310
n (%)	306 (98.7)
90% CI	97.1, 99.6
1-sided p-value[b]	0.9920

BCDVA = best-corrected distance visual acuity; CI = confidence interval; IOL = intraocular lens; ISO = International Organization for Standardization; logMAR = logarithm of the minimum angle of resolution; mITT = Modified Intent-to-Treat; SPE = Safety and Performance Endpoint.

[a]p-value based on a 1-sided exact binomial test comparing the proportion of eyes achieving BCDVA 0.3 logMAR or better to the ISO standard SPE rate of 92.5% for the mITT Set.

[b]p-value based on a 1-sided exact binomial test comparing the proportion of eyes achieving BCDVA 0.3 logMAR or better to the ISO standard SPE rate of 96.7% for the Best Case Set.

For each endpoint, if the p-value from the MI analysis of treatment effect was ≤ 0.05 and the treatment effect was ≤ -0.10 logMAR units for DCIVA or DCNVA, then it was concluded that the test IOL is statistically and clinically successful in the corresponding outcome.

Mean ± SD photopic monocular DCNVA at Visit 4 (4-6 Months) in first eyes (excluding Phase I participants) was 0.152 ± 0.1342 logMAR in the trifocal IOL group and 0.545 ± 0.1703 logMAR in the monofocal IOL group (Table 15). The LS mean ± SE difference between treatment groups was -0.392 ± 0.0142 logMAR, for a statistically significant difference demonstrating superiority of the trifocal IOL over the control IOL ($P < 0.0001$). Moreover, the treatment effect of 0.392 logMAR exceeded the protocol-defined performance standard for clinical significance of -0.10 logMAR. Similar results were observed for the PP Set.

Mean ± SD photopic monocular DCIVA at Visit 4 (4-6 Months) in first eyes (excluding Phase I participants) was 0.122 ± 0.1199 logMAR in the trifocal IOL group and 0.349 ± 0.1592 logMAR in the monofocal IOL group (Table 16). The LS mean ± SE difference between treatment groups was -0.225 ± 0.0133 logMAR, for a statistically significant difference demonstrating superiority of the trifocal IOL over the control IOL ($P < 0.0001$). Moreover, the treatment effect of 0.225 logMAR exceeded the protocol-defined performance standard for clinical significance of -0.10 logMAR. Similar results were observed for the PP Set.

Table 15: Photopic Monocular (First Eyes) DCNVA (40 cm) At Visit 4 (4-6 Months) – Excluding Phase I Participants (mITT Set; MI)

DCNVA, LogMAR	enVista Trifocal IOL (N=303)	enVista Monofocal IOL (N=156)
n	297	152
Mean (SD)	0.152 (0.1342)	0.545 (0.1703)
Median	0.120	0.560
Minimum, maximum	-0.17, 0.72	-0.05, 1.03
LS mean (SE)[a]	0.148 (0.0095)	0.539 (0.0126)
LS mean difference (SE)[a]	-0.392 (0.0142)	
2-sided 95% CI[a]	-0.419, -0.364	
p-value[a]	<0.0001	

ANCOVA = analysis of covariance; CI = confidence interval; DCNVA = distance-corrected near visual acuity; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; LS = least-squares; MI = multiple imputation; SD = standard deviation; SE = standard error.

Note: Missing data are imputed using the Markov chain Monte Carlo MI method. An ANCOVA model with DCNVA as the dependent variable and treatment and site as fixed factors is performed to obtain effect size and SE for each of complete imputed datasets.

[a]Overall statistics are from the MI method. The p-value is for a 2-sided treatment difference test.

Table 16: Photopic Monocular (First Eyes) DCIVA (66 cm) At Visit 4 (4-6 Months) – Excluding Phase I Participants (mITT Set; MI)

DCIVA, LogMAR	enVista Trifocal IOL (N=303)	enVista Monofocal IOL (N=156)
n	297	152
Mean (SD)	0.122 (0.1199)	0.349 (0.1592)
Median	0.100	0.350
Minimum, maximum	-0.26, 0.68	-0.08, 0.90
LS mean (SE)[a]	0.124 (0.0089)	0.349 (0.0119)
LS mean difference (SE)[a]	-0.225 (0.0133)	
2-sided 95% CI[a]	-0.251, -0.199	
p-value[a]	<0.0001	

ANCOVA = analysis of covariance; CI = confidence interval; DCIVA = distance-corrected intermediate visual acuity; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; LS = least-squares; MI = multiple imputation; SD = standard deviation; SE = standard error.

Note: Missing data are imputed using the Markov chain Monte Carlo MI method. An ANCOVA model with DCIVA as the dependent variable and treatment and site as fixed factors is performed to obtain effect size and SE for each of complete imputed datasets.

[a]Overall statistics are from the MI method. The p-value is for a 2-sided treatment difference test.

B. Secondary Effectiveness Variables

Mean ± SD/SE photopic binocular DCNVA at Visit 4 (4-6 months; excluding Phase I participants) was 0.080 ± 0.0977/0.0058 logMAR in the trifocal IOL group and 0.453 ± 0.1526/0.0128 logMAR in the monofocal IOL group. The LS mean ± SE difference between treatment groups was -0.374 ± 0.0114 logMAR, for a statistically significant difference demonstrating superiority of the trifocal IOL over the control IOL ($P < 0.0001$).

Mean ± SD photopic binocular UNVA at Visit 4 (4-6 months; excluding Phase I participants) was 0.096 ± 0.1056 logMAR in the trifocal IOL group and 0.418 ± 0.1454 logMAR in the monofocal IOL group. The LS mean ± SE difference between treatment groups was -0.321 ± 0.0119 logMAR, for a statistically significant difference demonstrating superiority of the trifocal IOL over the control IOL ($P < 0.0001$).

Mean ± SD/SE photopic binocular DCIVA at Visit 4 (4-6 months; excluding Phase I participants) was 0.041 ± 0.0976/0.0058 logMAR in the trifocal IOL group and 0.268 ± 0.1485/0.0125 logMAR in the monofocal IOL group. The LS mean ± SE difference between treatment groups was -0.225 ± 0.0111 logMAR, for a statistically significant difference demonstrating superiority of the trifocal IOL over the control IOL ($P < 0.0001$).

Mean ± SD photopic binocular UIVA at Visit 4 (4-6 months; excluding Phase I participants) was 0.064 ± 0.0988 logMAR in the trifocal IOL group and 0.217 ± 0.1442 logMAR in the monofocal IOL group. The LS mean ± SE difference between treatment groups was -0.151 ± 0.0115 logMAR, for a statistically significant difference demonstrating superiority of the trifocal IOL over the control IOL ($P < 0.0001$).

At Visit 5 (11-14 Months), mean ± SD photopic monocular BCDVA in first eyes was 0.027 ± 0.0920 logMAR in the trifocal IOL group and -0.020 ± 0.0826 logMAR in the monofocal IOL group (Table 17). At Visit 5 (11-14 Months), mean ± SD photopic monocular DCNVA in first eyes (excluding Phase I participants) was 0.143 ± 0.1284 logMAR in the trifocal IOL group and 0.533 ± 0.1843 logMAR in the monofocal IOL group. At Visit 5 (11-14 Months), mean ± SD photopic monocular DCIVA in first eyes (excluding Phase I participants) was 0.120 ± 0.1147 logMAR in the trifocal IOL group and 0.343 ± 0.1594 logMAR in the monofocal IOL group.

All of the secondary effectiveness endpoints that were tested for superiority were met, with the trifocal IOL showing statistical superiority to the monofocal IOL in photopic binocular DCNVA, UNVA, DCIVA, and UIVA (all $P < 0.0001$).

Table 17: Photopic Monocular (First Eyes) BCDVA (4 m), DCNVA (40 cm), And DCIVA (66 cm) At Visit 5 (11-14 Months) (mITT Set)

	enVista Trifocal IOL (N=332)	enVista Monofocal IOL (N=169)
BCDVA (4 m), logMAR		
n	308	152
Mean (SD)	0.027 (0.0920)	-0.020 (0.0826)
Median	0.000	-0.010
Minimum, maximum	-0.16, 0.46	-0.26, 0.30
DCNVA (40 cm), excluding Phase I participants, logMAR		
n	280	139
Mean (SD)	0.143 (0.1284)	0.533 (0.1843)
Median	0.120	0.540
Minimum, maximum	-0.12, 0.52	0.04, 1.00

	enVista Trifocal IOL (N=332)	enVista Monofocal IOL (N=169)
DCIVA (66 cm), excluding Phase I participants, logMAR		
n	280	139
Mean (SD)	0.120 (0.1147)	0.343 (0.1594)
Median	0.100	0.360
Minimum, maximum	-0.10, 0.60	-0.10, 1.00

BCDVA = best-corrected distance visual acuity; DCIVA = distance-corrected intermediate visual acuity; DCNVA = distance-corrected near visual acuity; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation.

C. Supportive Effectiveness Variables

Supportive effectiveness analyses included categorical summaries of photopic monocular and binocular corrected (BCDVA, DCNVA, and DCIVA) and uncorrected (UDVA, UNVA, and UIVA) VAs.

1. BCDVA

Photopic binocular BCDVA of 20/20-2 or better at Visit 4 (4-6 Months) was achieved by 85.3% (266/312) of participants in the trifocal IOL group and 89.7% (140/169) of participants in the monofocal IOL group; BCDVA of 20/40 or better was achieved by 100.0% (312/312 and 156/156) of participants in both treatment groups (Table 18).

In the mITT Set, photopic monocular BCDVA of 20/40-2 or better at Visit 4 (4-6 Months) was achieved by 98.7% (308/312) of first eyes in the trifocal IOL group versus 99.4% (155/156) of first eyes in the monofocal IOL group, by 99.0% (309/312) of second eyes in the trifocal IOL group versus 100.0% (155/155) of second eyes in the monofocal IOL group, and by 98.9% (617/624) of all eyes in the trifocal IOL group versus 99.7% (310/311) of all eyes in the monofocal IOL group; none of these percentages were statistically significantly worse than the ISO grid performance standard.

Table 18: Categorical Analysis Of Photopic Binocular BCDVA (4 m) At Visit 4 (4-6 Months) (mITT Set)

BCDVA	enVista Trifocal IOL (N=312) n (%)	enVista Monofocal IOL (N=156) n (%)
20/20-2 or better	266 (85.3)	140 (89.7)
20/25-2 or better	304 (97.4)	154 (98.7)
20/32-2 or better	311 (99.7)	156 (100.0)
20/40-2 or better	312 (100.0)	156 (100.0)
logMAR VA		
0.00 or better	220 (70.5)	133 (85.3)
0.10 or better	299 (95.8)	154 (98.7)
0.20 or better	309 (99.0)	156 (100.0)
0.30 or better	312 (100.0)	156 (100.0)

BCDVA = best-corrected distance visual acuity; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; VA = visual acuity.

2. UDVA

Photopic binocular UDVA of 20/20-2 or better was achieved at Visit 4 (4-6 Months) by 57.5% (180/313) of participants in the trifocal IOL group and 73.1% (114/156) of participants in the monofocal IOL group; UDVA of 20/40-2 or better was achieved by 99.7% (312/313) of participants in the trifocal IOL group and 100.0% (156/156) of participants in the monofocal IOL group (Table 19).

Table 19: Categorical Analysis Of Photopic Binocular UDVA (4 m) At Visit 4 (4-6 Months) (mITT Set)

UDVA	enVista Trifocal IOL (N=313) n (%)	enVista Monofocal IOL (N=156) n (%)
20/20-2 or better	180 (57.5)	114 (73.1)
20/25-2 or better	276 (88.2)	144 (92.3)
20/32-2 or better	306 (97.8)	154 (98.7)
20/40-2 or better	312 (99.7)	156 (100.0)
logMAR VA		
0.00 or better	125 (39.9)	93 (59.6)
0.10 or better	253 (80.8)	139 (89.1)
0.20 or better	302 (96.5)	153 (98.1)
0.30 or better	311 (99.4)	156 (100.0)
0.40 or better	312 (99.7)	156 (100.0)

IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; UDVA = uncorrected distance visual acuity; VA = visual acuity.

3. DCNVA

Photopic binocular DCNVA of 20/20-2 or better (excluding Phase I participants) was achieved at Visit 4 (4-6 Months) by 44.0% (125/284) of participants in the trifocal IOL group and no participants in the monofocal IOL group; DCNVA of 20/40-2 or better (excluding Phase I participants) was achieved by 98.9% (281/284) of participants in the trifocal IOL group and 24.6% (35/142) of participants in the monofocal IOL group (Table 20).

Table 20: Categorical Analysis Of Photopic Binocular DCNVA (40 cm) At Visit 4 (4-6 Months) – Excluding Phase I Participants (mITT Set)

DCNVA	enVista Trifocal IOL (N=284) n (%)	enVista Monofocal IOL (N=142) n (%)
20/20-2 or better	125 (44.0)	0
20/25-2 or better	225 (79.2)	1 (0.7)
20/32-2 or better	271 (95.4)	12 (8.5)
20/40-2 or better	281 (98.9)	35 (24.6)
logMAR VA		
0.00 or better	79 (27.8)	0
0.10 or better	181 (63.7)	0
0.20 or better	260 (91.5)	8 (5.6)
0.30 or better	279 (98.2)	27 (19.0)
0.40 or better	283 (99.6)	64 (45.1)
0.50 or better	284 (100.0)	98 (69.0)

DCNVA = distance-corrected near visual acuity; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; VA = visual acuity.

4. UNVA

Photopic binocular UNVA of 20/20-2 or better (excluding Phase I participants) was achieved at Visit 4 (4-6 Months) by 38.4% (109/284) of participants in the trifocal IOL group and no participants in the monofocal IOL group; UNVA of 20/40-2 or better (excluding Phase I participants) was achieved by 99.3% (282/284) of participants in the trifocal IOL group and 31.5% (45/143) of participants in the monofocal IOL group (Table 21).

