AN INSIDE LOOK AT INNOVATIONS IN OPHTHALMOLOGY

Innovation JOURNAL CLUB

Innovation Journal Club **explores recently published and presented data around innovations in eye care with a focus on how they might shape real-world practice.**

In the *Innovation Journal Club* (*IJC*) series on *Eyetube.net*, host I. Paul Singh, MD, of The Eye Centers of Racine & Kenosha in Wisconsin, interviews leading experts from across eye care subspecialties about emerging innovations and technologies that may prove influential to the real-world practice of ophthalmology. The series is editorially independent (supported by advertising from multiple companies), which allows the discussions to be broad in scope and candid in presentation.

The following is a summary of three episodes in which Dr. Singh sat down with Nandini Venkateswaran, MD, to talk about exciting new treatments during keratoplasty surgery with fibroblast-derived growth factors; took a deep dive into the latest workshop report from the Tear Film and Ocular Surface Society (TFOS) with Christopher E. Starr, MD; and explored the expanding options for treating dry eye disease with John Hovanesian, MD.

THE POTENTIAL OF FIBROBLAST GROWTH FACTORS IN CORNEAL DISEASE

WITH NANDINI VENKATESWARAN, MD

Innovation in ophthalmology has brought forth new tools for treating an array of eye diseases. Historically, research into newer therapeutics for diseases affecting the front and back surfaces of the cornea has taken time, but that may begin to change in the next few years as current pipeline products progress through their development cycle.

An area of research attracting attention in corneal disease is the potential for creating therapies that target fibroblast growth factors (FGF), which are ubiquitous throughout the body and are involved in myriad biologic processes. Specifically, FGF1 has attracted interest due to its role in protecting and healing endothelial and epithelial cells of the cornea.

One company, Trefoil Therapeutics, has been developing an engineered form of FGF1 (TTHX1114) that has entered into in-human studies with an intracameral injection at the time of Descemet stripping only (DSO) procedures in patients with Fuchs endothelial cell dystrophy. In the STORM 2 trial, a phase 2 study, the control group received DSO alone. Group 2 underwent DSO after a priming dose of TTHX1114 that was delivered 3 days before the procedure, and then these patients received 4 weekly doses, given at the time of the procedure and for 3 weeks thereafter. Group 3 underwent DSO along with one high dose of TTHX1114 dosed at the time of the procedure. Group 4 received DSO plus a dose of TTHX1114 at the time of the procedure, then three subsequent weekly doses.

"The outcomes of the phase 2 STORM study (Figure 1) showed an accelerated improvement of vision and a resolution of corneal edema in response to the injection of the synthetic FGF1," said Dr. Venkateswaran. She found it interesting that Group 3 had the most successful outcomes in the trial: gains in visual acuity at about 28 days post-injection and post-procedure, with continued improvement over the course of 2 months. This healing time was perhaps a little faster than with traditional DSO alone, but still longer than recovery times with DMEK.

Furthermore, 46% of the enrolled patients underwent cataract surgery concurrently with DSO, and the investigators found no difference in these patients' recovery compared to those who received DSO only, and no differences in their pachymetry readings. Dr. Venkateswaran was encouraged by these findings. "Clinically, the potential of TTHX1114 is very relevant, because DSO is not always an isolated procedure in a pseudophakic patient," she said. "Many of us

