AN INSIDE LOOK AT INNOVATIONS IN OPHTHALMOLOGY

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* 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 Darrell E. White, MD, to talk about how treating vitreous floaters can have a meaningful impact on patients' quality of life; with Leonard K. Seibold, MD, to discuss new and emerging options in MIGS; and with Laura Periman, MD, to discuss new understandings in the prevalence of *Demodex* blepharitis and the evolution in treatment.

HOW TO ADDRESS VITREOUS FLOATERS

WITH DARRELL E. WHITE, MD

For years, Dr. White listened to patients in his office describe how vitreous floaters affected their quality of vision, but without a treatment he believed in, there didn't seem much he could do. Adopting laser vitreolysis, though, changed his mindset—making him more attuned to just how severely floaters affected not only vision, but quality of life more generally.

"It doesn't matter how big or how small we think [the floaters are]," said Dr. White, "the impact on them is the only thing that matters." Dr. Singh agreed, adding that too often the definition of "clinically significant" is tied to the availability of treatment options, rather than accurately reflecting a patient's daily experience.

Before integrating Nd:YAG laser treatments for floaters, Dr. White says that he would base his determination of treatment necessity on the size and location of the floaters. Now, he lets the patient drive the conversation. "I'm not voting so much on the size of the floater," he explains. "I'm listening very hard to the patient as they tell me the size of them. And it totally changes the conversation."

Dr. Singh pointed to a 2022 single-center study by García et al[1] in which the authors examined the quality-of-life aspect of patients' outcomes after they underwent laser vitreolysis for floaters. The results of this study showed a significant reduction in the subjects' anxiety and marked improvement in the answers on the VFQ-25 and VFQ-39 Visual Function Questionnaires that preceded treatment. Dr. White said while he was not particularly surprised by the overall findings, those pertaining to anxiety were interesting. "We don't think about something like this being an anxiety trigger," he said.

Dr. White described his three criteria for treating vitreous floaters with the Nd:YAG laser: (1) they must cause enough interference in the patient's day-to-day life to warrant intervention; (2) they should be visible enough to determine if it will absorb the laser's energy; and (3) they have to be located far enough in front of the retina and behind the lens to be lasered safely, although in pseudophakic eyes, the margin of safety is a little wider. He generally performs the procedure at some point after having done a capsulotomy, and he tells patients to expect it to last between 4 and 8 minutes. Often, he can eliminate the floater in a single session.

Dr. Singh concluded the conversation by stressing how important it is not to ignore patients' complaints about perceived floaters now that vitreolysis is available. Dr. White agreed and pointed out that the procedure's learning curve is minimal. "Anybody who can do a YAG [laser capsulotomy] can do a YAG vitreolysis. If nobody in your area does it, there's no reason why you couldn't, or shouldn't." He acknowledged that the treatment has enabled him to improve patients' lives to a degree he did not anticipate. "It's much more impactful than I expected."

1. García BG, Orduna Magán C, Alvarez-Peregrina C, et al. Nd:YAG laser vitreolysis and health-related quality of life in patients with symptomatic vitreous floaters. *Eur J Ophthalmol*. 2021:11206721211008036.

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NEW AND NEXT IN MIGS

WITH LEONARD K. SEIBOLD, MD

Dr. Singh invited Dr. Seibold to talk about new and emerging options in the MIGS space: one targeting outflow in and beyond the trabecular meshwork (TM), and a new take on directing outflow to the subconjunctival space.

What is the Streamline Surgical System?

The concept of flushing the TM, canal of Schlemm, and adjacent anatomy with OVD, or viscodilation, has grown in popularity in recent years because surgeons have a better understanding of how complex the aqueous drainage pathway actually is. Although the TM is the most typical site of obstruction in primary-open glaucoma, blockades at other sites may inhibit outflow. Viscodilation