Table 21: Categorical Analysis Of Photopic Binocular UNVA (40 cm) At Visit 4 (4-6 Months) – Excluding Phase I Participants (mITT Set)

UNVA	enVista Trifocal IOL (N=284) n (%)	enVista Monofocal IOL (N=143) n (%)
20/20-2 or better	109 (38.4)	0
20/25-2 or better	208 (73.2)	4 (2.8)
20/32-2 or better	262 (92.3)	22 (15.4)
20/40-2 or better	282 (99.3)	45 (31.5)
logMAR VA		
0.00 or better	64 (22.5)	0
0.10 or better	174 (61.3)	1 (0.7)
0.20 or better	248 (87.3)	10 (7.0)
0.30 or better	278 (97.9)	38 (26.6)
0.40 or better	283 (99.6)	78 (54.5)

IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; UNVA = uncorrected near visual acuity; VA = visual acuity.

5. DCIVA

Photopic binocular DCIVA of 20/20-2 or better measured at a distance of 66 cm (excluding Phase I participants) was achieved at Visit 4 (4-6 Months) by 61.5% (174/283) of participants in the trifocal IOL group and 2.8% (4/142) of participants in the monofocal IOL group; DCIVA of 20/40-2 or better measured at a distance of 66 cm (excluding Phase I participants) was achieved by 98.6% (279/283) of participants in the trifocal IOL group and 73.9% (105/142) of participants in the monofocal IOL group (Table 22).

Table 22: Categorical Analysis Of Photopic Binocular DCIVA (66 cm) At Visit 4 (4-6 Months) – Excluding Phase I Participants (mITT Set)

DCIVA	enVista Trifocal IOL (N=283) n (%)	enVista Monofocal IOL (N=142) n (%)
20/20-2 or better	174 (61.5)	4 (2.8)
20/25-2 or better	257 (90.8)	34 (23.9)
20/32-2 or better	276 (97.5)	69 (48.6)
20/40-2 or better	279 (98.6)	105 (73.9)
logMAR VA		
0.00 or better	119 (42.0)	1 (0.7)
0.10 or better	235 (83.0)	21 (14.8)
0.20 or better	274 (96.8)	57 (40.1)
0.30 or better	278 (98.2)	95 (66.9)
0.40 or better	279 (98.6)	120 (84.5)

DCIVA = distance-corrected intermediate visual acuity; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; VA = visual acuity.

6. UIVA

Photopic binocular UIVA of 20/20-2 or better measured at a distance of 66 cm (excluding Phase I participants) was achieved at Visit 4 (4-6 Months) by 51.8% (147/284) of participants in the trifocal IOL group and 14.7% (21/143) of participants in the monofocal IOL group; UIVA of 20/40-2 or better measured at a distance of 66 cm (excluding Phase I participants) was achieved by 98.6% (280/284) of participants in the trifocal IOL group and 84.6% (121/143) of participants in the monofocal IOL group (Table 23).

Table 23: Categorical Analysis Of Photopic Binocular UIVA (66 cm) At Visit 4 (4-6 Months) – Excluding Phase I Participants (mITT Set)

UIVA	enVista Trifocal IOL (N=284) n (%)	enVista Monofocal IOL (N=143) n (%)
20/20-2 or better	147 (51.8)	21 (14.7)
20/25-2 or better	237 (83.5)	50 (35.0)
20/32-2 or better	273 (96.1)	89 (62.2)
20/40-2 or better	280 (98.6)	121 (84.6)
logMAR VA		
0.00 or better	93 (32.7)	12 (8.4)
0.10 or better	210 (73.9)	38 (26.6)
0.20 or better	268 (94.4)	75 (52.4)
0.30 or better	280 (98.6)	116 (81.1)
0.40 or better	282 (99.3)	132 (92.3)

IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; UIVA = uncorrected intermediate visual acuity; VA = visual acuity.

7. Sub-Study: Binocular Defocus Curves

Binocular defocus curves were evaluated at Visit 4 (4-6 Months) for a subset of participants, 53 in the trifocal IOL group and 41 in the monofocal IOL group.

Figure 2 shows that both treatment groups had similar corrected distance vision, as shown by the similar peaks near 20/20 at 0.0 D. However, in the intermediate and near vision range (-1.5 to -2.5 D), the trifocal IOL group demonstrated a plateau at approximately 20/25, whereas the monofocal IOL group decreased from approximately 20/40 to nearly 20/80. The trifocal IOL advantage was maintained throughout the extended near vision range (-2.5 to -3.5 D).

Participants were also subdivided by photopic pupil size. Those with the smallest pupil sizes (<3.0 mm; trifocal IOL group, n=12; monofocal IOL group, n=9) and those with medium pupil sizes (3.0 – 4.0 mm; trifocal IOL group, n=21; monofocal IOL group, n=23) showed a similar advantage for the trifocal IOL group in the intermediate and near vision ranges (Figure 3 and Figure 4, respectively). Those participants with the largest pupil sizes (>4.0 mm; trifocal IOL group, n=18; monofocal IOL group, n=9) showed the largest advantage for the trifocal IOL group in the intermediate and near vision ranges (Figure 5).

As measured by the binocular defocus curves from the data collected with a subset of participants (n=94), both IOL groups had similar distance vision, while the trifocal IOL group showed better VA compared with the monofocal IOL group in the intermediate vision range and maintained this throughout the near vision range. Photopic pupil size impacted depth of focus, with large pupil sizes demonstrating the largest VA benefit of the trifocal IOL.

Figure 2: Binocular Defocus Curves (LogMAR) By Defocus Lens Power At Visit 4 (4-6 Months) (mITT Set)

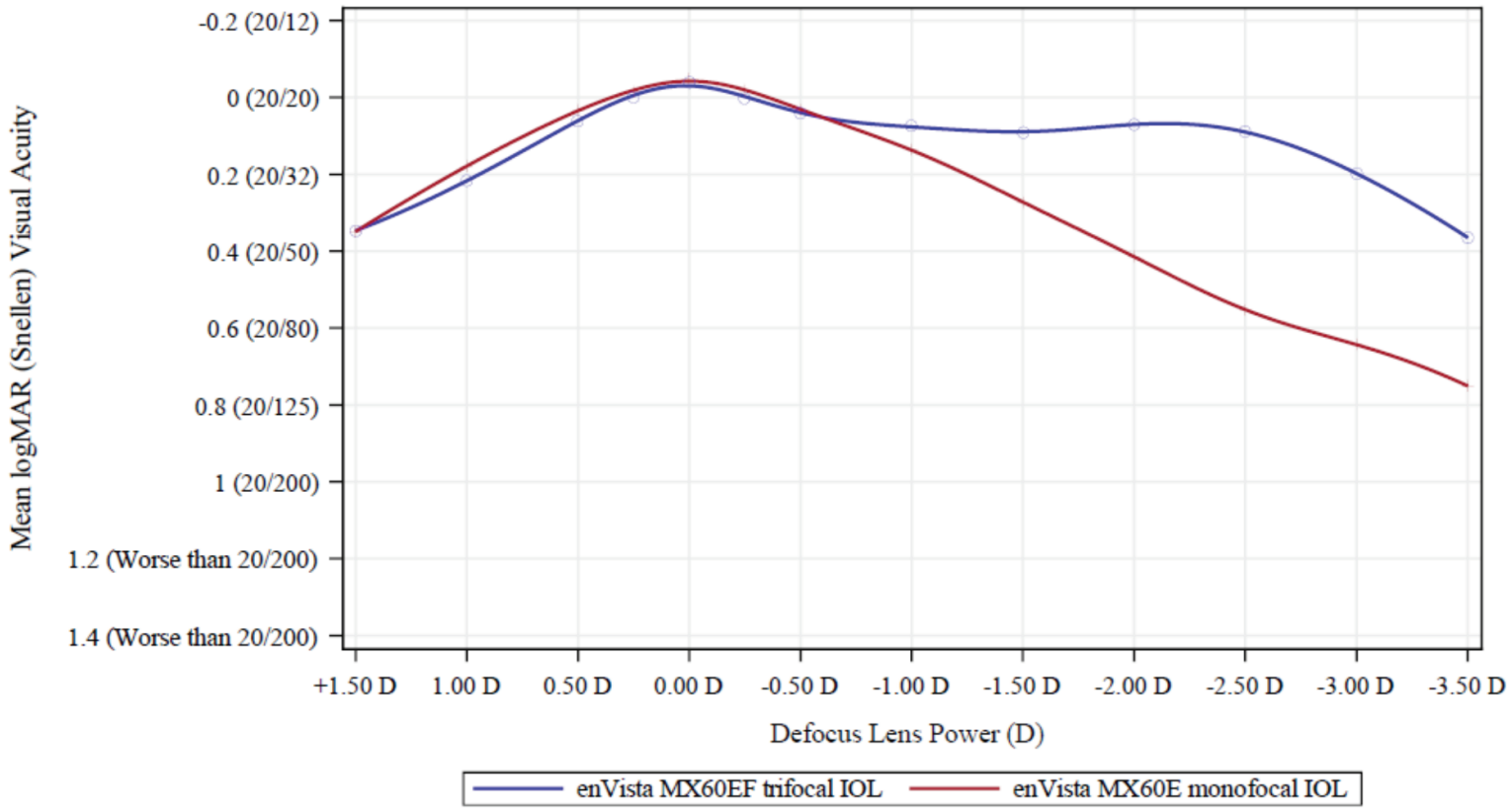


Figure 3: Binocular Defocus Curves (LogMAR) By Defocus Lens Power At Visit 4 (4-6 Months) For Participants With Small (<3.0 mm) Pupil Size (mITT Set)

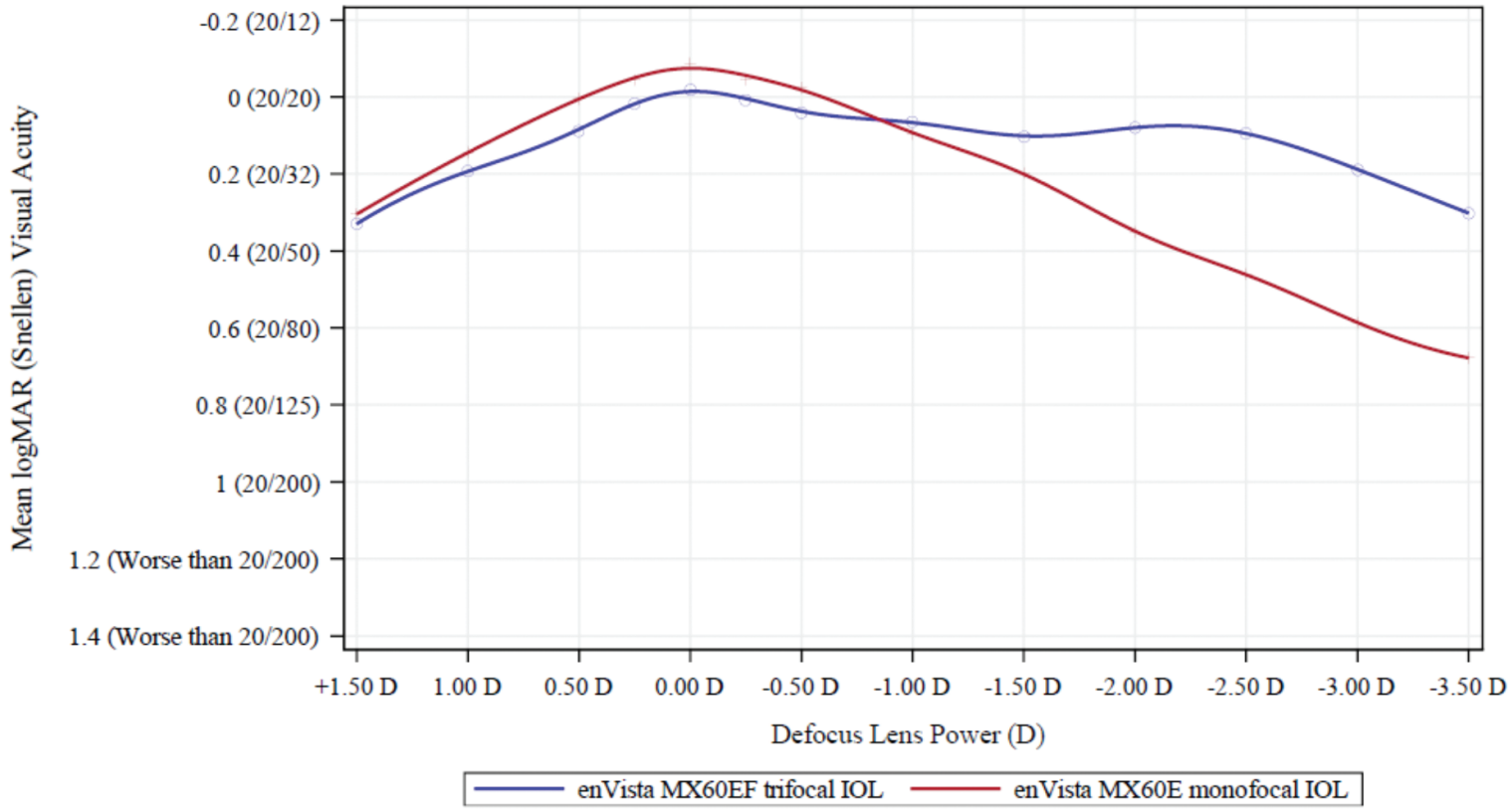


Figure 4: Binocular Defocus Curves (LogMAR) By Defocus Lens Power At Visit 4 (4-6 Months) For Participants With Medium (3.0 – 4.0 mm) Pupil Size (mITT Set)

