ARTICLE

Evaluation of the small-aperture intracorneal inlay: Three-year results from the cohort of the U.S. Food and Drug Administration clinical trial

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Purpose: To evaluate the safety and effectiveness of the Kamra small-aperture intracorneal inlay.

Setting: Centers in North America, Europe, Asia, and Australia.

Design: Prospective clinical trial.

Methods: Patients with emmetropic presbyopia had intracorneal implantation of the inlay in the nondominant eye.

Results: The study comprised 507 patients with emmetropic presbyopia who were aged 45 to 60 years old. The implanted eyes exhibited 3.5 diopters of defocus range above 20/40, with 363 (87.1%) of 417 patients and 391 (93.8%) of 417 patients having 20/40 or better monocular and binocular uncorrected near visual acuity (UNVA) at 36 months, respectively. Patients implanted via a femtosecond laser pocket procedure using a spot/line setting of 6 μm × 6 μm demonstrated further improved near vision, with 131 (90.3%) of 145 patients and 137 (94.5%) of 145 of patients having 20/40 or better monocular and binocular UNVA, respectively. Uncorrected distance visual acuity 20/25 or better was maintained in 135 (93.1%) of 145 of implanted eyes and 100% (145) of 145 of implanted eyes binocularly at 36 months. Less than 1.5% of eyes had a loss of 2 or more lines of corrected distance visual acuity for 3 months or more at any time after surgery. Forty-four inlays (8.7%) were removed from the full cohort over 3 years. The removal rate was significantly less in the 6 × 6 pocket group (3.0% for visual complaints) and further reduced with deeper implantation (0%). Less than 1.0% of the patients reported severe glare or halos postoperatively.

Conclusion: The small-aperture corneal inlay was found to be safe and effective, improving near vision both monocularly and binocularly with minimal effect on distance visual acuity.

J Cataract Refract Surg 2018; ■:■–■

The loss of accommodation and associated loss of near vision is a universal condition that is part of the normal aging process. Presbyopia is generally associated with substantial negative effect on vision-related quality of life.

The Kamra small-aperture corneal inlay (Acufocus, Inc.) is implanted intrastromally in a corneal pocket in the nondominant eye of phakic patients for the correction of presbyopia. The inlay design is based on the well-established concept of small-aperture optics. Depth of focus is increased by reducing aperture size: the smaller the aperture, the greater the depth of focus at the image plane and the greater the depth of field at the object plane (object of regard). The opaque annulus of the small-aperture corneal inlay effectively reduces the aperture of the eye to 1.6 mm to improve near vision by narrowing the retinal blur circle, thereby providing an increased depth of focus in the implanted eye without significantly affecting unaided distance vision in the implanted eye or binocularity.

This paper provides the results of a prospective nonrandomized multicenter open-label single-arm 36-month United States Investigational Device Exemption (IDE) clinical trial.[A,B] The clinical trial evaluated the effectiveness and safety of the small-aperture corneal inlay. This U.S. IDE clinical trial was performed both in the U.S. and outside the U.S. under the same study protocol.

Submitted: October 30, 2017 | Final revision submitted: February 20, 2018 | Accepted: February 28, 2018

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0886-3350/$ - see frontmatter
https://doi.org/10.1016/j.jcrs.2018.02.023

PATIENTS AND METHODS

Patients at 24 clinical sites (15 U.S. and 9 non-U.S.) were implanted in the IDE study (1 additional patient was operated but not implanted because of a thin flap). The study was conducted in the U.S., England, Austria, Germany, Singapore, Philippines, New Zealand, and Australia. Patients provided informed consent before being screened for eligibility and participation in the study. Patients received free surgery and the study device and were modestly compensated for their participation time. The study was performed in accordance with the tenets of the Declaration of Helsinki and was approved by the institutional review board or the ethics committee of each respective investigational site. Contrast sensitivity, defocus curve, and visual field subgroups were predetermined before study initiation.

Patients eligible for inclusion in the clinical trial were emmetropic presbyopes between 45 years and 60 years of age with corrected distance visual acuity (CDVA) corrected to 20/20 in both eyes. The eye to be implanted had uncorrected near visual acuity (UNVA) between 20/40 and 20/100 and cycloplegic refractive spherical equivalent of +0.50 diopters (D) to −0.75 D with 0.75 D or less of refractive cylinder, and required a near correction of +1.00 D to +2.50 D of reading addition (add). The eye to be implanted had a minimum central corneal thickness (CCT) of 500 μm or more, corneal power of 41.00 D or more, and 47.00 D or less in all meridians and endothelial cell count of more than 2000 cells/mm^2. Key exclusion criteria included previous ocular surgery, anterior or posterior segment disease or degeneration, diagnosed diabetes or autoimmune disease, chronic use of systemic medications with significant ocular side effects, patients with latent hyperopia, history of steroid-responsive rise in intraocular pressure (IOP) or preoperative IOP over 21 mm Hg, and dry eyes as determined by the Schirmer test less than 10 mm or tear breakup time less than 10 seconds. The eye to be implanted was the nondominant eye based on motor dominance determined preoperatively. If equal between the 2 eyes, then sensory dominance was used to assess preoperative dominance.