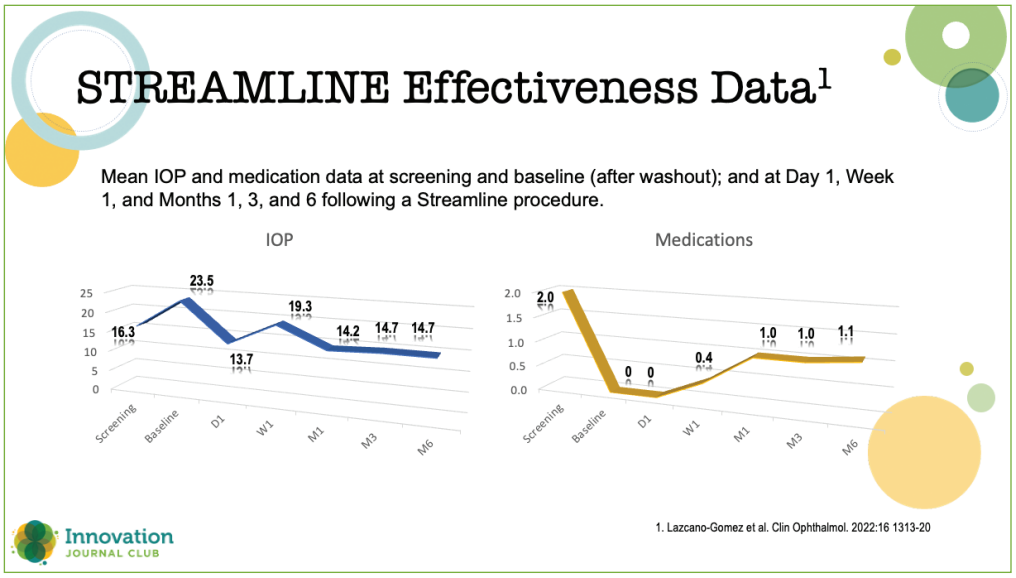

Figure 1. Results from an interim analysis of an ongoing prospective, nonrandomized, open-label, interventional, first-in-human case series of Streamline.

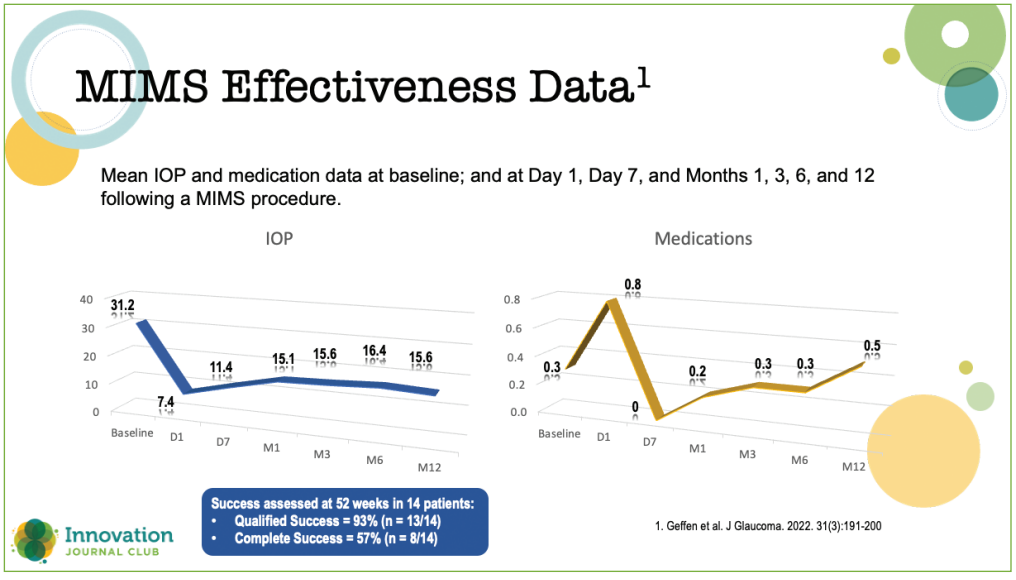

Figure 2. Results from a prospective, open-label clinical trial of patients undergoing MIMS or MIMS plus cataract surgery.

provides a means to open up herniations and blockages, even without knowing the exact location of collector channels.

Dr. Seibold has been using the Streamline Surgical System (New World Medical, Inc.) since its FDA approval more than a year ago. The device is designed to perform a 150-µm goniotomy and deliver OVD in a single step, thereby opening a drainage pathway, stretching open the TM, and flushing the canal and distal collector channels. The treatment can be titrated, as it can be performed up to eight times across the nasal angle. As well, the surgeon can extend the goniotomies by using the cannula to create a linear goniotomy for a few clock hours.

These features add tremendous versatility, yet the device is also very minimally traumatic to the ocular tissues, according to Dr. Seibold. Early evidence suggests a role for the procedure in treating mild and early glaucoma, although recent evidence has demonstrated a benefit in more advanced cases.