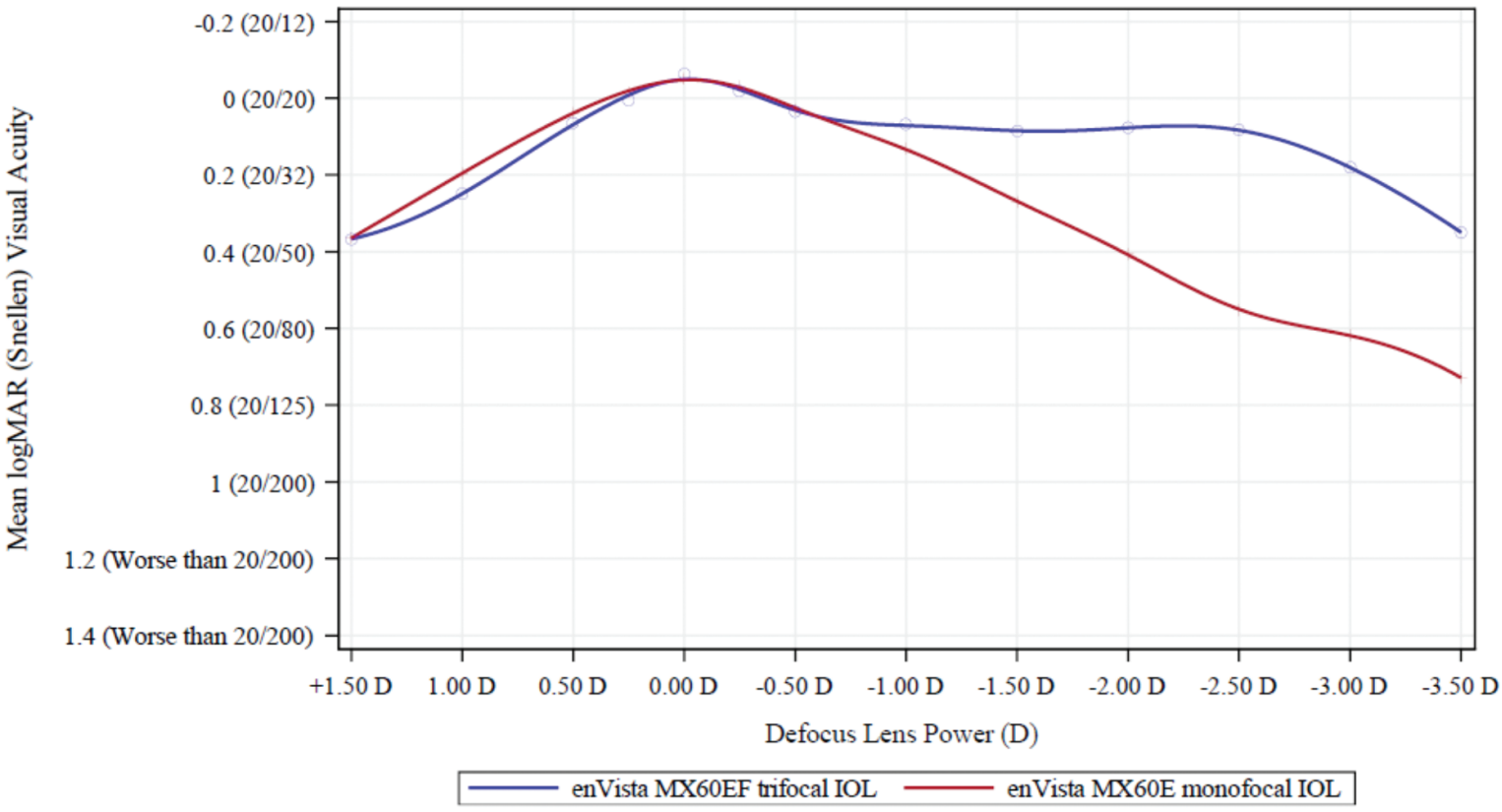
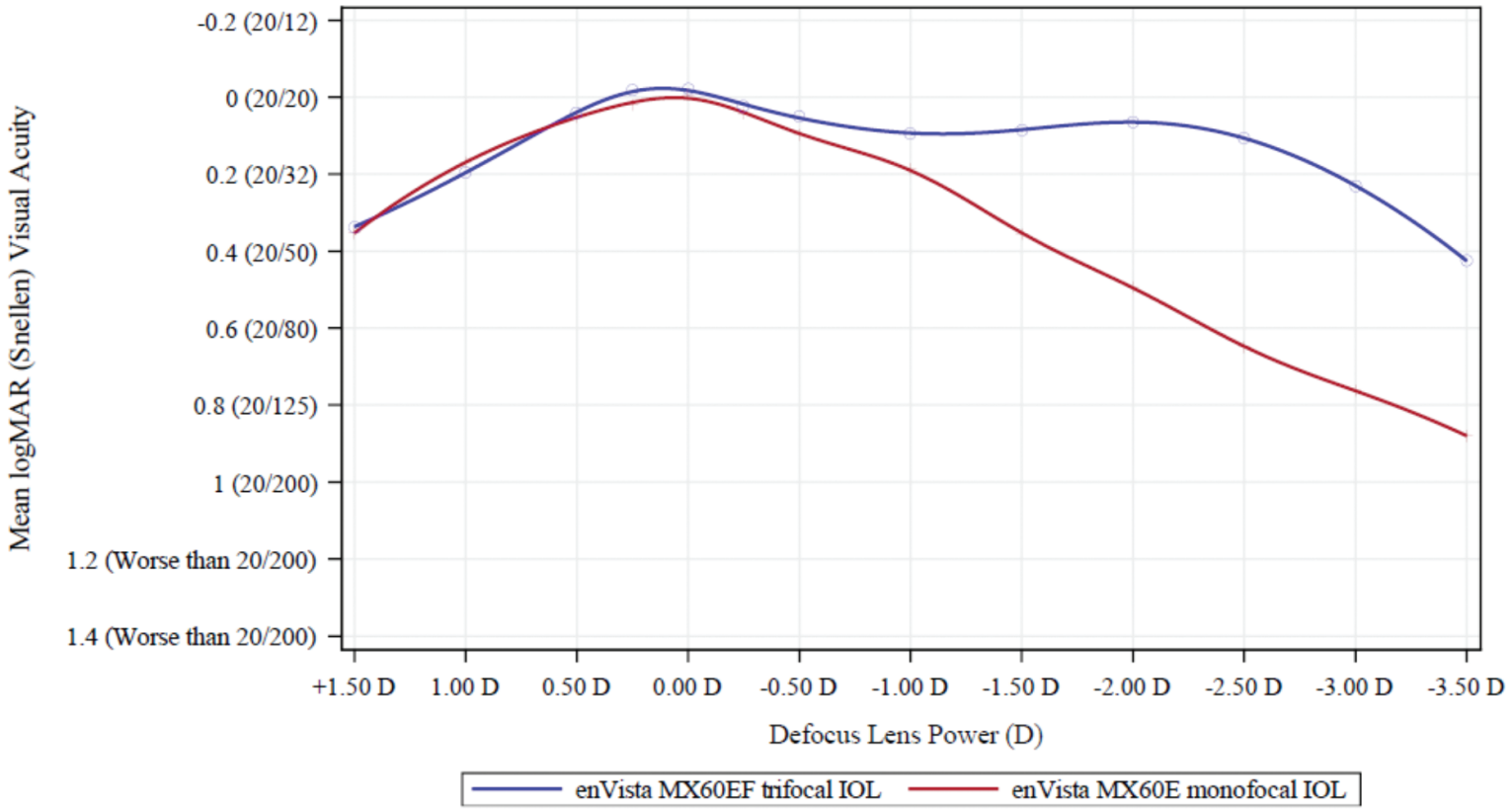


Figure 5: Binocular Defocus Curves (LogMAR) By Defocus Lens Power At Visit 4 (4-6 Months) For Participants With Large (>4.0 mm) Pupil Size (mITT Set)



D. Safety Evaluation

Adverse Events

The incidences of cumulative adverse events for the enVista Envy IOL and the control Monofocal IOL as compared to the ISO 11979-7:2018 historical grid rates are provided in Tables 24 and 30. The rate of secondary surgical interventions (SSIs) did not exceed the ISO grid rate for the enVista Envy IOL or the Monofocal IOL group.

1. Primary Safety Variables

1.1 ISO Grid Adverse Events In First Eyes

Three ISO grid cumulative or persistent AEs, all secondary surgical interventions were reported in first eyes of the trifocal IOL group (Table 24). The three secondary surgical interventions that occurred with the first eye for the enVista Envy IOL were suturing of a Seidel positive wound, a Pars Plana Vitrectomy with internal limiting membrane peeling due to a macular hole and an Argon laser retinopexy for an operculated retinal role. The trifocal IOL was statistically successful in this endpoint because no observed rate was statistically significantly greater than the corresponding SPE rate.

Table 24: ISO Grid Adverse Events (First Eyes; Modified Safety Set)

Adverse Event	Observed Event Rate For enVista Trifocal IOL n (%)	2-Sided 95% CI	1-Sided 95% LCL	SPE Rate (%)[b]
Cumulative[a]	N=332			
Cystoid macular oedema[c]	0	(0.00, 1.10)	0.00	3.0
Hypopyon	0	(0.00, 1.10)	0.00	0.3
Endophthalmitis	0	(0.00, 1.10)	0.00	0.1
Lens dislocated from posterior chamber[d]	0	(0.00, 1.10)	0.00	0.1
Pupillary block	0	(0.00, 1.10)	0.00	0.1
Retinal detachment[e]	0	(0.00, 1.10)	0.00	0.3
SSI	3 (0.9)	(0.19, 2.62)	0.25	0.8
Persistent[a]	N=314			
Corneal stroma oedema[f]	0	(0.00, 1.17)	0.00	0.3
Cystoid macular oedema	0	(0.00, 1.17)	0.00	0.5
Iritis[g]	0	(0.00, 1.17)	0.00	0.3
Raised IOP requiring treatment[h]	0	(0.00, 1.17)	0.00	0.4

AE = adverse event; CI = confidence interval; IOL = intraocular lens;
IOP = intraocular pressure; ISO = International Organization for Standardization; LCL = lower confidence limit;
SPE = Safety and Performance Endpoint; SSI = secondary surgical intervention.

[a]For cumulative AEs, observed AE rate is calculated as 100 multiplied by the number of eyes with the specific treatment-emergent event divided by the number of eyes (N). For persistent AE rates, the number of eyes (N) present at Visit 5 (11-14 Months) is the denominator.

[b]The ISO standard SPE rate in ISO 11979-7:2018.

[c]Per protocol, the definition of CME on this study was cystoid macular edema diagnosed by clinical exam and adjunct testing (e.g., OCT, FA or other method), resulting in BCDVA of ≤ 20/40 at Visit 3 or later. No participants were diagnosed with CME based on OCT alone.

[d]IOL decentration or tilt likely to affect visual outcome and resulting in secondary intervention.

[e]Per protocol, Retinal detachment includes Partial or complete Retinal Detachment associated with retinal tear. There were no retinal detachments without retinal tears.

[f]Corneal edema or corneal wound edema resulting in BCDVA of ≤ 20/40 at Visit 3A or later in the first implanted eye or at Visit 3B or later in the second implanted eye, or any persistent corneal or corneal wound edema present at Visit 5 (11-14 Months), per protocol.

[g]Per protocol, Iritis/cells/flare is characterized by grade 1+ cells or greater using SUN criteria if persistent for greater than 3 months after surgery, or relapses in less than 3 months after discontinuation of therapy, or the participant is maintained on therapy for more than 3 months to control inflammation.

[h]Defined per protocol as Elevation of IOP by ≥ 10 mmHg above baseline (pre-operative) to a minimum of 25 mmHg (Masket S, et al. Special Report: The American Academy of Ophthalmology Task Force Consensus Statement on Adverse Events with Intraocular Lenses. Ophthalmology 2017;124(1):142-144) after IOL implantation, or elevated IOP requiring treatment if present at Visit 5 (11-14 Months).

1.2 Secondary Surgical Interventions In First Eyes

One of the co-primary safety endpoints was to estimate the cumulative rate of secondary surgical interventions (SSIs) related to the optical properties of the IOL for the first operative eye up to Month 6. No SSIs due to the optical properties of the study lens were reported in first eyes. Therefore, the trifocal IOL was statistically noninferior to the monofocal IOL in this endpoint.

1.3 Ocular Serious Adverse Events In First Eyes

Four of 332 participants (1.2%) in the trifocal IOL group and one of 169 participants (0.6%) in the monofocal IOL group experienced an ocular TE-SAE in first eyes (Table 25). The ocular TE-SAEs were macular hole, retinal tear, retinal vein occlusion, and Seidel test positive in the trifocal IOL group and ophthalmic herpes zoster in the monofocal IOL group. The rates of ocular TE-SAEs were low and similar between the treatment groups.

Table 25: Ocular Treatment-Emergent Serious Adverse Events By Treatment (First Eyes; Modified Safety Set)

Adverse Event Term	enVista Trifocal IOL (N=332) n (%)	enVista Monofocal IOL (N=169) n (%)
All ocular TE-SAEs	4 (1.2)	1 (0.6)
Macular hole	1 (0.3)	0
Retinal tear	1 (0.3)	0
Retinal vein occlusion	1 (0.3)	0
Ophthalmic herpes zoster	0	1 (0.6)
Seidel test positive	1 (0.3)	0

IOL = intraocular lens.

Note: When reporting incidence, an eye is counted only once if the eye experiences more than 1 event of the same type. Adverse event term is coded from the verbatim using the Medical Dictionary for Regulatory Activities (MedDRA V 21).

2. Secondary Safety Variables

2.1 Quality Of Vision Questionnaire – Summary Of Visual Disturbances

The Quality of Vision (QoV) Questionnaire (McAlinden et al., 2010[1]; 2013[2]) was used to provide a standardized measure of subjective vision as a secondary safety endpoint, and allowed for subjective evaluation of visual disturbances for the IOLs of each treatment group.

The QoV was provided to participants in the clinical study to evaluate visual disturbances such as glare, halo and starbursts before and after surgery.

Participants rated each type of visual disturbance for frequency, severity and bothersomeness. Table 26 displays the percentage of clinical study participants reporting the frequency, bothersomeness, and severity of 11 types of visual disturbances at 4-6 months after surgery. While the clinical study was not designed to determine which lens had higher rates of each visual disturbance, study findings can help identify trends in potential differences between this lens and the monofocal control. This table does not display rates of visual disturbances before surgery. These results showed that participants who received either lens had a reduction in most visual disturbances.

[1]McAlinden C, Pesudovs K, Moore JE. The development of an instrument to measure quality of vision: the Quality of Vision (QoV) questionnaire. *Invest Ophthalmol Vis Sci*. 2010;51:5537-5545.

