Implantable Telescope Not Recommended for Approval, But There is Reason for Optimism

Despite significant visual acuity and quality of life gains, the FDA panel had concerns.

BY CONNI BERGMANN KOURY, EDITOR-IN-CHIEF

A US Food and Drug Administration (FDA) advisory panel found the Implantable Miniature Telescope (IMT) "not approvable" in July by a 10-to-3 vote.[1] The FDA Ophthalmic Devices Advisory Panel is an outside panel of experts that is called on to recommend if a device should be approved. Historically, the FDA usually follows the advice of the panel, although it is not required to do so. Ultimately, continuing dialogue with FDA will be necessary to get the investigational telescope prosthesis to an "approvable" form.

Manufactured by Visioncare Ophthalmic Technologies (Saratoga, Calif), the IMT was developed by Isaac Lipshitz, MD. It is designed for patients with bilateral visual impairment due to age-related macular degeneration (AMD), according to Visioncare. The device is designed to improve visual acuity by reducing scotoma size relative to objects in the central visual field (Figure 1).

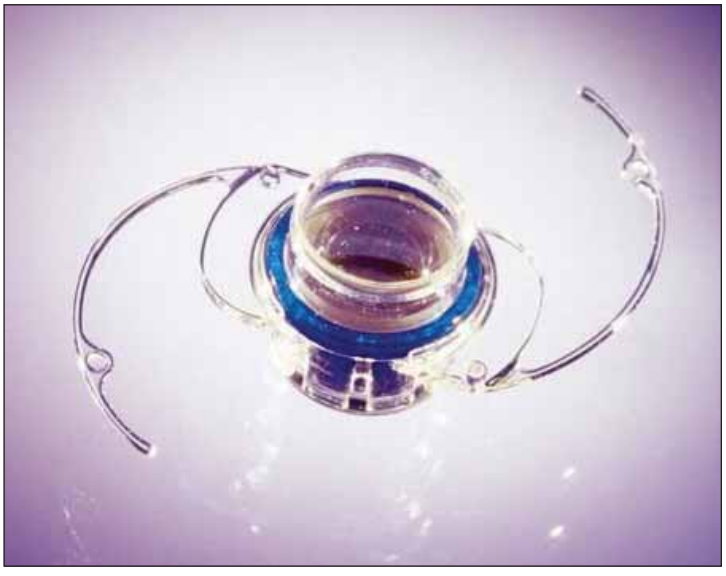

Figure 1. The IMT is in clinical trials for central vision loss due to AMD.

CLINICAL TRIAL

The company conducted a prospective multicenter clinical trial of 217 patients at 28 sites, according to FDA documents. The mean age of patients was 76 years, and the mean preoperative visual acuity was 20/316. The primary safety endpoint for the trial was the mean percentage of endothelial cell density loss ≤17% at 1-year post-IMT implantation. The secondary safety endpoint was preservation of BCVA — no more than 10% of implanted eyes were to experience a loss of more than two lines of either near or distance BCVA without a corresponding improvement in BCVA (gain of two lines or more).

The primary effectiveness endpoint for the study was defined as an improvement of two lines or greater in either near or distance BCVA in 50% of implanted eyes at 12 months postimplantation. Quality-of-life surveys and the National Eye Institute Visual Function Questionnaire were used as secondary measurements of efficacy.

Investigator R. Doyle Stulting, MD, PhD, said that 90%

of the patients included in the trial had profound or severe visual impairment at the beginning of the study, and they experienced positive improvements in quality of life postimplantation.

"It is not a perfect device that cures macular degeneration or even stops its progress," Dr. Stulting said in a Web cast of the panel meeting. But, the data support its approval under limited circumstances." Dr. Stulting is in the department of ophthalmology at Emory University.

RESULTS NOW PUBLISHED

The results of the trial have also now been published in *Ophthalmology*.[2] "This is truly a breakthrough because it is the first clinical trial to show the potential for improved vision and quality of life specifically in patients with bilateral, irreversible AMD," said Henry L. Hudson, MD, lead author of the study and a retina specialist at Retina Centers, PC, in Tucson. "From an efficacy standpoint we hoped that half of this study population with untreatable forms of AMD could achieve at least a two-line visual acuity gain. The results surpassed our expectations because 90% achieved the efficacy endpoint, and, furthermore, over two-thirds of our patients improved by at least three lines and one-quarter improved by at least five lines in distance vision."

At 1 year after implantation, 67% of patients achieved a three-line or greater improvement in their study eye distance visual acuity, compared with 13% of unimplanted fellow eye controls. Approximately 25% of telescope-implanted eyes achieved a five line or greater improvement in visual acuity compared with 2% of fellow eyes. Loss of three lines or more was encountered in 1.6% of implanted eyes compared with 3.1% of fellow eyes, according to the report in *Ophthalmology*.

ENDOTHELIAL CELL DENSITY

One-year postimplantation, mean endothelial cell density had decreased 25.3% in the eyes that received the IMT, and 90.1% of the implanted eyes had an improvement of two lines or better in either near or distance BCVA. Ten patients had a loss in either distance or near visual acuity and eight patients had their devices removed.

In the 10-to-3 nonapprovable vote, the panel said, "The data did not provide reasonable assurance that the device is safe and effective under the conditions of use prescribed, recommended or suggested in the proposed labeling."

Panel member Neil M. Bressler, MD, who made the motion to not approve the device, said his decision was specifically due to the 20% endothelial cell loss seen in the first 3 months after implantation. Dr. Bressler is the James P. Gills Professor of Ophthalmology at the Wilmer Eye Institute of Johns Hopkins University.