Lazcano-Gomez and colleagues recently reported an interim analysis of an ongoing prospective, nonrandomized, open-label, interventional, first-in-human case series to characterize the safety and IOP-lowering effectiveness of incisional goniotomies and canal of Schlemm viscodilation in patients with mild to severe POAG undergoing cataract surgery."[1] At the 6-month readout, about 90% of patients achieved more than a 20% reduction in IOP, and over 40% were free of medication (Figure 1).

"The mean medication use fell in half," Dr. Seibold said, "with 40% or a little bit more achieving medication-free status. This is really important. These are the home runs we want to hit with our patients with MIGS."

MINIMALLY INVASIVE MICRO SCLEROSTOMY

When it comes to unguarded filtration surgery, glaucoma surgeons would not be wholly unjustified in responding with a "been there, done that" mindset. However, minimally invasive micro sclerostomy (MIMS), being developed by Sanoculis, Ltd., because it is performed via an *ab interno* approach, may be a viable option for effecting subconjunctival drainage without leaving an implant in place and without opening conjunctiva like traditional incisional glaucoma surgeries.

"With MIMS, we also don't have to worry about implant placement," Dr. Seibold said.

The surgery is performed with a disposable handpiece that creates a precise and repeatable 100-µm microsclerotomy from an *ab interno* approach. Then, the surgeon advances a small trephine into the sclera to extract a plug of tissue and create a fistula pathway into the subconjunctival space. The energy delivery is controlled via a footpedal.

Geffen et al published results of a prospective, open-label clinical trial of a MIMS procedure performed by a single surgeon in Chennai, India (Figure 2).[2] Adults with uncontrolled open-angle glaucoma underwent either phacoemulsification plus MIMS (n = 21) or MIMS alone (n = 10). The criteria for success included a post-procedure IOP ≥ 5 mm Hg and ≤ 18 mm Hg; a reduction in IOP of > 20% compared with baseline; and no need for filtration surgery at 12 and 24 weeks after surgery.

The authors reported no intraoperative complications, serious adverse events, or device malfunctions; however, five patients

(16.12%) experienced iris clogging of the internal ostium between 1 and 24 weeks following the procedure: two were treated with a laser iris retraction and thereafter maintained a stable IOP, and three required a trabeculectomy and were considered surgical failures.

"I think there was a little bit of AC shallowing, and that allowed the iris to adhere to that sclerotomy and occlude it," Dr. Seibold said. "[The authors] presented a number of different ways to prevent this, [including] some good suggestions on using a miotic agent like pilocarpine and leaving viscoelastic in the eye, which I think makes a lot of sense."

Although he does not have personal experience with the procedure, Dr. Seibold said he will be monitoring clinical trials with the technique for answers to some lingering questions: "How do these patients behave early postoperatively? Can we leave a little viscoelastic? I think we can manage those things, and this could potentially be a nice option for patients who maybe want to stay away from a stent … [or who] have thin conjunctiva. I think this would give us a nice alternative."

1. Lazcano-Gomez G, Garg SJ, Yeu E, Kahook MY. Interim analysis of STREAMLINE® Surgical System clinical outcomes in eyes with glaucoma. *Clin Ophthalmol*. 2022;16(4):1313-1320.
2. Geffen N, Kumar DA, Barayev E, et al. Minimally invasive micro sclerostomy (MIMS) procedure: a novel glaucoma filtration procedure. *J Glaucoma*. 2021;31(3):191-200.

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INNOVATIONS IN DEMODEX BLEPHARITIS

WITH LAURA PERIMAN, MD

Demodex blepharitis is more prevalent than previously thought, and yet it is still dramatically underdiagnosed in real-world ophthalmology patients, according to a recent multicenter study of consecutive patients undergoing slit-lamp exams.[1] However, a new treatment option, lotilaner ophthalmic solution, 0.25% (Tarsus), which is currently being reviewed for approval by the US FDA, has demonstrated impressive results in clinical trials and stands poised to significantly alter how the common lid margin disease is managed.

"Blepharitis is sort of the bane of our clinical experience," Dr. Periman explained. "Every specialty in ophthalmology deals with it on a daily basis—or ignores it on a daily basis. And to be fair, we haven't had super effective strategies for addressing blepharitis. But we're starting to get things in our toolkit that make treating blepharitis more precise and effective."