[2]McAlinden C, Skiadaresi E, Gatinel D, et al. The Quality of Vision questionnaire: subscale interchangeability. *Optom Vis Sci.* 2013;90:760-767.

Responses to the questionnaire generally showed improvements after surgery in both the Trifocal and Monofocal groups with similar postoperative results for frequency, severity, and bothersomeness in most visual disturbance categories. Participants in the Trifocal group stated a greater frequency of halos (36.9% [116/314] quite often or very often) compared to the Monofocal IOL (7.1% [11/154]). Moderate to severe difficulty with focusing and depth perception was reported by 8.8% (27/309) and 5.5% (15/310) of participants with the Trifocal group compared to 13.2% (20/151) and 7.9% (10/151) of participants in the Monofocal group respectively.

At 4-6 months after surgery, results show a trend of more participants who received this lens (enVista Trifocal IOL) reporting having halos compared to participants who received the monofocal lens although 80% (247/309) of the Trifocal group reported the halos as being not at all to a little bothersome. About 10% more participants experienced glare and starbursts at least occasionally in the Trifocal group compared to the monofocal group.

The Trifocal IOL results monitoring difficulty in Judging distance and depth perception showed a trend of lower rate of frequency stated as "very often", "severe", and "very bothersome" when compared to the Monofocal group.

Table 26: Quality Of Vision Questionnaire Responses At Visit 4 (4-6 Months) (Modified Safety Set)

		Frequency (%)				Severity (%)				Bothersome (%)			
Visual Disturbance	**Device**	**Never**	**Occasionally**	**Quite often**	**Very often**	**Not at all**	**Mild**	**Moderate**	**Severe**	**Not at all**	**A little**	**Quite**	**Very**
Glare	Monofocal	N=154				N=151				N=151			
		73 (47.4)	67 (43.5)	9 (5.8)	5 (3.2)	76 (50.3)	49 (32.5)	23 (15.2)	3 (2.0)	85 (56.3)	48 (31.8)	16 (10.6)	2 (1.3)
	This device	N=314				N=310				N=310			
		118 (37.6)	152 (48.4)	28 (8.9)	16 (5.1)	124 (40.0)	129 (41.6)	47 (15.2)	10 (3.2)	148 (47.7)	125 (40.3)	23 (7.4)	14 (4.5)
Halos	Monofocal	N=154				N=151				N=151			
		91 (59.1)	52 (33.8)	8 (5.2)	3 (1.9)	95 (62.9)	41 (27.2)	13 (8.6)	2 (1.3)	104 (68.9)	36 (23.8)	9 (6.0)	2 (1.3)
	This device	N=314				N=309				N=309			
		84 (26.8)	114 (36.3)	62 (19.7)	54 (17.2)	90 (29.1)	114 (36.9)	86 (27.8)	19 (6.1)	126 (40.8)	120 (38.8)	41 (13.3)	22 (7.1)
Starbursts	Monofocal	N=154				N=151				N=151			
		101 (65.6)	41 (26.6)	6 (3.9)	6 (3.9)	109 (72.2)	29 (19.2)	7 (4.6)	6 (4.0)	118 (78.1)	23 (15.2)	4 (2.6)	6 (4.0)
	This device	N=314				N=311				N=311			
		168 (53.5)	106 (33.8)	28 (8.9)	12 (3.8)	175 (56.3)	91 (29.3)	37 (11.9)	8 (2.6)	204 (65.6)	78 (25.1)	19 (6.1)	10 (3.2)
Hazy Vision	Monofocal	N=154				N=152				N=152			
		102 (66.2)	44 (28.6)	6 (3.9)	2 (1.3)	101 (66.4)	36 (23.7)	14 (9.2)	1 (0.7)	104 (68.4)	37 (24.3)	11 (7.2)	0 (0.0)
	This device	N=314				N=311				N=311			
		211 (67.2)	81 (25.8)	17 (5.4)	5 (1.6)	214 (68.8)	73 (23.5)	22 (7.1)	2 (0.6)	222 (71.4)	64 (20.6)	21 (6.8)	4 (1.3)
Blurred Vision	Monofocal	N=153				N=153				N=154			
		82 (53.6)	55 (35.9)	13 (8.5)	3 (2.0)	86 (56.2)	48 (31.4)	17 (11.1)	2 (1.3)	93 (60.4)	46 (29.9)	13 (8.4)	2 (1.3)
	This device	N=314				N=311				N=311			
		195 (62.1)	103 (32.8)	12 (3.8)	4 (1.3)	200 (64.3)	92 (29.6)	15 (4.8)	4 (1.3)	214 (68.8)	76 (24.4)	15 (4.8)	6 (1.9)
Distortion	Monofocal	N=154				N=151				N=151			
		130 (84.4)	23 (14.9)	1 (0.6)	0 (0.0)	128 (84.8)	20 (13.2)	3 (2.0)	0 (0.0)	129 (85.4)	19 (12.6)	2 (1.3)	1 (0.7)
	This device	N=313				N=310				N=310			
		280 (89.5)	29 (9.3)	4 (1.3)	0 (0.0)	281 (90.6)	25 (8.1)	4 (1.3)	0 (0.0)	283 (91.3)	22 (7.1)	5 (1.6)	0 (0.0)
Double Or Multiple Images	Monofocal	N=154				N=152				N=152			
		127 (82.5)	20 (13.0)	6 (3.9)	1 (0.6)	127 (83.6)	15 (9.9)	9 (5.9)	1 (0.7)	128 (84.2)	19 (12.5)	4 (2.6)	1 (0.7)
	This device	N=314				N=309				N=309			
		276 (87.9)	32 (10.2)	5 (1.6)	1 (0.3)	275 (89.0)	24 (7.8)	9 (2.9)	1 (0.3)	275 (89.0)	25 (8.1)	7 (2.3)	2 (0.6)
Fluctuation In Vision	Monofocal	N=154				N=153				N=153			
		78 (50.6)	72 (46.8)	4 (2.6)	0 (0.0)	84 (54.9)	62 (40.5)	7 (4.6)	0 (0.0)	95 (62.1)	52 (34.0)	5 (3.3)	1 (0.7)
	This device	N=314				N=311				N=311			
		179 (57.0)	119 (37.9)	14 (4.5)	2 (0.6)	187 (60.1)	102 (32.8)	18 (5.8)	4 (1.3)	207 (66.6)	88 (28.3)	11 (3.5)	5 (1.6)
Focusing Difficulties	Monofocal	N=154				N=151				N=151			
		70 (45.5)	67 (43.5)	16 (10.4)	1 (0.6)	72 (47.7)	59 (39.1)	20 (13.2)	0 (0.0)	75 (49.7)	62 (41.1)	13 (8.6)	1 (0.7)
	This device	N=314				N=309				N=309			
		134 (42.7)	159 (50.6)	17 (5.4)	4 (1.3)	146 (47.2)	136 (44.0)	24 (7.8)	3 (1.0)	172 (55.7)	116 (37.5)	17 (5.5)	4 (1.3)
Judging Distance Or Depth Perception	Monofocal	N=154				N=151				N=151			
		108 (70.1)	35 (22.7)	9 (5.8)	2 (1.3)	107 (70.9)	32 (21.2)	8 (5.3)	4 (2.6)	110 (72.8)	31 (20.5)	6 (4.0)	4 (2.6)
	This device	N=314				N=310				N=310			
		224 (71.3)	79 (25.2)	10 (3.2)	1 (0.3)	228 (73.5)	65 (21.0)	16 (5.2)	1 (0.3)	231 (74.5)	64 (20.6)	14 (4.5)	1 (0.3)

Abbreviations: IOL = intraocular lens; Op = Operative; This device = enVista MX60EF Trifocal IOL; Monofocal = enVista MX60E monofocal IOL.

2.2 Sub-Study: Binocular Contrast Sensitivity

At Visit 4 (4-6 Months), mean ± SD photopic binocular CS with glare ranged from 0.841 ± 0.3384 log units in the trifocal IOL group and 0.999 ± 0.3294 log units in the monofocal IOL group for 18 cpd to 1.718 ± 0.3642 log units in the trifocal IOL group and 1.921 ± 0.3114 log units in the monofocal IOL group for 3 cpd (Figure 6 and Table 27). The largest observed mean difference between the treatment group means was -0.327 log units at 6 cpd.

At Visit 4 (4-6 Months), mean ± SD mesopic binocular CS with glare ranged from 0.751 ± 0.3139 log units in the trifocal IOL group and 0.959 ± 0.3528 log units in the monofocal IOL group for 12 cpd to 1.607 ± 0.3373 log units in the trifocal IOL group and 1.798 ± 0.2796 log units in the monofocal IOL group for 3 cpd (Figure 7 and Table 28). The largest observed mean difference between the treatment group means was -0.279 log units at 6 cpd.

At Visit 4 (4-6 Months), mean ± SD mesopic binocular CS without glare ranged from 0.969 ± 0.2998 log units in the trifocal IOL group and 1.098 ± 0.3358 log units in the monofocal IOL group for 12 cpd to 1.995 ± 0.2899 log units in the trifocal IOL group for 1.5 cpd and 2.075 ± 0.2576 log units in the monofocal IOL group for 3 cpd (Figure 8 and Table 29). The largest observed mean difference between the treatment group means was -0.174 log units at 6 cpd.

The differences in mean binocular contrast sensitivity between the Trifocal and Monofocal IOLs were clinically insignificant, i.e., <0.15 log unit for 4 of the 12 test conditions (Mesopic with and without glare at 1.5 cpd, Mesopic without glare at 3 and 12 cpd); clinically significant differences favored the Monofocal IOL for the remaining test conditions. The mean binocular contrast sensitivity was worse in the trifocal cohort than monofocal cohort for all tested conditions, except for the lowest spatial frequency tested (i.e., thickest stripes) for the mesopic with glare, and mesopic without glare conditions.

Figure 6: Binocular Contrast Sensitivity – Photopic Lighting With Glare By Spatial Frequency At Visit 4 (4-6 Months) (Modified Safety Set)

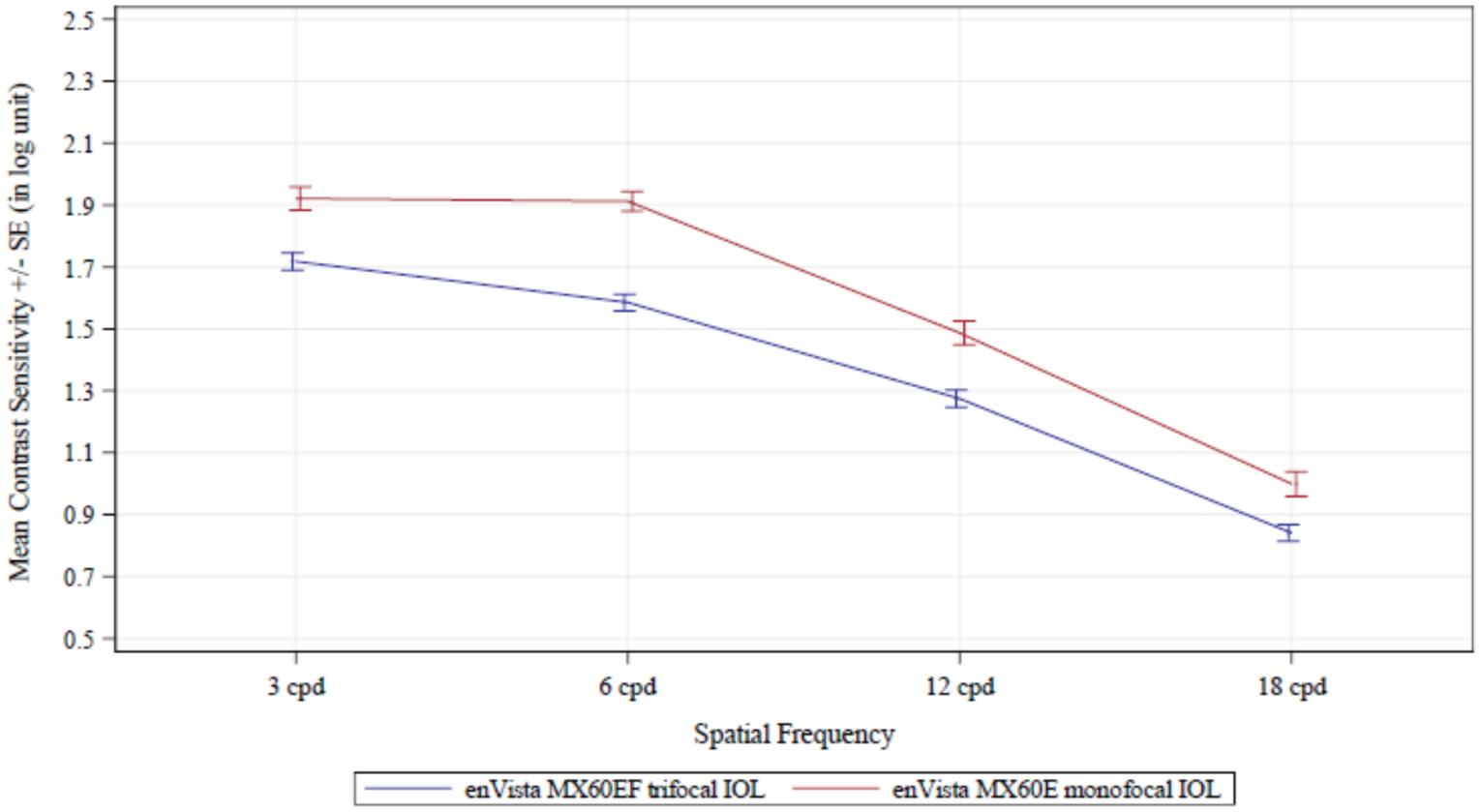


Figure 7: Binocular Contrast Sensitivity – Mesopic Lighting With Glare By Spatial Frequency At Visit 4 (4-6 Months) (Modified Safety Set)