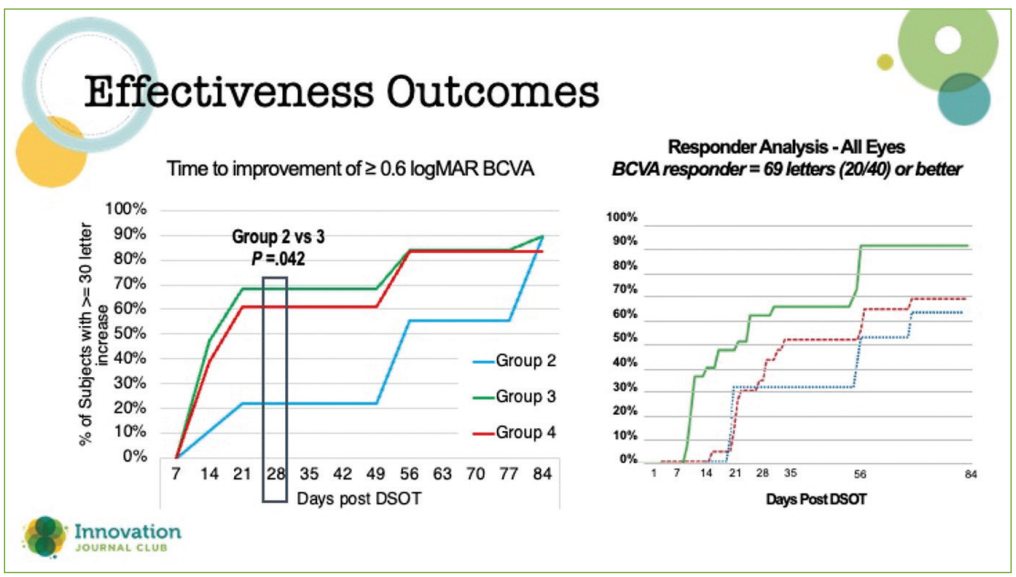

Figure 1. Effectiveness outcomes with TTHX1114 in the Storm 2 clinical trial.

are doing DSO at the time of cataract surgery, too. If we are able to accelerate healing time after cataract surgery in patients with endothelial disease such as Fuchs dystrophy, that's important."

Dr. Venkateswaran stressed that the STORM studies are still ongoing, with data still needed on the long-term safety and efficacy profile of TTHX1114. Still, she sees its potential as an adjunctive therapy to traditional corneal surgeries. Although she prefers DMEK because of its expedited recovery for patients, there are some people who simply don't do well with EK. "The compliance with drops, the positioning, the long-term effects of graft failure—graft longevity is limited, especially in eyes that have had multiple surgeries. If I can offer these patients DSO, plus start the process of endothelial recovery with a synthetic FGF1, maybe we can now have a more viable transplant-less option. It might open up that door for more patients."

NANDINI VENKATESWARAN, MD
- Assistant Professor of Ophthalmology, Harvard Medical School, Boston
- Cataract, cornea, and refractive surgeon, Massachusetts Eye and Ear, Lexington
- Member, *CRST* Editorial Advisory Board
- nandini.venkat89@gmail.com; X (formerly Twitter) @nandinivenkatmd
- Financial disclosure: No relevant disclosures

A VALUABLE DRY EYE EDUCATION TOOL FOR CLINICIANS AND PATIENTS: THE TFOS LIFESTYLE REPORT

WITH CHRISTOPHER E. STARR, MD

The multifactorial nature of ocular surface disease continues to present challenges for eye care practitioners who want effective management strategies for their patients. With so many factors contributing to DED—environmental, lifestyle, nutritional, hormonal, pharmacological, etc.—physicians need evidence-based data to guide their patients in making or breaking daily habits that can ease or exacerbate their condition. "Ocular surface disease is so complex, it almost warrants its own subspecialty," Christopher E. Starr, MD, told Dr. Singh.

> **"Ocular surface disease is so complex, it almost warrants its own subspecialty,"**
> **– Christopher E. Starr, MD**

Dr. Starr is a global ambassador and US affiliate for the Tear Film and Ocular Surface Society (TFOS), a nonprofit organization that facilitates research and education on ocular health. The organization's most recent series of publications, "A Lifestyle Epidemic: Ocular Surface Disease," focuses on lifestyle behaviors that have been shown in research to contribute to ocular surface disease.[1] These behaviors include digital eye strain, the use of cosmetics, nutritional deficiencies, contact lens use, and others. "The task here was to look at all the evidence-based literature published over the past 10 years relating to decisions that patients make on a daily basis that can impact the health of their eyes and ocular surfaces, such as cosmetics, nutrition, and digital screen usage," explained Dr. Starr. This undertaking required 158 noted researchers and experts from 38 countries, as well as a subcommittee to evaluate the quality of the evidence that would be used in the report.