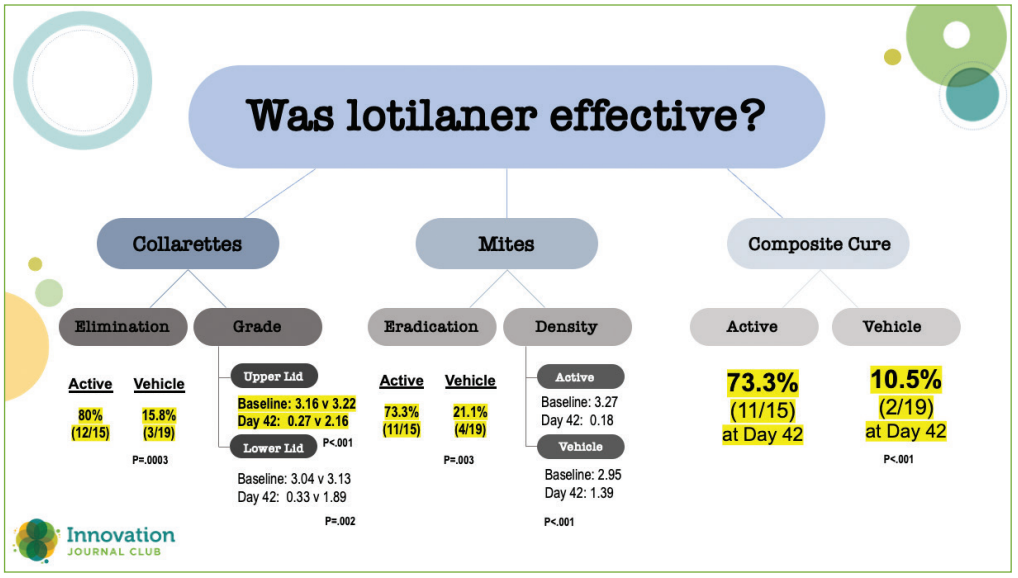

Figure 3. Results from a 54-patient randomized, controlled, double-masked clinical trial comparing lotilaner ophthalmic solution, 0.25% and vehicle.

MULTICENTER STUDY DEMONSTRATES PREVALENCE OF DEMODEX BLEPHARITIS

In a study involving seven investigators at six clinics, consecutive patients undergoing slit-lamp examinations were reviewed for *Demodex* blepharitis by the presence of collarettes.[1] Of the 1,032 patients enrolled in the study, 57.7% were found to have *Demodex* blepharitis, but the investigators also found evidence that its prevalence may be higher in the general population. Perhaps unsurprisingly, 44% of patients with collarettes had not previously been diagnosed with blepharitis, suggesting that degree of symptom bother is a less accurate depiction of disease burden compared to the pathognomonic sign of collarette presence.

According to the study, the prevalence of collarettes was higher in select subgroups: patients with a known diagnosis of blepharitis (69.1%) and those with glaucoma (64.8%). Furthermore, although 64.8% were diagnosed with collarettes during an annual eye examination, 60.8% were diagnosed during an exam for glaucoma, 59.9% during a cataract evaluation, and 53.5% during a dry eye evaluation.

As part of the screening protocol for the study, patients were asked whether they were currently using tea tree oil. Of those who answered yes, 74.5% were eventually diagnosed with blepharitis; of those who answered no, 56.7% were ultimately diagnosed with blepharitis.

"The temptation is to say, well, tea tree oil doesn't work, but maybe these patients are self-selecting due to more severe symptoms, looking for different relief and are trying different products that contain tea tree oil," Dr. Periman said.

NEW TREATMENT OPTION

As is the case with many ophthalmic conditions, when viable treatments come to the clinic, specialists' awareness of the disease tends to heighten. According to Dr. Periman, upon looking at the data from clinical trials involving lotilaner ophthalmic