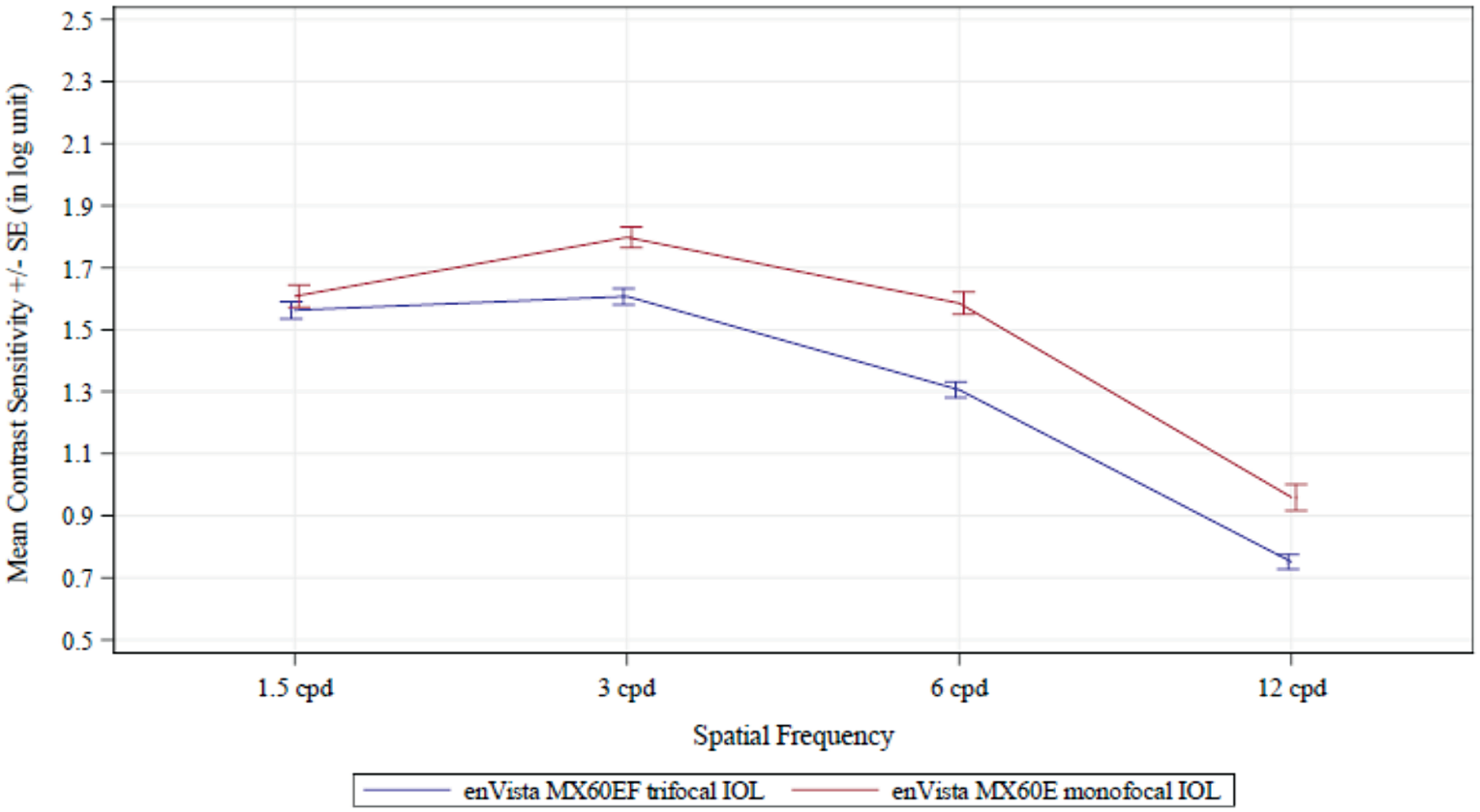


Figure 8: Binocular Contrast Sensitivity – Mesopic Lighting Without Glare By Spatial Frequency At Visit 4 (4-6 Months) (Modified Safety Set)

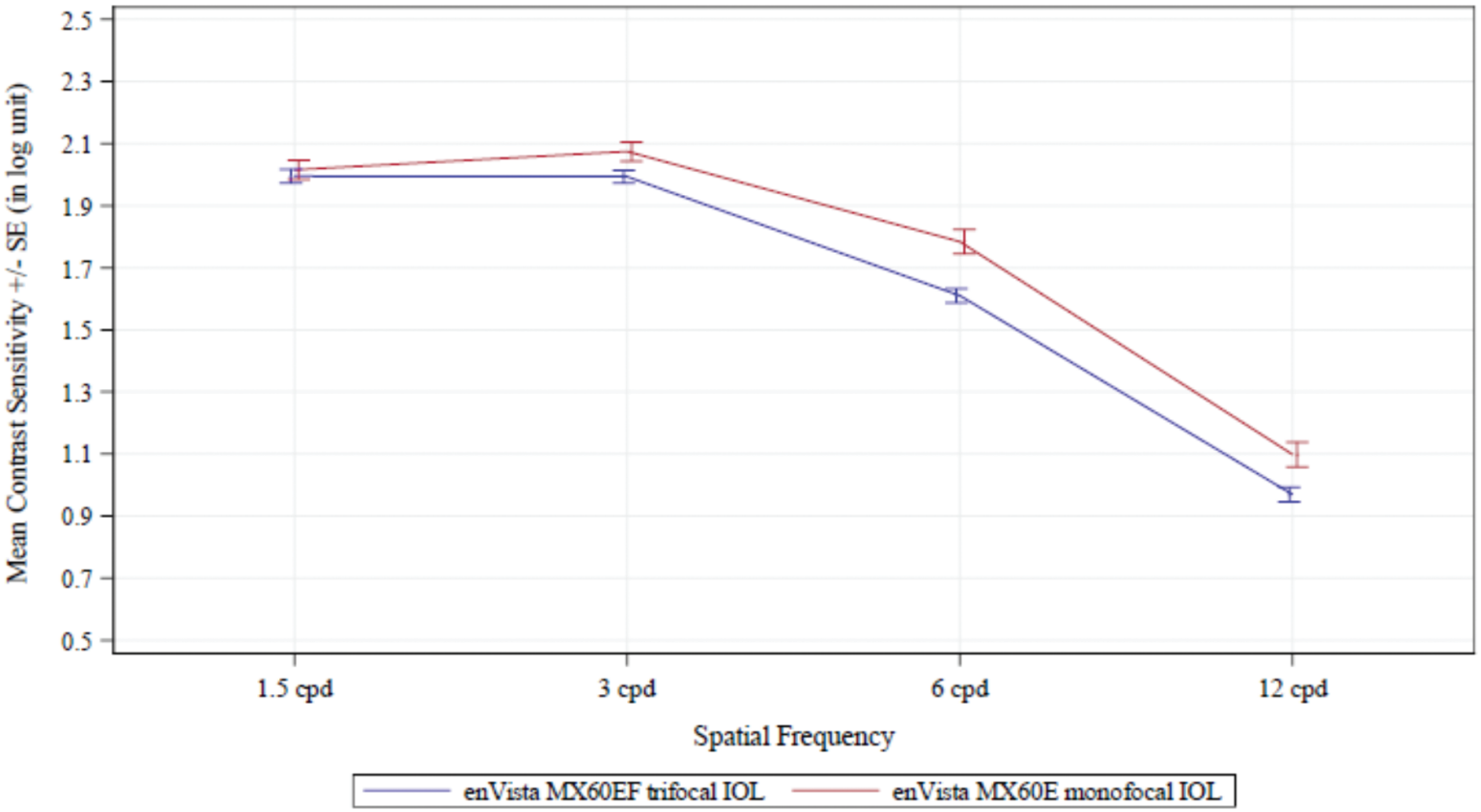


Table 27: Photopic Binocular Contrast Sensitivity With Glare In Log Value By Spatial Frequency At Visit 4 (4-6 Months) (Modified Safety Set)

	enVista Trifocal IOL (N=327)	enVista Monofocal IOL (N=168)
Photopic CS with glare at 3 cpd, log units		
n	168	70
Mean (SD)	1.718 (0.3642)	1.921 (0.3114)
Median	1.750	1.925
Minimum, maximum	0.00, 2.40	0.60, 2.40
95% CI for mean	1.662, 1.773	1.847, 1.995
Mean difference (trifocal – monofocal)	-0.203	
95% CI for mean difference	-0.301, -0.105	
Photopic CS with glare at 6 cpd, log units		
n	168	70
Mean (SD)	1.585 (0.3468)	1.912 (0.2712)
Median	1.625	1.925
Minimum, maximum	0.00, 2.24	1.27, 2.40
95% CI for mean	1.532, 1.638	1.847, 1.977
Mean difference (trifocal – monofocal)	-0.327	
95% CI for mean difference	-0.418, -0.235	
Photopic CS with glare at 12 cpd, log units		
n	168	70
Mean (SD)	1.274 (0.3635)	1.487 (0.3238)
Median	1.300	1.548
Minimum, maximum	0.00, 2.00	0.57, 2.20
95% CI for mean	1.219, 1.330	1.409, 1.564
Mean difference (trifocal – monofocal)	-0.212	
95% CI for mean difference	-0.311, -0.114	
Photopic CS with glare at 18 cpd, log units		
n	166	69
Mean (SD)	0.841 (0.3384)	0.999 (0.3294)
Median	0.875	1.000
Minimum, maximum	0.00, 1.80	0.28, 1.85
95% CI for mean	0.789, 0.893	0.920, 1.078
Mean difference (trifocal – monofocal)	-0.158	
95% CI for mean difference	-0.253, -0.064	

CI = confidence interval; cpd = cycles per degree; CS = contrast sensitivity; IOL = intraocular lens; SD = standard deviation.

Table 28: Mesopic Binocular Contrast Sensitivity With Glare In Log Value By Spatial Frequency At Visit 4 (4-6 Months) (Modified Safety Set)

	enVista Trifocal IOL (N=327)	enVista Monofocal IOL (N=168)
Mesopic CS with glare at 1.5 cpd, log units		
n	168	70
Mean (SD)	1.563 (0.3597)	1.608 (0.2981)
Median	1.648	1.670
Minimum, maximum	0.25, 2.34	0.63, 2.40
95% CI for mean	1.508, 1.618	1.537, 1.679
Mean difference (trifocal – monofocal)	-0.045	
95% CI for mean difference	-0.141, 0.051	
Mesopic CS with glare at 3 cpd, log units		
n	168	70
Mean (SD)	1.607 (0.3373)	1.798 (0.2796)
Median	1.650	1.820
Minimum, maximum	0.45, 2.34	0.80, 2.30
95% CI for mean	1.556, 1.659	1.731, 1.864
Mean difference (trifocal – monofocal)	-0.190	
95% CI for mean difference	-0.280, -0.100	
Mesopic CS with glare at 6 cpd, log units		
n	168	70
Mean (SD)	1.306 (0.3309)	1.585 (0.3019)
Median	1.323	1.610
Minimum, maximum	0.50, 2.24	0.75, 2.24
95% CI for mean	1.256, 1.356	1.513, 1.657
Mean difference (trifocal – monofocal)	-0.279	
95% CI for mean difference	-0.370, -0.189	
Mesopic CS with glare at 12 cpd, log units		
n	167	69
Mean (SD)	0.751 (0.3139)	0.959 (0.3528)
Median	0.750	1.020
Minimum, maximum	0.10, 1.77	0.25, 1.70
95% CI for mean	0.703, 0.799	0.874, 1.044
Mean difference (trifocal – monofocal)	-0.208	
95% CI for mean difference	-0.300, -0.116	

CI = confidence interval; cpd = cycles per degree; CS = contrast sensitivity; IOL = intraocular lens; SD = standard deviation.

Table 29: Mesopic Binocular Contrast Sensitivity Without Glare In Log Value By Spatial Frequency At Visit 4 (4-6 Months) (Modified Safety Set)

	enVista Trifocal IOL (N=327)	enVista Monofocal IOL (N=168)
Mesopic CS without glare at 1.5 cpd, log units		
n	168	70
Mean (SD)	1.995 (0.2899)	2.015 (0.2634)
Median	2.050	2.075
Minimum, maximum	0.80, 2.40	1.15, 2.40
95% CI for mean	1.951, 2.039	1.953, 2.078
Mean difference (trifocal – monofocal)	-0.020	
95% CI for mean difference	-0.100, 0.059	
Mesopic CS without glare at 3 cpd, log units		
n	168	70
Mean (SD)	1.993 (0.2722)	2.075 (0.2576)
Median	2.075	2.125
Minimum, maximum	0.95, 2.40	1.49, 2.40
95% CI for mean	1.952, 2.035	2.013, 2.136
Mean difference (trifocal – monofocal)	-0.081	
95% CI for mean difference	-0.156, -0.006	
Mesopic CS without glare at 6 cpd, log units		
n	168	70
Mean (SD)	1.610 (0.2877)	1.784 (0.3248)
Median	1.620	1.770
Minimum, maximum	0.77, 2.30	1.05, 2.34
95% CI for mean	1.566, 1.654	1.706, 1.861
Mean difference (trifocal – monofocal)	-0.174	
95% CI for mean difference	-0.258, -0.090	
Mesopic CS without glare at 12 cpd, log units		
n	168	70
Mean (SD)	0.969 (0.2998)	1.098 (0.3358)
Median	0.950	1.110
Minimum, maximum	0.15, 1.85	0.30, 1.75
95% CI for mean	0.924, 1.015	1.018, 1.178
Mean difference (trifocal – monofocal)	-0.129	
95% CI for mean difference	-0.216, -0.042	

CI = confidence interval; cpd = cycles per degree; CS = contrast sensitivity; IOL = intraocular lens; SD = standard deviation.

2.3 ISO Grid Adverse Events In Second Eyes

Among second eyes, the trifocal IOL group had 3/329 participants (95% Confidence interval between 0.2-2.6) with cystoid macular edema, which was not statistically significantly greater than the SPE rate of 3.0%, and 1/329 participants (0.3%, 95% CI: 0.0-1.7) with endophthalmitis which was not significantly greater than the SPE rate of 0.1%. In addition, there were 2/329 participants (0.6%, 95% CI: 0.07-2.18%) with secondary surgical interventions, which were not significantly greater than the SPE rate of 0.8% (Table 30). The two secondary surgical interventions that occurred in the second eyes for the enVista Envy IOL were a Pars Plana Vitrectomy for endophthalmitis and removal of a retained lens fragment. None of the other ISO grid cumulative AEs or any persistent AEs were reported in the trifocal IOL group.