One subcommittee explored the impact that watching/reading screens and devices has on the ocular surface. Notably, they advocated for using the term *digital eye strain* to describe the "development or exacerbation of recurrent ocular symptoms and/or signs related specifically to digital device screen viewing."[1] In a separate part of the report, the committee reviewed results of an analysis of treatment options for digital eye strain. Interestingly, Dr. Starr noted, the literature review revealed that supplementation with omega-3 essential fatty acids is one of the best ways to combat the symptoms of digital eye strain. Glasses that block blue light, on the other hand, had no measurable effect.

Cosmetic products were the focus of another of the lifestyle subcommittees. In this largely unregulated industry, patients need to be informed and screen labels for ingredients such as formaldehyde (a known carcinogen), BAK, parabens, and other toxins, which may be present at levels many times higher than what has been proven to be damaging to the ocular surface.

FUTURE OF THE TFOS AND OCULAR SURFACE DISEASE TREATMENT

Dr. Starr noted that recruitment is already underway for the TFOS DEWS III report. Additionally, he is excited for the recent proliferation in pharmacologic DED treatment options that have come to market this year alone. These include MIEBO (perfluorohexyloctane ophthalmic solution; Bausch + Lomb), with no preservatives and no inactive ingredients, and a new product to treat *Demodex* blepharitis, lotilaner ophthalmic solution 0.25% (XDEMVY; Tarsus Pharmaceuticals). "There is so much going on in this field that, 10 years from now, I would expect the dry eye literature to double or triple again," said Dr. Starr. "The role of the TFOS is to evaluate high-quality, evidence-based research to cut through marketing and hyperbole, and that's why I'm very proud to be a part of it."

1. Craig JP, Alves M, Wolffsohn JS, et al. TFOS Lifestyle Report Executive Summary: A Lifestyle Epidemic - Ocular Surface Disease. *Ocul Surf*. 2023;30:240–253.

CHRISTOPHER E. STARR, MD
- Associate Professor of Ophthalmology, Director of Refractive Surgery, and Director of Ophthalmic Education, Weill Cornell Medicine, New York-Presbyterian Hospital, New York
- Member, *CRST* Editorial Advisory Board
- cestarr@med.cornell.edu; www.StarrMD.com
- Financial disclosure: None

INNOVATIONS IN DRY EYE: USE OF AMNIOTIC MEMBRANES AND A NEW OPTION FOR MGD-ASSOCIATED DRY EYE

WITH JOHN HOVANESIAN, MD

Ocular surface disease is well known to be a major cause of visual disability. While an array of options are available for treatment, there always seems to be a place for more, especially when they fulfill persisting unmet needs.

In an episode where they explored the expanding options for treating dry eye disease (DED), John Hovanesian, MD, and Dr. Singh stressed the importance of identifying and treating ocular surface disease in any patient, but particularly for those exploring surgical options, be they cataract or refractive.

"It's a must-treat condition—if we don't address it, it will cause problems with the outcome," Dr. Hovanesian said.

AMNIOTIC MEMBRANE FOR SEVERE DED

Amniotic membranes are typically thought of in the context of treating chronically symptomatic ocular surface disease, such as herpes simplex and neurotrophic keratopathy, where the surface doesn't heal despite advanced treatments. However, according to a study by McDonald et al, they may have utility in refractory DED cases in which other treatments have failed.[1] In the study, outcomes from 94 eyes of 84 patients from 10 clinical sites with severe DED treated with a cryopreserved amniotic membrane (CAM) were retrospectively reviewed. The affected eyes received a CAM for 5.4±2.8 days, and they were followed for 3 months. Clinical manifestations and comorbidities were common among eyes in the study, including superficial punctate keratitis (86%), filamentary keratitis (13%), exposure keratitis (19%), neurotrophic keratitis (2%), and corneal epithelial defect (7%).The study's primary outcome was the change in patients' dry eye workshop (DEWS) scores following the treatment (Figure 2).

