Glaucoma Management: The case for preserving trabeculectomy, *p. 51*

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Also inside

VABYSMO™
faricimab-svoa injection 6 mg

WHERE 2 WORLDS MEET

The First and Only Dual-Pathway Inhibitor in Retinal Disease[1-5]

VABYSMO Is the First IVT Injection Approved for Q4W-Q16W Dosing Intervals in nAMD and DME[1-4]*

Image not intended to be a patient portrayal.

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INDICATIONS

VABYSMO (faricimab-svoa) is a vascular endothelial growth factor (VEGF) inhibitor and angiopoietin-2 (Ang-2) inhibitor indicated for the treatment of patients with Neovascular (Wet) Age-Related Macular Degeneration (nAMD) and Diabetic Macular Edema (DME).

IMPORTANT SAFETY INFORMATION

Contraindications

VABYSMO is contraindicated in patients with ocular or periocular inflammation, in patients with active intraocular inflammation, and in patients with known hypersensitivity to faricimab or any of the excipients in VABYSMO.

Warnings and Precautions

- Endophthalmitis and retinal detachments may occur following intravitreal injections. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management.
- Increases in intraocular pressure have been seen within 60 minutes of an intravitreal injection.
- There is a potential risk of arterial thromboembolic events (ATEs) associated with VEGF inhibition.

Adverse Reactions

The most common adverse reaction (≥5%) reported in patients receiving VABYSMO was conjunctival hemorrhage (7%).

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

Please see Brief Summary of VABYSMO full Prescribing Information on the following page.

*Dosing Information:

In nAMD, the recommended dose for VABYSMO is 6 mg (0.05 mL of 120 mg/mL solution) IVT Q4W for the first 4 doses, followed by OCT and visual acuity evaluations 8 and 12 weeks later to inform whether to extend to: 1) Q16W (weeks 28 and 44); 2) Q12W (weeks 24, 36, and 48); or 3) Q8W (weeks 20, 28, 36, and 44).

In DME, the recommended dose for VABYSMO is 6 mg (0.05 mL of 120 mg/mL solution) IVT Q4W for ≥4 doses until CST is ≤325 µm (by OCT), followed by treat-and-extend dosing with 4-week interval extensions or 4- to 8-week interval reductions based on CST and visual acuity evaluations through week 52. Alternatively, VABYSMO can be administered IVT Q4W for the first 6 doses, followed by Q8W dosing over the next 28 weeks.

Although VABYSMO may be dosed as frequently as Q4W, additional efficacy was not demonstrated in most patients when VABYSMO was dosed Q4W vs Q8W. Some patients may need Q4W dosing after the first 4 doses. Patients should be assessed regularly and the dosing regimen reevaluated after the first year.

CST=central subfield thickness; IVT=intravitreal; OCT=optical coherence tomography; Q4W=every 4 weeks; Q8W=every 8 weeks; Q12W=every 12 weeks; Q16W=every 16 weeks.

References: 1. VABYSMO [package insert]. South San Francisco, CA: Genentech, Inc; 2022. **2.** Beovu® (brolucizumab) [package insert]. East Hanover, NJ: Novartis; 2020. **3.** Eylea® (aflibercept) [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc; 2021. **4.** LUCENTIS® (ranibizumab) [package insert]. South San Francisco, CA: Genentech, Inc; 2018. **5.** SUSVIMO™ (ranibizumab injection) [package insert]. South San Francisco, CA: Genentech, Inc; 2022.

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VABYSMO™
faricimab-svoa injection 6 mg

VABYSMO™ (faricimab-svoa) injection, for intravitreal use

This is a brief summary. Before prescribing, please refer to the full Prescribing Information

1 INDICATIONS AND USAGE

VABYSMO is a vascular endothelial growth factor (VEGF) and angiopoietin 2 (Ang-2) inhibitor indicated for the treatment of patients with:

1.1 Neovascular (wet) Age-Related Macular Degeneration (nAMD)

1.2 Diabetic Macular Edema (DME)

4 CONTRAINDICATIONS

4.1 Ocular or Periocular Infections

VABYSMO is contraindicated in patients with ocular or periocular infections.