Table 30: ISO Grid Adverse Events (Second Eyes; Modified Safety Set)

Adverse Event	Observed Event Rate For enVista Trifocal IOL n (%)	2-Sided 95% CI	1-Sided 95% LCL	SPE Rate (%)[b]
Cumulative[a]	N=329			
Cystoid macular oedema[c]	3 (0.9)	(0.19, 2.64)	0.25	3.0
Hypopyon	0	(0.00, 1.11)	0.00	0.3
Endophthalmitis	1 (0.3)	(0.01, 1.68)	0.02	0.1
Lens dislocated from posterior chamber[d]	0	(0.00, 1.11)	0.00	0.1
Pupillary block	0	(0.00, 1.11)	0.00	0.1
Retinal detachment[e]	0	(0.00, 1.11)	0.00	0.3
SSI	2 (0.6)	(0.07, 2.18)	0.11	0.8
Persistent[a]	N=314			
Corneal stroma oedema[f]	0	(0.0, 1.17)	0.00	0.3
Cystoid macular oedema	0	(0.0, 1.17)	0.00	0.5
Iritis[g]	0	(0.0, 1.17)	0.00	0.3
Raised IOP requiring treatment[h]	0	(0.0, 1.17)	0.00	0.4

AE = adverse event; CI = confidence interval; IOL = intraocular lens; IOP = intraocular pressure; ISO = International Organization for Standardization; LCL = lower confidence limit; SPE = Safety and Performance Endpoint; SSI = secondary surgical intervention.

[a]For cumulative AEs, observed AE rate is calculated as 100 multiplied by the number of eyes with the specific treatment-emergent event divided by the number of eyes (N). For persistent AE rates, the number of eyes (N) present at Visit 5 (11-14 Months) is the denominator.

[b]The ISO standard SPE rate in ISO 11979-7:2018.

[c]Per protocol, the definition of CME on this study was cystoid macular edema diagnosed by clinical exam and adjunct testing (e.g., OCT, FA or other method), resulting in BCDVA of ≤ 20/40 at Visit 3 or later. No participants were diagnosed with CME based on OCT alone.

[d]IOL decentration or tilt likely to affect visual outcome resulting in secondary intervention.

[e]Partial or complete Retinal Detachment associated with retinal tear. There were no retinal detachments without retinal tears.

[f]Corneal or corneal wound edema resulting in BCDVA of ≤ 20/40 at Visit 3A or later in the first implanted eye or at Visit 3B or later in the second implanted eye, or any persistent corneal or corneal wound edema present at Visit 5 (11-14 Months).

[g]Iritis/cells/flare characterized by grade 1+ cells or greater using SUN criteria if persistent for greater than 3 months after surgery, or relapses in less than 3 months after discontinuation of therapy, or the participant is maintained on therapy for more than 3 months to control inflammation.

[h]Elevation of IOP by ≥ 10 mmHg above baseline (pre-operative) to a minimum of 25 mmHg (Masket S, et al. Special Report: The American Academy of Ophthalmology Task Force Consensus Statement on Adverse Events with Intraocular Lenses. Ophthalmology 2017;124(1):142-144) after IOL implantation, or elevated IOP requiring treatment if present at Visit 5.

2.4 Secondary Surgical Interventions In Second Eyes

Two SSIs were reported in second eyes of the trifocal IOL group.

2.5 Ocular Treatment-Emergent Serious Adverse Events In Second Eyes And All Eyes

One participant of 329 (0.3%) in the trifocal IOL group and 1 participant of 168 (0.6%) in the monofocal IOL group experienced an ocular TE-SAE in second eyes (Table 31). The ocular TE-SAEs were one instance of endophthalmitis in the trifocal IOL group and one cataract operation complication in the monofocal IOL group.

Adding the 5 ocular TE-SAEs from first eyes (trifocal IOL group, n=4; monofocal IOL group, n=1), 5 of 661 participant eyes (0.8%) in the trifocal IOL group and 2 of 337 participant eyes (0.6%) in the monofocal IOL group experienced an ocular TE-SAE in all eyes. The rates of ocular TE-SAEs were similar between the treatment groups.

Table 31: Ocular Treatment-Emergent Serious Adverse Events By Treatment (Second Eyes And All Eyes; Modified Safety Set)

	Second Eyes		All Eyes	
Adverse Event Term	enVista Trifocal IOL (N=329) n (%)	enVista Monofocal IOL (N=168) n (%)	enVista Trifocal IOL (N=661) n (%)	enVista Monofocal IOL (N=337) n (%)
All ocular TE-SAEs	1 (0.3)	1 (0.6)	5 (0.8)	2 (0.6)
Macular hole	0	0	1 (0.2)	0
Retinal tear	0	0	1 (0.2)	0
Retinal vein occlusion	0	0	1 (0.2)	0
Endophthalmitis	1 (0.3)	0	1 (0.2)	0
Ophthalmic herpes zoster	0	0	0	1 (0.3)
Cataract operation complication	0	1 (0.6)	0	1 (0.3)
Seidel test positive	0	0	1 (0.2)	0

IOL = intraocular lens; MedDRA = Medical Dictionary for Regulatory Activities; TE-SAE = treatment-emergent serious adverse event.

Note: When reporting incidence, an eye is counted only once if the eye experiences more than 1 event of the same type. Adverse event term is coded from the verbatim using the Medical Dictionary for Regulatory Activities (MedDRA V 21).

2.6 All Other Types Of Adverse Events

Refer to Section 3.

3. Adverse Events

3.1 Brief Summary Of Adverse Events

In the Modified Safety Set, 49.4% (164/332) of participants in the trifocal IOL group and 40.8% (69/169) of participants in the monofocal IOL group experienced ocular TEAEs. Two participants in each treatment group experienced severe ocular TEAEs. Two participants in each treatment group had ocular TEAEs that were related to the study device. A total of 125 of 332 participants (37.7%) in the trifocal IOL group and 51 of 169 participants (30.2%) in the monofocal IOL group had ocular TEAEs that were related to the surgical procedure.

Five of 332 participants (1.5%) in the trifocal IOL group and 2 of 169 participants (1.2%) in the monofocal group had ocular TE-SAEs; 3 had moderate TE-SAEs and 2 had severe TE-SAEs in the trifocal IOL group, and 1 each had moderate and severe TE-SAEs in the monofocal IOL group. None of the ocular TE-SAEs were related to the study device. Two participants in the trifocal IOL group and 1 participant in the monofocal IOL group had ocular TE-SAEs that were related to the surgical procedure.

Twelve of 332 participants (3.6%) in the trifocal IOL group and 13 of 169 participants (7.7%) in the monofocal IOL group had non-ocular TE-SAEs.

In the Modified Safety Set, 37.7% (249/661) of all eyes in the trifocal IOL group and 28.8% (97/337) of all eyes in the monofocal IOL group experienced ocular TEAEs. Two eyes in each treatment group had severe ocular TEAEs. Four eyes in the trifocal IOL group and 3 eyes in the monofocal IOL group had ocular TEAEs that were related to the study device. A total of 178 of 661 eyes (26.9%) in the trifocal IOL group and 68 of 337 eyes (20.2%) in the monofocal IOL group had ocular TEAEs that were related to the surgical procedure. The trifocal IOL group had 2 of 332 (0.6%) participants with a nonserious TEAE related to the study device (both halo vision) and 37.7% (125/332) related to the surgical procedure (primarily punctate keratitis, intraocular pressure increased, and vitreous detachment).

Five of 661 eyes (0.8%) in the trifocal IOL group and 2 of 337 eyes (0.6%) in the monofocal group

had ocular TE-SAEs; 3 had moderate TE-SAEs and 2 had severe TE-SAEs in the trifocal IOL group, and 1 each had moderate and severe TE-SAEs in the monofocal IOL group. None of the ocular TE-SAEs were related to the study device. Two eyes in the trifocal IOL group and 1 eye in the monofocal IOL group had ocular TE-SAEs that were related to the surgical procedure.

Two participants required a surgical exchange of the IOL during the initial phacoemulsification and IOL procedure due to bent haptics and both incidences were recorded as a device deficiency.

The results of adverse events analyses based on the consensus definitions as set forth by American Academy of Ophthalmology's Task Force (Masket et al. Ophthalmology 2017) are shown in Tables 32 and 33. In addition, see Tables 34 and 35 for all ocular serious and non-serious adverse events.

Table 32: Ocular Adverse Events Based On A Modified Version Of AAO Consensus (Masket et al., 2017), First Eye (Modified Safety Set)

	enVista Trifocal IOL (N=332)			enVista Monofocal IOL (N=169)		
Adverse Event	**n (%)**	**2-Sided 95% CI**	**E**	**n (%)**	**2-Sided 95% CI**	**E**
Chronic anterior uveitis	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Clinically significant cystoid macular edema	0	(0.00, 1.10)	0	1 (0.6)	(0.01, 3.25)	1
Visually significant corneal edema	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Endophthalmitis	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Mechanical pupillary block	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Increased IOP	26 (7.8)	(5.18, 11.26)	27	15 (8.9)	(5.05, 14.22)	15
Rhegmatogenous RD	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Toxic anterior segment syndrome	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Secondary IOL intervention - Exchange	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Secondary IOL intervention - Removal	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Secondary IOL intervention - Reposition	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0

Percentage calculated as (n/N) * 100

Table 33: Ocular Adverse Events Based On A Modified Version Of AAO Consensus (Masket et al., 2017), Second Eye (Modified Safety Set)

	enVista Trifocal IOL (N=329)			enVista Monofocal IOL (N=168)		
Adverse Event	**n (%)**	**2-Sided 95% CI**	**E**	**n (%)**	**2-Sided 95% CI**	**E**
Chronic anterior uveitis	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Clinically significant cystoid macular edema	3 (0.9)	(0.19, 2.64)	3	3 (1.8)	(0.37, 5.13)	4
Visually significant corneal edema	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Endophthalmitis	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Mechanical pupillary block	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Increased IOP	26 (7.9)	(5.23, 11.37)	26	8 (4.8)	(2.08, 9.17)	8
Rhegmatogenous RD	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Toxic anterior segment syndrome	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Secondary IOL intervention - Exchange	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Secondary IOL intervention - Removal	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0
Secondary IOL intervention - Reposition	0	(0.00, 1.10)	0	0	(0.00, 2.16)	0

Percentage calculated as (n/N) * 100

Table 34: Ocular Adverse Events (Serious And Non-Serious Combined), First Eye (Modified Safety Set)

	enVista Trifocal IOL (N=332)			enVista Monofocal IOL (N=169)		
Preferred Term	**n (%)**	**2-Sided 95% CI**	**E**	**n (%)**	**2-Sided 95% CI**	**E**
Punctate keratitis	48 (14.5)	(10.86, 18.71)	53	13 (7.7)	(4.16, 12.79)	14
Intraocular pressure increased	26 (7.8)	(5.18, 11.26)	27	15 (8.9)	(5.05, 14.22)	15
Vitreous detachment	22 (6.6)	(4.20, 9.86)	22	10 (5.9)	(2.87, 10.61)	10
Dry eye	7 (2.1)	(0.85, 4.30)	7	3 (1.8)	(0.37, 5.10)	4
Blepharitis	5 (1.5)	(0.49, 3.48)	5	4 (2.4)	(0.65, 5.95)	4
Meibomian gland dysfunction	5 (1.5)	(0.49, 3.48)	5	3 (1.8)	(0.37, 5.10)	3
Visual acuity reduced	5 (1.5)	(0.49, 3.48)	5	2 (1.2)	(0.14, 4.21)	2
Cystoid macular oedema	0	(0.00, 1.10)	0	1 (0.6)	(0.01, 3.25)	1
Vitreous floaters	2 (0.6)	(0.07, 2.16)	2	1 (0.6)	(0.01, 3.25)	1
Diplopia	3 (0.9)	(0.19, 2.62)	3	0	(0.00, 2.16)	0
Iritis	3 (0.9)	(0.19, 2.62)	3	1 (0.6)	(0.01, 3.25)	1
Blepharochalasis	2 (0.6)	(0.07, 2.16)	2	1 (0.6)	(0.01, 3.25)	1
Macular fibrosis	3 (0.9)	(0.19, 2.62)	3	0	(0.00, 2.16)	0
Chalazion	3 (0.9)	(0.19, 2.62)	3	0	(0.00, 2.16)	0
Glare	1 (0.3)	(0.01, 1.67)	1	1 (0.6)	(0.01, 3.25)	1
Halo vision	2 (0.6)	(0.07, 2.16)	2	0	(0.00, 2.16)	0
Conjunctivitis allergic	1 (0.3)	(0.01, 1.67)	1	1 (0.6)	(0.01, 3.25)	1
Eye irritation	2 (0.6)	(0.07, 2.16)	2	0	(0.00, 2.16)	0
Eyelid irritation	2 (0.6)	(0.07, 2.16)	2	0	(0.00, 2.16)	0
Conjunctival hyperaemia	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Conjunctivochalasis	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Diabetic retinopathy	0	(0.00, 1.10)	0	1 (0.6)	(0.01, 3.25)	1
Iridocyclitis	0	(0.00, 1.10)	0	1 (0.6)	(0.01, 3.25)	1
Retinal tear	2 (0.6)	(0.07, 2.16)	2	0	(0.00, 2.16)	0
Corneal epithelium defect	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Eye pruritus	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Macular hole	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Retinal vein occlusion	1 (0.3)	(0.01, 1.67)	2	0	(0.00, 2.16)	0
Trichiasis	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Ulcerative keratitis	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Vitreous haemorrhage	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Seidel test positive	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Cataract operation complication	1 (0.3)	(0.01, 1.67)	1	2 (1.2)	(0.14, 4.21)	2
Corneal abrasion	2 (0.6)	(0.07, 2.16)	2	0	(0.00, 2.16)	0
Foreign body in eye	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Ocular procedural complication	0	(0.00, 1.10)	0	1 (0.6)	(0.01, 3.25)	1
Conjunctivitis	1 (0.3)	(0.01, 1.67)	1	1 (0.6)	(0.01, 3.25)	1
Hordeolum	1 (0.3)	(0.01, 1.67)	1	2 (1.2)	(0.14, 4.21)	2
Ophthalmic herpes simplex	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Ophthalmic herpes zoster	0	(0.00, 1.10)	0	1 (0.6)	(0.01, 3.25)	2
Visual field defect	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Dermatitis contact	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0
Madarosis	0	(0.00, 1.10)	0	1 (0.6)	(0.01, 3.25)	1
Seasonal allergy	1 (0.3)	(0.01, 1.67)	1	0	(0.00, 2.16)	0