The Kamra inlay (model ACI 7000PDT) is made from a biocompatible material, polyvinylidene difluoride,[1] impregnated with nanoparticles of carbon, and was proven to be stable in the eye.[2] The small-aperture corneal inlay has a 3.8 mm overall diameter, with a 1.6 mm central aperture, is approximately 6 μm thick, and has 8400 laser-drilled porosity holes to facilitate nutrient flow and waste transport. The holes vary in diameter between 5 μm and 11 μm and are arranged in a pseudorandom pattern to minimize diffractive aberrations. The light transmission through these microperforations is 5.4%. Figure 1 shows the appearance of the inlay from the anterior perspective.

The corneal inlay was implanted under a lamellar resection, either a corneal pocket created by a femtosecond laser (with a mask) using the same laser settings as for a standard laser in situ keratomileusis (LASIK) procedure or under a corneal flap created by a mechanical microkeratome. The majority (over 90%) of dissection diameters were between 9.2 mm and 9.5 mm in the corneal pockets while the remaining few pockets varied between 5.0 mm and 9.1 mm, which depended on the type of femtosecond laser being used. The dissection diameter ranged between 9.0 mm and 10.2 mm in corneal flaps. The target dissection depth was a minimum of 180 μm. The resultant pocket depth ranged between 185 μm and 270 μm: 79% of patients at or below 210 μm, 6% between 220 μm to 250 μm, and 15% at 270 μm. The small-aperture corneal inlay was centered on or close to the first Purkinje image. Patients followed a standardized regimen of postoperative topical ophthalmic medications, including 1 week use of antibiotic solution and 1 month tapered use of corticosteroids.

Clinical Measurements

Monocular and binocular uncorrected and corrected distance (6 m), intermediate (80 cm), and near (40 cm) visual acuities were measured in all patients using high-contrast back-lit Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity charts in the Optec 6500 Vision Tester (Stereo Optical Co, Inc.) and were recorded in letters. The spectacle correction for distance vision was determined with midpoint refraction (ie, the arithmetic average of the most plus lens and most minus lens through which CDVA is maintained). The midpoint refraction established the center of the range of clear vision in the eyes implanted with the small-aperture corneal inlay as a result of extended depth of focus.

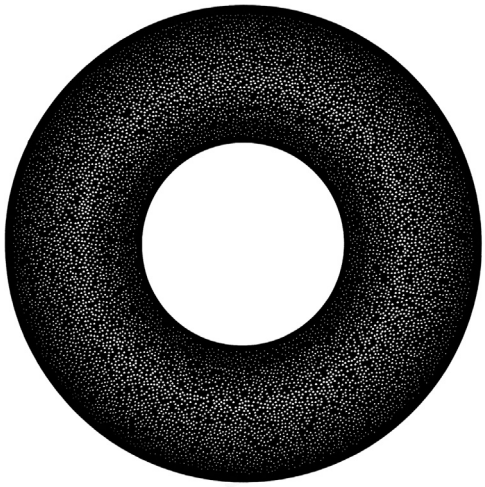

Figure 1. Image of the small-aperture corneal inlay.

Defocus curves for the predetermined subgroup were measured both preoperatively and at 12 months using a distance back-lit ETDRS visual acuity chart and the midpoint refraction as the starting point. Visual acuities were determined by adding plus and minus lenses to the midpoint refraction ranging from +5.00 to −5.00 D in 0.50 D steps.

Contrast sensitivity testing was performed in the predetermined subgroup preoperatively and postoperatively. Contrast sensitivity was measured monocularly and binocularly with the Optec 6500 Vision Tester using the Functional Acuity Contrast Test chart under photopic and mesopic conditions with and without glare. Threshold visual fields using the 24-2 paradigm on the Humphrey Visual Field (Carl Zeiss Meditec AG) was performed in a predetermined subgroup of patients preoperatively and at 12, 24, and 36 months. Specular microscopy was performed preoperatively and postoperatively to evaluate endothelial cell density (ECD) and morphology.

Subjective satisfaction and visual symptoms were assessed using a subjective questionnaire with a 7-point Likert scale. The 46-item questionnaire was administered preoperatively and at 3, 6, 12, 18, 24, 30, and 36 months postoperatively.

Statistical Analysis

Statistical analysis was performed using the JMP statistical package (version 11.2, SAS Institute, Inc.). Correlation tests were conducted using analysis of variance (ANOVA). Continuous parameters were compared with *t* tests. Categorical parameters were compared with Pearson chi-square tests. Logistic regression multivariate analyses were used to examine the possible effects of clinical parameters such as patient demographics, preoperative characteristics, surgical parameters, and clinical site. A *P* value less than 0.05 was considered statistically significant.

The safety analyses were based on the safety cohort of all available eyes. The effectiveness analyses were based on the effectiveness cohort that excluded data after several patients had inlay repositioning secondary surgical interventions during the study. The primary effectiveness outcome for the study was the percentage of eyes with a UNVA of 20/40 or better. The primary safety