4.2 Active Intraocular Inflammation

VABYSMO is contraindicated in patients with active intraocular inflammation.

4.3 Hypersensitivity

VABYSMO is contraindicated in patients with known hypersensitivity to faricimab or any of the excipients in VABYSMO. Hypersensitivity reactions may manifest as rash, pruritus, urticaria, erythema, or severe intraocular inflammation.

5 WARNINGS AND PRECAUTIONS

5.1 Endophthalmitis and Retinal Detachments

Intravitreal injections have been associated with endophthalmitis and retinal detachments *[see Adverse Reactions (6.1)]*. Proper aseptic injection techniques must always be used when administering VABYSMO. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management *[see Dosage and Administration (2.6) and Patient Counseling Information (17)]*.

5.2 Increase in Intraocular Pressure

Transient increases in intraocular pressure (IOP) have been seen within 60 minutes of intravitreal injection, including with VABYSMO *[see Adverse Reactions (6.1)]*. IOP and the perfusion of the optic nerve head should be monitored and managed appropriately *[see Dosage and Administration (2.6)]*.

5.3 Thromboembolic Events

Although there was a low rate of arterial thromboembolic events (ATEs) observed in the VABYSMO clinical trials, there is a potential risk of ATEs following intravitreal use of VEGF inhibitors. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause).

The incidence of reported ATEs in the nAMD studies during the first year was 1% (7 out of 664) in patients treated with VABYSMO compared with 1% (6 out of 662) in patients treated with aflibercept *[see Clinical Studies (14.1)]*.

The incidence of reported ATEs in the DME studies during the first year was 2% (25 out of 1,262) in patients treated with VABYSMO compared with 2% (14 out of 625) in patients treated with aflibercept *[see Clinical Studies (14.2)]*.

6 ADVERSE REACTIONS

The following potentially serious adverse reactions are described elsewhere in the labeling:

- Hypersensitivity *[see Contraindications (4)]*
- Endophthalmitis and retinal detachments *[see Warnings and Precautions (5.1)]*
- Increase in intraocular pressure *[see Warnings and Precautions (5.2)]*
- Thromboembolic events *[see Warnings and Precautions (5.3)]*

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in other clinical trials of the same or another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to VABYSMO in 1,926 patients, which constituted the safety population in four Phase 3 studies *[see Clinical Studies (14.1, 14.2)]*.

Table 1: Common Adverse Reactions (≥ 1%)

Adverse Reactions	VABYSMO		Active Control (aflibercept)	
	AMD N=664	DME N=1262	AMD N=622	DME N=625
Conjunctival hemorrhage	7%	7%	8%	6%
Vitreous floaters	3%	3%	2%	2%
Retinal pigment epithelial tear[a]	3%		1%	
Intraocular pressure increased	3%	3%	2%	2%
Eye pain	3%	2%	3%	3%
Intraocular inflammation[b]	2%	1%	1%	1%
Eye irritation	1%	1%	< 1%	1%
Ocular discomfort	1%	1%	< 1%	< 1%
Vitreous hemorrhage	< 1%	1%	1%	< 1%

[a]AMD only
[b]Including iridocyclitis, iritis, uveitis, vitritis

Less common adverse reactions reported in < 1% of the patients treated with VABYSMO were corneal abrasion, eye pruritus, lacrimation increased, ocular hyperemia, blurred vision, eye irritation, sensation of foreign body, endophthalmitis, visual acuity reduced transiently, retinal tear and rhegmatogenous retinal detachment.

6.2 Immunogenicity

The immunogenicity of VABYSMO was evaluated in plasma samples. The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to VABYSMO in immunoassays. The detection of an immune response is highly dependent on the sensitivity and specificity of the assays used, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to VABYSMO with the incidence of antibodies to other products may be misleading.

There is a potential for an immune response in patients treated with VABYSMO. In the nAMD and DME studies, the pre-treatment incidence of anti-faricimab antibodies was approximately 1.8% and 0.8%, respectively. After initiation of dosing, anti-faricimab antibodies were detected in approximately 10.4% and 8.4% of patients with nAMD and DME respectively, treated with VABYSMO across studies and across treatment groups. As with all therapeutic proteins, there is a potential for immunogenicity with VABYSMO.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of VABYSMO administration in pregnant women.