Table 35: Ocular Adverse Events (Serious And Non-Serious Combined), Second Eye (Modified Safety Set)

	enVista Trifocal IOL (N=329)			enVista Monofocal IOL (N=168)		
Preferred Term	n (%)	2-Sided 95% CI	E	n (%)	2-Sided 95% CI	E
Punctate keratitis	46 (14.0)	(10.42, 18.21)	50	11 (6.5)	(3.31, 11.41)	12
Intraocular pressure increased	26 (7.9)	(5.23, 11.37)	26	8 (4.8)	(2.08, 9.17)	8
Vitreous detachment	21 (6.4)	(3.99, 9.59)	21	7 (4.2)	(1.69, 8.40)	7
Dry eye	6 (1.8)	(0.67, 3.93)	6	4 (2.4)	(0.65, 5.98)	5
Blepharitis	5 (1.5)	(0.50, 3.51)	5	4 (2.4)	(0.65, 5.98)	4
Meibomian gland dysfunction	5 (1.5)	(0.50, 3.51)	5	4 (2.4)	(0.65, 5.98)	4
Visual acuity reduced	4 (1.2)	(0.33, 3.08)	4	2 (1.2)	(0.14, 4.23)	2
Cystoid macular oedema	3 (0.9)	(0.19, 2.64)	3	3 (1.8)	(0.37, 5.13)	4
Vitreous floaters	0	(0.00, 1.11)	0	4 (2.4)	(0.65, 5.98)	5
Diplopia	3 (0.9)	(0.19, 2.64)	3	0	(0.00, 2.17)	0
Iritis	2 (0.6)	(0.07, 2.18)	2	0	(0.00, 2.17)	0
Blepharochalasis	2 (0.6)	(0.07, 2.18)	2	0	(0.00, 2.17)	0
Macular fibrosis	1 (0.3)	(0.01, 1.68)	1	1 (0.6)	(0.02, 3.27)	1
Chalazion	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Glare	1 (0.3)	(0.01, 1.68)	1	1 (0.6)	(0.02, 3.27)	1
Halo vision	2 (0.6)	(0.07, 2.18)	2	0	(0.00, 2.17)	0
Conjunctivitis allergic	0	(0.00, 1.11)	0	1 (0.6)	(0.02, 3.27)	1
Eye irritation	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Eyelid irritation	0	(0.00, 1.11)	0	1 (0.6)	(0.02, 3.27)	1
Ocular hypertension	2 (0.6)	(0.07, 2.18)	2	1 (0.6)	(0.02, 3.27)	1
Conjunctival hyperaemia	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Conjunctivochalasis	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Diabetic retinopathy	0	(0.00, 1.11)	0	1 (0.6)	(0.02, 3.27)	1
Iridocyclitis	0	(0.00, 1.11)	0	1 (0.6)	(0.02, 3.27)	1
Anterior chamber cell	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Conjunctival cyst	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Conjunctival haemorrhage	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Eye discharge	0	(0.00, 1.11)	0	1 (0.6)	(0.02, 3.27)	1
Eye inflammation	0	(0.00, 1.11)	0	1 (0.6)	(0.02, 3.27)	1
Eye pain	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Photopsia	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Vitreous prolapse	0	(0.00, 1.11)	0	1 (0.6)	(0.02, 3.27)	1
Seidel test positive	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Cataract operation complication	1 (0.3)	(0.01, 1.68)	1	1 (0.6)	(0.02, 3.27)	2
Corneal abrasion	2 (0.6)	(0.07, 2.18)	2	0	(0.00, 2.17)	0
Iris injury	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Conjunctivitis	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Endophthalmitis	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Visual field defect	2 (0.6)	(0.07, 2.18)	2	0	(0.00, 2.17)	0
Dermatitis contact	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Corneal dystrophy	1 (0.3)	(0.01, 1.68)	1	0	(0.00, 2.17)	0
Device dislocation	0	(0.00, 1.11)	0	1 (0.6)	(0.02, 3.27)	1

3.2 Deaths, Other Serious Adverse Events, And Other Significant Adverse Events

3.2.1 Deaths

Four deaths, all of which were unrelated to the control or test IOLs, occurred during this study.

3.2.2 Serious Adverse Events

Five of 332 participants (1.5%) in the trifocal IOL group and 2 of 169 participants (1.2%) in the monofocal IOL group experienced ocular TE-SAEs (Table 31). The ocular TE-SAEs, occurring in 1 participant each, were macular hole, retinal tear, retinal vein occlusion, endophthalmitis, and Seidel test positive in the trifocal IOL group and ophthalmic herpes zoster and cataract operation complication in the monofocal IOL group.

3.2.3 Non-Ocular Treatment-Emergent Serious Adverse Events

Twelve of 332 participants (3.6%) in the trifocal IOL group and 13 of 169 participants (7.7%) in the monofocal IOL group experienced non-ocular TE-SAEs. The most common system organ classes associated with non-ocular TE-SAEs were nervous system disorders (1.2% [4/332]) and neoplasms benign, malignant and unspecified (incl cysts and polyps) (1.2% [4/332]) in the trifocal IOL group and nervous system disorders (2.4% [4/169]) and general disorders and administration site conditions (1.8% [3/169]) in the monofocal IOL group. The only preferred terms that occurred in more than one participant were cerebrovascular accident (trifocal IOL group, n=2; monofocal IOL group, n=2) and chest pain (monofocal IOL group, n=2).

4. Sub-Study: Trial Frame Astigmatism

The Trial Frame astigmatism simulation was a sub-study conducted at Visit 6 (Day 2-30 after otherwise last Visit/Postoperative Visit 5 at 11-14 Months), at up to 10 sites. Approximately 30 Group 1 participants and 15 Group 2 participants were enrolled with a goal of a total of 50 participants enrolled. Enrollment was sequential with consecutive participants enrolled at each site in order of their completion of post-operative Visit 5 (11-14 Months) and based on their eligibility. The sub-study noted a first participant on July 21, 2022, and a completion with last participant on February 21, 2023. The purpose of the Trial Frame Astigmatism Simulation sub-study was to assess the potential effect of residual astigmatism on visual performance. It was conducted in subjects implanted with the non-toric enVista Envy IOL and the study was performed to support approval of toric models greater than 3.75 D in the IOL plane.

Eligibility was confirmed at completion of Visit 5 (11-14 Months) and the participant once consented was brought back to undergo the trial frame evaluation at Visit 6 (Day 2 to 30 after otherwise last visit/Postoperative Visit 5). The Inclusion criteria included a completed Visit 5 (11-14 Months) with a signed consent; a BCDVA of 20/25 or better at Visit 5 (11-14 Months); no Adverse/Serious Adverse Events including corneal edema/increased Intraocular Pressure and acceptance to complete Visit 6 between 2 and 30 days after completion of Visit 5 (11-14 Months). Participants with oblique post-operative residual astigmatism (axis between 30 to 60 degrees or 120 to 150 degrees) were excluded.

To assess the potential effect of residual astigmatism on the visual performance of enVista Envy Trifocal IOL in relation to enVista monofocal IOL, various levels of astigmatic blur (1.00 D, 1.50 D, 2.00 D in with-the-rule and against-the-rule orientations) were added to each participant's distance corrected visual acuities. Visual acuity was tested at 4 m, 66 cm, and 40 cm for each eye of the participant using the Clinical Trial Suite system (M&S Technologies, Niles, IL). To ensure the spherical equivalent was kept at a constant, a correction (-0.50 sph added with +1.00 cylinder, -0.75 sph added with +1.50 cylinder, -1.00 sph added with +2.00 cylinder) was added to each plus cylinder power added to the trial frame to modify the spherical power.

The logMAR VA for each assessed combination of distance, cylinder power and axis were summarized by treatment group using the sample size, mean, standard deviation, minimum, first through third quartiles, and maximum. Also summarized was the within-eye difference in logMAR VA between without astigmatic correction (0.00 D cylinder power) and with astigmatic correction, for each combination of distance, non-zero cylinder power, and axis.

Results

A total of 33 participants implanted with the enVista Envy Trifocal IOL and 17 implanted with enVista monofocal IOL consented to participate in the trial frame astigmatism sub-study. The mean age of the participants was 65.4 ± 9.51 years in the enVista Envy Trifocal group and 71.3 ± 6.16 years in the enVista monofocal IOL group. Most of the study participants were females in both groups (57.6%; 19/33 in the enVista Envy Trifocal group and 58.8%; 10/17 in the monofocal IOL group). In the enVista Envy Trifocal group, 97%; 32/33 of the participants were White, and 3%; 1/33 were Asian, whereas in the enVista monofocal IOL group, all (100%; 17/17) of the study participants were White with a larger subset of participants falling under the non-Hispanic or non-Latino ethnicity in both groups. The mean photopic pupil size (for the first eye) was 4.0 ± 0.71 mm in the Envy Trifocal group and 3.9 ± 0.82 mm in the monofocal IOL group. The mesopic pupil size was 4.8 ± 0.74 mm in the enVista Envy Trifocal group and 4.5 ± 0.80 mm in the monofocal IOL group. The mean absolute refractive cylinder (in the first eye) was -0.60 ± 0.99 D in the Envy Trifocal group and 0.00 ± 0.74 D in the monofocal IOL group.

The tolerance to induced astigmatism, when assessed using trial frame astigmatism blur, showed that (Table 36):

- The baseline (no additional sphere, cylinder, or axis) mean BCDVA (± SD) among all eyes was 0.01 (± 0.07) logMAR in the trifocal IOL group and 0.01 (± 0.11) logMAR in the monofocal IOL group.
- With simulated astigmatism, change from baseline mean BCDVA (± SD) ranged from 0.14 (± 0.14) logMAR (+1.00 D, cylinder 180°) to 0.46 (± 0.18) logMAR (+2.00 D, cylinder 90°) in the trifocal IOL group and from 0.08 (± 0.10) logMAR (+1.00 D, cylinder 180°) to 0.44 (± 0.20) logMAR (+2.00 D, cylinder 90°) in the monofocal IOL group.
- The baseline (no additional sphere, cylinder, or axis) mean DCIVA (± SD) among all eyes was 0.12 (± 0.10) logMAR in the trifocal IOL group and 0.40 (± 0.14) logMAR in the monofocal IOL group.
- With simulated astigmatism, change from baseline mean DCIVA (± SD) ranged from 0.04 (± 0.09) logMAR (+1.00 D, cylinder 180°) to 0.22 (± 0.14) logMAR (+2.00 D, cylinder 90°) in the trifocal IOL group and from -0.01 (± 0.12) logMAR (+1.00 D, cylinder 90°) to 0.03 (± 0.11) logMAR (+2.00 D, cylinder 180°) in the monofocal IOL group.
- The baseline (no additional sphere, cylinder, or axis) mean DCNVA (± SD) was 0.15 (± 0.11) logMAR in the trifocal IOL group and 0.56 (± 0.14) logMAR in the monofocal IOL group.
- With simulated astigmatism, change from baseline mean DCNVA (± SD) ranged from 0.08 (± 0.11) logMAR (+1.00 D, cylinder 180°) to 0.21 (± 0.15) logMAR (+2.00 D, cylinder 90°) in the trifocal IOL group and from -0.01 (± 0.09) logMAR (+1.00 D, cylinder 90°) to 0.04 ± 0.08 logMAR (+2.00 D, cylinder 180°) in the monofocal IOL group.

Conclusion

Visual acuity results for eyes with higher levels of induced astigmatism (1.50 D and 2.00 D) were generally reduced compared to visual acuity results for eyes without induced astigmatism. For DCNVA mean acuity was within 2.2 lines of vision for all induced astigmatism levels compared to eyes with induced astigmatism with a mean difference of about 1.5 lines for 1.50 D and about 2.2 lines for 2.00 D.

The results of this clinical investigation indicate that the effects of 1.00 D of induced astigmatism on distance, intermediate and near visual acuities are about 1.4 to 2.0 lines, 0.4 to 0.7 lines and 0.8 to 0.9 lines, respectively, compared to acuities without induced astigmatism. Non toric enVista Envy IOLs provide improved intermediate and near vision while preserving good distance vision compared to standard monofocal IOLs. The results from this simulation provide reasonable assurance that eyes implanted with high-cylinder toric enVista Envy trifocal IOLs may generally achieve reasonably similar results but indicate that eyes with significant toric lens misalignment from the intended position or errors in the estimated postoperative astigmatism are likely to achieve somewhat poorer results.

Table 36: Photopic Monocular LogMAR Distance Corrected Visual Acuities With The Trial Frame Astigmatism Simulation Sub-Study And Within Eye Difference Of LogMAR Visual Acuities With And Without Astigmatic Correction At Visit 6 (Day 2 To 30 After Otherwise Last Visit/Postoperative Visit 5) (Modified Safety Set: All Eyes).