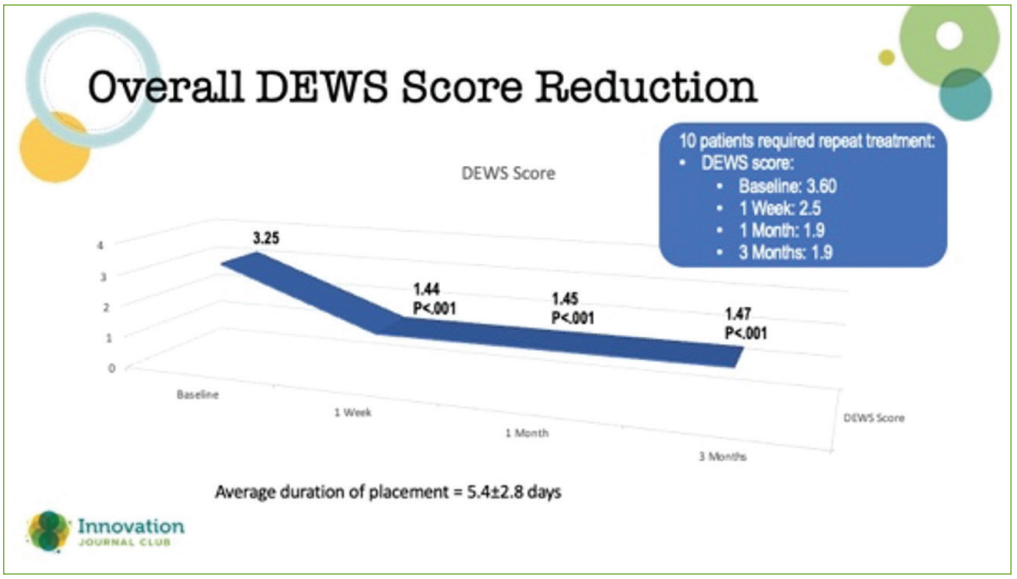

Figure 2. Reduction in DEWS score out to 3 months after use of an amniotic membrane for the treatment of refractory dry eye disease.

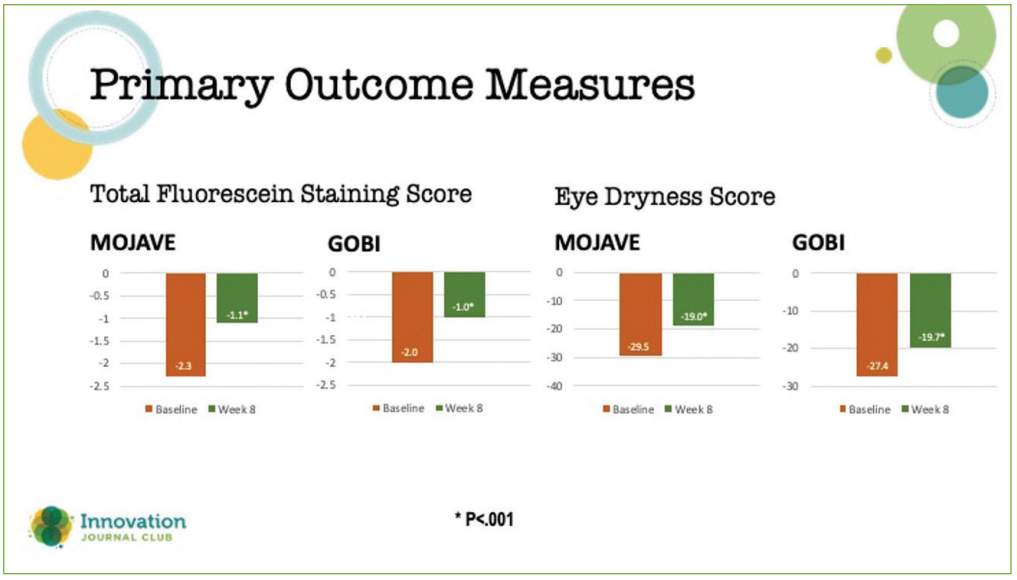

Figure 3. Primary outcome measures in the two phase 3 studies on MIEBO.