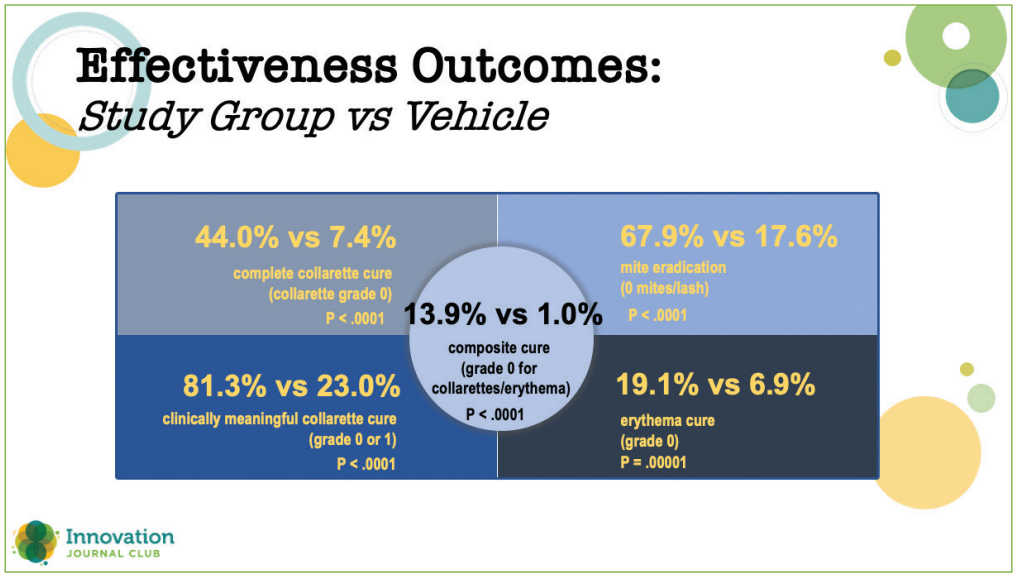

Figure 4. In the phase 3 Saturn-1 study, all outcomes were statistically significantly higher at day 43 for patients treated with topical lotilaner ophthalmic solution, 0.25% compared to vehicle.

solution, 0.25%, it is not hard to see why eye care providers who deal with a lot of lid margin disease are very excited about how it may change clinical practice.

In a randomized, controlled, double-masked clinical trial, 54 patients with *Demodex* blepharitis were randomized 1:1 to topical lotilaner ophthalmic solution, 0.25%, or vehicle.[2] At the topline, all outcomes were statistically significantly higher at day 42 for patients treated with topical lotilaner ophthalmic solution, 0.25%, dosed BID compared to vehicle. A closer look at the numbers, however, shows just how effective lotilaner was in eliminating collarettes, eradicating mites, clearing erythema, and achieving a statistically significantly higher rate of composite cure (73.3% vs 10.5% in vehicle; *P*<.001) (Figure 3).

While those results were impressive, Dr. Periman said the real proof of lotilaner's effectiveness is in the 421-patient phase 3 Saturn-1 trial that compared lotilaner to vehicle at BID dosing. As with the other study, all outcomes were statistically significantly higher for lotilander versus vehicle (Figure 4). What was slightly unprecedented, though, was the degree of separation between the two study arms.

"There are so few ocular surface disease treatment options that we have, procedure-based or drop-based, that have this kind of crazy-good data. I don't know if I've seen this before in ocular surface disease," Dr. Singh said.

Dr. Periman agreed: "When we look from a 30,000-foot view of how frustrating ocular surface disease can be for our colleagues and for patients alike, one of the reasons for that is we haven't had targeted and specific, strategic therapeutics to address very common contributors. Turns out, *Demodex* blepharitis is involved in about 60% of your MGD cases. To have an eyedrop that is a 6-week course, that has an 81% clinically meaningful cure, is a very straightforward, time efficient, positively reinforcing approach for these ocular surface disease patients." ■

1. Trattler W, Karpecki P, Rapoport Y, et al. The prevalence of Demodex blepharitis in US eye care clinic patients as determined by collarettes: a pathognomonic sign. *Clin Ophthalmol*. 2022;16:1153-1164.
2. Yeu E, Holdbrook M, Baba SN, et al. Treatment of Demodex blepharitis: a prospective, randomized, controlled, double-masked clinical trial comparing topical lotilaner ophthalmic solution, 0.25% eyedrops to vehicle. *Ocul Immunol Inflamm*. 2022:1-9.
3. Yeu E, Wirta DL, Karpecki Pet al; Saturn I Study Group. Lotilaner ophthalmic solution, 0.25%, for the treatment of demodex blepharitis: results of a prospective, randomized, vehicle-controlled, double-masked, pivotal trial (Saturn-1). *Cornea*. 2023;42(4):435-443.

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