Administration of VABYSMO to pregnant monkeys throughout the period of organogenesis resulted in an increased incidence of abortions at intravenous (IV) doses 158 times the human exposure (based on C_{max}) of the maximum recommended human dose *[see Animal Data]*. Based on the mechanism of action of VEGF and Ang-2 inhibitors, there is a potential risk to female reproductive capacity, and to embryo-fetal development. VABYSMO should not be used during pregnancy unless the potential benefit to the patient outweighs the potential risk to the fetus.

All pregnancies have a background risk of birth defect, loss, and other adverse outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects is 2%-4% and of miscarriage is 15%-20% of clinically recognized pregnancies.

Data

Animal Data

An embryo fetal developmental toxicity study was performed on pregnant cynomolgus monkeys. Pregnant animals received 5 weekly IV injections of VABYSMO starting on day 20 of gestation at 1 or 3 mg/kg. A non-dose dependent increase in pregnancy loss (abortions) was observed at both doses evaluated. Serum exposure (C_{max}) in pregnant monkeys at the low dose of 1 mg/kg was 158 times the human exposure at the maximum recommended intravitreal dose of 6 mg once every 4 weeks. A no observed adverse effect level (NOAEL) was not identified in this study.

8.2 Lactation

Risk Summary

There is no information regarding the presence of faricimab in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. Many drugs are transferred in human milk with the potential for absorption and adverse reactions in the breastfed child.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for VABYSMO and any potential adverse effects on the breastfed child from VABYSMO.

8.3 Females and Males of Reproductive Potential

Contraception

Females of reproductive potential are advised to use effective contraception prior to the initial dose, during treatment and for at least 3 months following the last dose of VABYSMO.

Infertility

No studies on the effects of faricimab on human fertility have been conducted and it is not known whether faricimab can affect reproduction capacity. Based on the mechanism of action, treatment with VABYSMO may pose a risk to reproductive capacity.

8.4 Pediatric Use

The safety and efficacy of VABYSMO in pediatric patients have not been established.

8.5 Geriatric Use

In the four clinical studies, approximately 60% (1,149/1,929) of patients randomized to treatment with VABYSMO were ≥ 65 years of age. No significant differences in efficacy or safety of faricimab were seen with increasing age in these studies. No dose adjustment is required in patients 65 years and above.

17 PATIENT COUNSELING INFORMATION

Advise patients that in the days following VABYSMO administration, patients are at risk of developing endophthalmitis. If the eye becomes red, sensitive to light, painful, or develops a change in vision, advise the patient to seek immediate care from an ophthalmologist *[see Warnings and Precautions (5)]*.

Patients may experience temporary visual disturbances after an intravitreal injection with VABYSMO and the associated eye examinations *[see Adverse Reactions (6)]*. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

VABYSMO™ [faricimab-svoa]
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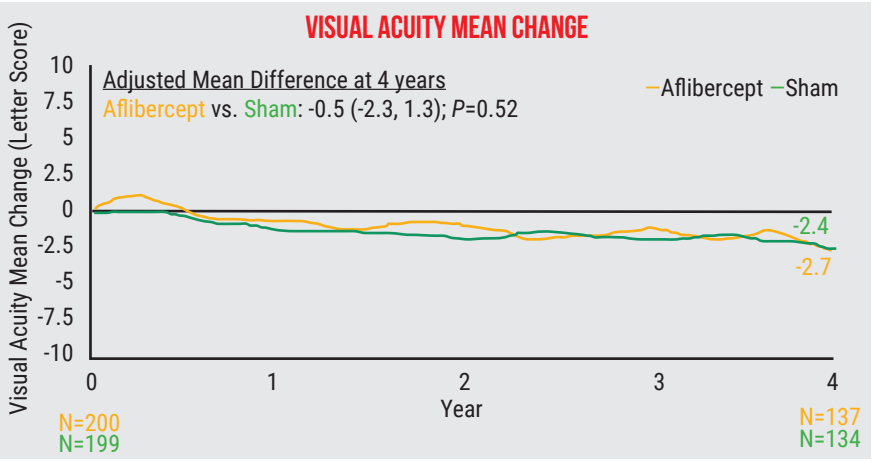
Early Anti-VEGF Treatment Doesn't Improve VA in DR