Dr. Hovanesian said that it was impressive that the effects of the CAM treatment did not wane in 3 months. He added that amniotic membranes can be used more than once if a patient's corneas start to regress over time. Typically, these membranes are left on the eye for a few weeks to promote healing.

"The anti-inflammatory property is not just healing the cells that are defective, it's keeping them healed. It keeps the ocular surface in a homeostatic state for quite a long time," Dr. Hovanesian said.

Dr. Singh commented that, when it comes to treating DED, symptomatology drives his decision-making. Dr. Hovanesian agreed, adding that one of the most telling symptoms for him is intermittent blurring: "Often, this symptom indicates a problem with the ocular surface," he said.

MIEBO: AN UNPRESERVED, NO-VEHICLE TOPICAL DROP TO TREAT MGD-ASSOCIATED DED

Dr. Hovanesian and Dr. Singh next discussed MIEBO (perfluorohexyloctane ophthalmic solution; formerly known as NOV03), the new preservative-free treatment from Bausch + Lomb that is indicated for the signs and symptoms of DED associated with meibomian gland dysfunction (MGD). MIEBO works by reducing tear evaporation from the ocular surface. "Evaporation happens because there's no hydrophobic layer to prevent evaporation of the aqueous, and the mucin layer becomes diminished when there's a disruption in the aqueous layer," Dr. Hovanesian explained.

He described how MIEBO's FDA approval stemmed from two 57-day, multicenter, randomized, double-masked, saline-controlled studies, GOBI and MOJAVE,[2,3] wherein investigators randomized more than 1,200 patients with a history of DED and clinical signs of MGD to receive either perfluorohexyloctane or hypotonic saline. "This was well-done science," said Dr. Hovanesian.

There were two primary endpoints in these studies: (1) a change from baseline in total corneal fluorescein staining (tCFS) at 8 weeks, and (2) patients' ocular dryness scoring on the Visual Analog Scale (VAS). Results from both studies showed that relief of patients' symptoms began as early as day 15 and continued through day 57, plus a significant reduction in dryness scores on the VAS (Figure 3).

Dr. Hovanesian stressed that perfluorohexyloctane is a highly dispersive compound with both hydrophillic and lipiphillic components that form a monolayer over the eye. The molecule requires a very small drop size: 15–20 microliters compared to the 50-microliter size of a typical topical eye drop. "I'm excited, because this is an entirely different kind of approach to dry eye."

He was also impressed with MIEBO's safety profile. "We saw a very low rate of adverse events of blepharitis, about 1.6%. And in the phase 3 GOBI study, we saw a 9.6% rate of AEs compared to 7.5% with the saline group."[2,3] In his own practice, Dr. Hovanesian said that his patients' tolerability of MIEBO has been excellent.

In conclusion, Dr. Hovanesian said that, although some DED patients will continue to need immunomodulators and anti-inflammatories because of their different mechanisms of action, there will be some individuals for whom MIEBO could replace these treatments, and be better tolerated. ■

1. McDonald MB, Sheha H, Tighe S, et al. Treatment outcomes in the DRy Eye Amniotic Membrane (DREAM) study. *Clin Ophthalmol.* 2018;12:677–681.
2. Tauber J, Berdy GJ, Wirta DL, et al. NOV03 for dry eye disease associated with meibomian gland dysfunction: results of the randomized phase 3 GOBI study. *Ophthalmology*. 2023;130(5):516–524.
3. Sheppard J, Kurata F, Epitropoulos AT, et al. NOV03 for signs and symptoms of dry eye disease associated with meibomian gland dysfunction: the randomized phase 3 Mojave study. *Am J Ophthalmol.* 2023;252:265–274.

JOHN HOVANESIAN, MD
- Private practice, Harvard Eye Associates, Laguna Hills, California
- Clinical Instructor, Jules Stein Eye Institute, University of California, Los Angeles
- Founder, MDbackline
- Member, *CRST* Editorial Advisory Board
- drhovanesian@harvardeye.com; X (formerly Twitter) @DrHovanesian
- Financial disclosure: Consultant or investor (Alcon, Bausch + Lomb, Carl Zeiss Meditec, Johnson & Johnson Vision)