DCVA, LogMAR	Assignment	Baseline (No Additional Sphere, Cylinder, Or Axis)	+2.00 D, Cylinder 180°	+2.00 D, Cylinder 90°	+1.50 D, Cylinder 180°	+1.50 D, Cylinder 90°	+1.00 D, Cylinder 180°	+1.00 D, Cylinder 90°
Mean (SD) BCDVA	enVista Trifocal IOL (N=66)	0.01 (0.07)	0.39 (0.20)	0.47 (0.17)	0.27 (0.17)	0.33 (0.15)	0.15 (0.14)	0.21 (0.15)
	enVista Monofocal IOL (N=34)	0.01 (0.11)	0.27 (0.19)	0.45 (0.22)	0.17 (0.13)	0.30 (0.20)	0.09 (0.11)	0.22 (0.20)
Mean (SD) BCDVA: Change From Baseline	enVista Trifocal IOL (N=66)	-	0.38 (0.21)	0.46 (0.18)	0.26 (0.18)	0.32 (0.14)	0.14 (0.14)	0.20 (0.14)
	enVista Monofocal IOL (N=34)	-	0.26 (0.19)	0.44 (0.20)	0.16 (0.15)	0.29 (0.18)	0.08 (0.10)	0.21 (0.16)
Mean (SD) DCIVA	enVista Trifocal IOL (N=66)	0.12 (0.10)	0.31 (0.13)	0.34 (0.13)	0.23 (0.12)	0.26 (0.12)	0.16 (0.11)	0.19 (0.10)
	enVista Monofocal IOL (N=34)	0.40 (0.14)	0.43 (0.14)	0.39 (0.16)	0.42 (0.16)	0.40 (0.15)	0.42 (0.14)	0.39 (0.14)
Mean (SD) DCIVA: Change From Baseline	enVista Trifocal IOL (N=66)	-	0.19 (0.11)	0.22 (0.14)	0.11 (0.11)	0.14 (0.14)	0.04 (0.09)	0.07 (0.12)
	enVista Monofocal IOL (N=34)	-	0.03 (0.11)	-0.01 (0.18)	0.02 (0.18)	0.00 (0.13)	0.02 (0.11)	-0.01 (0.12)
Mean (SD) DCNVA	enVista Trifocal IOL (N=66)	0.15 (0.11)	0.36 (0.14)	0.37 (0.13)	0.30 (0.12)	0.29 (0.12)	0.23 (0.13)	0.24 (0.12)
	enVista Monofocal IOL (N=34)	0.56 (0.14)	0.61 (0.14)	0.56 (0.15)	0.60 (0.13)	0.57 (0.15)	0.60 (0.13)	0.55 (0.15)
Mean (SD) DCNVA: Change From Baseline	enVista Trifocal IOL (N=66)	-	0.21 (0.15)	0.22 (0.15)	0.15 (0.13)	0.14 (0.13)	0.08 (0.11)	0.09 (0.13)
	enVista Monofocal IOL (N=34)	-	0.05 (0.09)	0.00 (0.09)	0.04 (0.07)	0.004 (0.08)	0.04 (0.08)	-0.01 (0.09)

DCVA = Distance corrected visual acuity; BCDVA = best-corrected distance visual acuity; DCIVA = Distance corrected intermediate visual acuity; DCNVA = Distance corrected near visual acuity; D = diopter; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation.

5. Optical Coherence Tomography Imaging Sub-Study

A total of 26 first eyes in Group 1 (test lens) and 13 first eyes in Group 2 (control lens) underwent imaging of the macula and/or optic nerve by anterior-segment OCT at 3 sites using the Zeiss Cirrus. Images were rated to have excellent quality in 37 eyes and good quality in 2 eyes. In all cases, the images were readable and provided sufficient information to diagnose the condition of the posterior segment (i.e., data on macular thickness and a clear image of Bruch's membrane in macular scans, retinal nerve fiber layer thickness, cup-to-disc ratio, and other parameters of optic disc morphology in optic nerve head scans).

6. Manifest Refraction, Residual Refractive Error And Keratometric Cylinder

Table 37 presents residual refractive error and postoperative keratometric cylinder for first eyes. The mean sphere and spherical equivalent in both the Trifocal and Monofocal groups demonstrate refractive accuracy to target with values close to zero. Approximately 97% (598/616 in the Trifocal IOL group and 295/304 in the Monofocal IOL group) of all eyes in both treatment groups were within ± 1.00 D of intended spherical equivalent at the end of the study.

Table 37: First Eye Residual Refractive Error And Keratometric Cylinder 4 To 6 Months After Surgery By Treatment Group (Modified Safety Set)

Parameter	Statistic	enVista Trifocal IOL (N=332)	enVista Monofocal IOL (N=169)
Sphere (D)	n	312	156
	Mean (SD)	0.095 (0.4473)	0.093 (0.4537)
	Median	0.000	0.000
	Min, Max	-1.25, 2.00	-1.00, 1.25
Cylinder (D)	n	312	156
	Mean (SD)	-0.460 (0.3913)	-0.465 (0.3518)
	Median	-0.500	-0.500
	Min, Max	-1.75, 0.00	-1.50, 0.00
Spherical Equivalent (D)	n	312	156
	Mean (SD)	-0.135 (0.3875)	-0.139 (0.4036)
	Median	-0.125	-0.188
	Min, Max	-1.25, 1.38	-1.50, 1.00
Keratometric Cylinder (D)	n	310	156
	Mean (SD)	0.576 (0.4123)	0.596 (0.3149)
	Median	0.500	0.560
	Min, Max	0.00, 3.92	0.00, 1.58

7. Intraocular Pressure

Among all eyes, baseline mean ± SD IOP was 15.8 ± 2.85 mmHg in the trifocal IOL group and 15.4 ± 2.95 mmHg in the monofocal IOL group. At Visit 5 (11-14 Months), mean ± SD IOP was 14.2 ± 2.66 mmHg (change from baseline, -1.6 ± 2.78 mmHg) in the trifocal IOL group and 13.8 ± 2.85 mmHg (change from baseline, -1.4 ± 2.96 mmHg) in the monofocal IOL group. Among all eyes, IOP showed a modest decline in both treatment groups from baseline to Visit 5 (11-14 Months) (~1.5 mmHg).

8. Quality Of Vision Questionnaire

See Section 2.1, "Secondary Safety Variables", Table 26

Conclusions

All 3 co-primary effectiveness endpoints examined in this study were met, with the trifocal IOL showing statistical noninferiority to the monofocal IOL in photopic monocular BCDVA, satisfactory BCDVA performance compared to the ISO grid performance standards, statistical superiority in photopic monocular DCNVA and DCIVA and statistical superiority at Visit 4 (4-6 Months) in binocular outcomes of DCNVA, DCIVA, UNVA, and UIVA compared to the monofocal. No unexpected safety findings were observed.

Binocular defocus curve testing demonstrated that the trifocal IOL produces an advantage in intermediate and near vision compared to the monofocal IOL group, with the largest benefit evident among eyes with large pupil sizes.

Per the safety analyses, three ISO grid cumulative or persistent AEs, all secondary surgical interventions, were reported in first eyes of the trifocal IOL group and the AEs did not exceed the ISO grid SPE rates; no SSIs due to the optical properties of the study lens were reported in first eyes of the trifocal IOL group; and no first eyes in the trifocal IOL group had an ocular TE-SAE that was related to the study device. Responses to the questionnaire generally showed improvements after surgery in both the Trifocal and Monofocal groups with similar postoperative results for frequency, severity, and bothersomeness in most visual disturbance categories. Participants in the Trifocal group stated a greater frequency of halos (36.9% [116/314] quite often or very often) compared to the control (7.1% [11/154]) with 6.1% (19/309) of the Trifocal participants describing the halos as severe and 7.1% (22/309) calling them very bothersome. Moderate to severe difficulty with focusing and depth perception was reported by 8.8% (27/309) and 5.5% (15/310) of participants with the Trifocal group compared to 13.2% (20/151) and 7.9% (10/151) of participants in the Monofocal group respectively. About 10% (31/311) more participants experienced glare and starbursts at least occasionally in the Trifocal group compared to the Monofocal group. At 4-6 months after surgery, results show a trend of more participants who received this lens (enVista Trifocal IOL) reporting having halos compared to participants who received the monofocal lens, although 80% (247/309) of the Trifocal group reported the halos as being not at all to a little bothersome.

The differences in mean binocular contrast sensitivity between the Trifocal and Monofocal IOLs were clinically insignificant, i.e., <0.15 log unit for 4 of the 12 test conditions (Mesopic with and without glare at 1.5 cpd, Mesopic without glare at 3 and 12 cpd); clinically significant differences favored the Monofocal IOL for the remaining test conditions.

The proportion of eyes implanted with the trifocal IOL that achieved 0.3 logMAR or better in photopic monocular BCDVA at Visit 4 (4-6 Months) exceeded the ISO standard SPE rates for the ITT and Best Case Sets, with 98.9% (617/624) and 99.0% (614/620), respectively. A similar proportion of participants and eyes across treatment groups had at least 1 ocular TEAE (trifocal IOL, 49.4% (164/332) of participants and 37.7% (249/661) of all eyes; monofocal IOL, 40.8% (69/169) of participants and 28.8% (97/337) of all eyes). The most common ocular TEAEs in both treatment groups were punctate keratitis, intraocular pressure increased, and vitreous detachment. By study completion there were 17/635 (2.7%) cases of moderate punctate keratitis in all eyes of the trifocal group, while there were 4/314 (1.3%) cases of moderate punctate keratitis in all eyes of the control group. There were 29/635 (4.6%) cases of mild punctate keratitis in all eyes of the trifocal group, while there were 4/314 (1.3%) cases of mild punctate keratitis in all eyes of the control group.

There were 4 deaths, all of which were unrelated to the control or test IOLs; no discontinuations due to AEs related to the study device or surgical procedure; and no ocular TE-SAEs related to the study device. The trifocal IOL group had 2 of 332 (0.6%) participants with a nonserious TEAE related to the

study device (both halo vision) and 37.7% (125/332) related to the surgical procedure (primarily punctate keratitis, intraocular pressure increased, and vitreous detachment).

Two participants required a surgical exchange of the IOL during the initial phacoemulsification and IOL procedure due to bent haptics and both incidences were recorded as a device deficiency.

The Trial Frame astigmatism blur sub-study revealed that at higher levels of induced astigmatism up to 2.00 D, the DCIVA, and DCNVA of the trifocal IOL were within 2.2 lines compared to that without induced astigmatism. The results from the sub-study provide reasonable assurance that eyes implanted with high-cylinder toric enVista Envy trifocal IOLs may generally achieve reasonably similar results to the non toric enVista trifocal IOL (improved intermediate and near vision while preserving good distance vision compared to a standard monofocal). However, eyes with significant toric lens misalignment from the intended position or errors in the estimated postoperative astigmatism are likely to achieve somewhat poorer results.

In summary, data presented in this study report show the enVista One-Piece Hydrophobic Acrylic Trifocal IOL (now known as the enVista Envy™ toric hydrophobic acrylic IOL (intraocular lens)) is safe and effective for participants undergoing cataract extraction.

Other Clinical Findings

The enVista IOL, model MX60, is the parent lens for all models listed in the device description. For the enVista MX60 clinical study (Study 658), all participants in the safety analysis set were evaluated for IOL glistenings at Form 3 and Form 4 visits. IOL glistenings were evaluated via retroillumination slit lamp examination utilizing a photographic grading scale provided in the protocol. The grading scale consisted of (in order of severity), "none, grade 0 (trace), grade 1, 2, 3, or 4." No glistenings of any grade were reported for any participant at any visit in the clinical study.

Adverse Event Reporting

Adverse events and/or potentially sight-threatening complications that may be regarded as lens related and that were not previously expected in nature, severity or degree of incidence should be reported within five (5) days to Bausch & Lomb Incorporated. This information is being requested from all surgeons in order to document potential long-term effects of IOL implantation. Should any of these incidents take place in the European Union (EU), the event should also be reported to the competent authority of the EU member state in which the user is established.

Physicians are encouraged to report these events in order to aid in identifying emerging or potential problems with IOL. These problems may be related to a specific lot of lenses or may be indicative of long-term effects associated with these lenses or with IOLs in general. If you wish to report a problem, in the USA, please call Bausch + Lomb at 1-800-338-2020. Outside the USA, contact information can be found on www.bausch.com/contactus. In case of device explant/extraction from a patient, keep the device and contact Customer Service for return instructions.

How Supplied

Non-preloaded IOL:

The enVista Envy toric IOL (model: ETN) is individually packaged in a sterile vial (containing blood bank saline), within a peel pouch, and should only be opened under sterile conditions.

Preloaded IOL:

The enVista Envy toric IOL (model: ETPN) is preloaded in the SnapSet IOL shuttle and individually packaged in a sterile vial (containing blood bank saline), within a peel pouch, and should only be opened under sterile conditions.

A patient card and self-adhesive labels are supplied to provide traceability of the lens. The package is sterilized by gamma irradiation.

Expiry Date

Sterility is guaranteed unless the pouch is damaged or opened. The expiry date on the lens package is the sterility expiry date. This lens should not be implanted after the indicated sterility expiry date.

Safe Disposal

Dispose/discard of the unused or contaminated device/equipment and/or packaging by following applicable safe disposal procedures, and in accordance with applicable laws and regulations regarding the disposal of biohazardous materials.

Patient Registration Instructions And Reporting Registration

Each patient who receives an enVista IOL must be registered with Bausch + Lomb at the time of lens implantation. Registration is accomplished by completing the Implant Registration Card that is enclosed in the lens package and mailing it to:

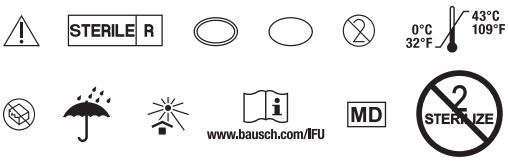
Bausch & Lomb Incorporated
3365 Tree Court Ind. Blvd.
St. Louis, MO 63122

Patient registration is essential and will assist Bausch + Lomb in responding to adverse reaction reports and/or potentially sight-threatening complications. The Patient Identification Card included in the package is to be completed and given to the patient, together with instructions to keep the card as a permanent record to be shown to any eye care practitioner that the patient consults in the future.

Symbols And Abbreviations Used On Labeling

Symbol Or Abbreviation	Symbol Or Abbreviation Title
SE	Spherical Equivalent
CYL	Cylinder
IOL	Intraocular Lens
PC	Posterior Chamber
UV	Ultraviolet
D	Diopter
$Ø_B$	Body Diameter (Optic Diameter)
$Ø_T$	Overall Diameter (Overall Length)
Rx ONLY	Caution: Federal (US) law restricts this device to sale by or on the order of a physician
	Fee paid for waste management
	Trifocal Intraocular Lens
	Preloaded Trifocal Intraocular Lens

www.bausch.com/symbols



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