According to the FDA document, the panel decision was based on unresolved safety concerns, in addition to uncertainty regarding the efficacy of the device. The panel said the absence of morphometric analysis of the endothelial cell density data did not allow them to adequately evaluate the chronic rate of endothelial cell density loss in eyes that received the prosthesis, a major safety concern for this device. Confounding factors may have influenced the efficacy of the IMT, the panel members added.

> Despite endothelial cell loss from surgery, the investigators believe that corneal health was maintained.

"Despite endothelial cell loss from surgery, we believe that corneal health was maintained," said Stephen S. Lane, MD, the trial's medical monitor who is an adjunct professor ophthalmology, University of Minnesota and in private practice at Associated Eye Care, Stillwater, Minn. "There was a significant correlation between the postoperative cell loss and the level of corneal edema on the first postoperative day. Therefore, it appears that the majority of cell loss was due to the impact of the surgical procedure. Stabilization of cell density 3 to 12 months after surgery was consistent with what we would expect after large-incision intraocular surgery. While the techniques required to implant the device are well within the skills et of anterior segment surgeons, a surgeon training program will be utilized to address the risk of acute endothelial cell density loss during implant."

DATA ALREADY EXISTS

Panel member Michael Grimmett, MD, said, "We need to know whether the endothelial loss is due to remodeling or whether the endothelial loss is due to a chronically stressed endothelium due to the IMT device." Dr. Grimmett is assistant professor of ophthalmology at the Bascom Palmer Eye Institute of the University of Miami School of Medicine. He continued: "Endothelial cell migration that is remodeling occurs after surgical trauma to the eye. It can occur for prolonged periods. With remodeling, the coefficient of

variation and percent hexagonality return to baseline levels do not show progressive deterioration. On the other hand, an unstable or chronically stressed endothelium will have abnormal morphometric values that do not return to baseline. Morphometric data are a more sensitive indicator of endothelial health than central endothelial cell density measurements alone."

According to Chet Kumar, director of business and market development for Visioncare, although the FDA did not request morphometric data before the panel meeting, that data is available from existing trial specular microscopy photos. This is why, in his closing remarks at the end of the panel meeting, Dr. Grimmett said, "My primary concern is with safety, and if the sponsor produces sufficient data, which they should be able to easily do, then I believe that it could be approvable with conditions. I don't really have an effectiveness gripe at this point."

> Morphometric data is available from existing trial specular microscopy photos.

PERMANENT IMPLANT

The prosthetic telescope implant is intended to be a permanent solution for vision loss due to AMD in a subpopulation of patients with bilateral disciform scars or geographic atrophy, and in whom no other medical treatments are available, according to Mr. Kumar. It is implanted in the posterior chamber of the eye in place of the crystalline lens and is held in position by haptic loops. The telephoto system enlarges images 2.2 or 3 times, depending on the device model. The telephoto effect allows images in the central visual field to not focus directly on the damaged macula, but over other healthy areas of the central and peripheral retina. Generally, this helps reduce the blind spot impairing vision in patients with AMD, hopefully improving their ability to recognize images that were either difficult or impossible to see.

The IMT is implanted in one eye to provide central vision, while the nonimplanted eye provides peripheral vision for mobility and navigation. After the surgical procedure, the patient participates in a structured vision rehabilitation program to maximize their ability to perform daily activities. Situated in the eye, the device allows patients to use natural eye movements to scan the environment and reading materials.

TEAM APPROACH FOR PATIENTS

Assuming the morphometric data analyses demonstrate corneal stability for long-term corneal health, retina specialists should prepare to understand the multidisciplinary approach required to manage this AMD subpopulation. Dr. Hudson said that patient expectations play a crucial role in whether or not they are good candidates for the device.

The investigators have now developed a team approach in response to the evolution of the device. "The very first patients to be implanted in the phase 1 study had a different device which offered a smaller field of view and really had no preoperative evaluation beyond whether they could anatomically tolerate the telescope," Dr. Hudson said in an interview with RETINA TODAY. The researchers determined that there was a degree of patient dissatisfaction with that early version of the implant that was unacceptable. The device in the phase 2/3 study included wide-angle microoptics that doubled the patients' field of view in the implanted eye.

"In the pivotal study we performed a preoperative evaluation, we had a telescopic refraction that had proved that the patient had to improve with the telescope in the lane, and the patient was sent home with a practice telescope. At the time we really did not understand too much about the value of a preoperative assessment by a low-vision specialist and getting a feel for what the patient expects following the surgery."

There are several reasons for patient dissatisfaction following the procedure, Dr. Hudson explained, such as unreasonable expectations, expectations that are not compatible with the device's capabilities, false motivations or motivations that are dependent upon another family member, as well as patients who are anatomically not good candidates.

"Now we have created a more advanced version of a the multidisciplinary approach. This will include a low-vision evaluation by a low-vision occupational therapist. The other members of the team include a low-vision optometrist, the implanting surgeon, the retina physician and a clinical coordinator. The clinical coordinator's job will be to ask a lot of questions and administer a survey. In combining the survey and these multiple assessments, we will have a better idea of who is a good potential candidate. We also have an external telescopic simulator, which will enable the patients to get more of an idea of what it is like to have a telescope in the eye.

"Let us not deny hope to the one group who has been deemed hopeless — up until now — it would be a disservice to our community," Dr. Hudson said. ■

1. Panel Meeting Summary - July 14, 2006 Meeting of the Ophthalmic Devices Panel. Accessed at www.fda.gov/cdrh/panel/summary/ophthsum071406.html.
2. Hudson HL, Lane SS, Heier JS, et al for the IMT-002 Study Group. Implantable miniature telescope for the treatment of visual acuity loss resulting from end-stage age-related macular degeneration. *Ophthalmology.* 2006;113:1987-2001.