The four-year findings from the NEI-supported Protocol W clinical trial show that early treatment of non-proliferative diabetic retinopathy with anti-VEGF agents confers no visual acuity benefit in the long term.[1]

Protocol chair Raj Maturi, MD, of Indiana University School of Medicine and Retina Partners Midwest, explains that "monitoring patients for signs of disease progression, such as vision loss, retinal edema and neovascularization, and treating only as needed once complications develop is the best course of action."

In the study, 328 patients (399 eyes) were randomized to 2-mg aflibercept injections or sham injections. During the first two years, eight injections were administered at one month, two months, four months and every four months. Injections were then continued quarterly through year four unless the eye improved to mild disease. Eyes in either group that developed vision-threatening complications were treated with additional anti-VEGF as necessary.

The cumulative probability of developing proliferative diabetic retinopathy or center-involved diabetic macular edema was 33.9 percent in the treatment group and 56.9 percent in the sham group ($p<0.001$). The visual acuity change from baseline to four years wasn't significant, with a mean change of -2.7 ±6.5 letters in the treatment group and -2.4 ±5.8 letters in the sham group ($p=0.52$).



At the start of the study, the researchers had hypothesized that early injections would have a protective effect on moderate and severe non-proliferative diabetic retinopathy, but the four-year results showed that almost one-third of eyes still developed complications despite early treatment and saw no significant functional vision gains.

"Treating prophylactically doesn't cause significant harm, but we found that holding off on treatment until disease worsening resulted in a reduction in the average number of injections," Dr. Maturi says. "There was an average of 13 injections in the early-treatment group and just 3.5 injections in the group that waited until worsening. This study demonstrated that there's no difference in visual acuity whether we wait or not, but there is a substantial difference in treatment burden.

"By treating early, we increase the number of injections given to patients and therefore increase the patient burden, cost, and risk of injection related complications," he continues. "We want to decrease this number. An average injection of aflibercept costs around $2,000. A difference of 10 injections, as we saw in our study, is almost $20,000 per patient, on average, over four years.

Does early treatment ever make sense for certain patients? "Prophylactic treatment will slow some disease progression, but it won't change many of the aspects we worry about such as nonperfusion," Dr. Maturi says. "Anti-VEGF treatment for diabetic retinopathy is a long-term commitment. Some patients may

(Continued on p. 8)

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(Continued from p. 4)

Early NPDR Treatment

be okay with that and want a treatment that will keep the disease from progressing. That's up to them. Many doctors feel that way too. But many of us also look for an endpoint, and one of those endpoints may be that we treat with injections only to prevent bleeding and vision loss. So, if we treat patients when their situation is more advanced, we also prevent it from happening, in a way. Many others, however, wish to decrease treatment burden for patients and now have very clear evidence that waiting until the disease progresses is not going to compromise their patient's visual acuity.

"It may make sense to treat poorly compliant patients prophylactically but, unfortunately, the protection offered by early treatment goes away if the patient isn't treated regularly," he continues. "So, it'll delay worsening but if the patient doesn't return for follow-up, they'll still progress to worsening retinopathy."

Dr. Maturi adds that the compliance data in the study points to a need for improving loss-to-follow-up. "We worked hard to ensure patients came back in this study," he says. "We had a research coordinator follow up with patients, reimbursed patients for their time and travel, and other things of that nature. Even with that, at the end of four years, we had a follow-up rate of only around 80 percent. So, 20 percent of patients—one in five—couldn't come for follow-up in a study where we were really pushing them to come back. Looking at data from large datasets, we see that diabetic patients, unfortunately, will often miss those follow-up exams due to various socio-economic factors. Treating patients with more permanent solutions is an important area of development. We have to do more to minimize treatment burden so patients can maintain visual function."

Ultimately, Dr. Maturi says that it's crucial to monitor diabetic retinopathy carefully and treat patients as soon as they meet high-risk criteria for proliferative diabetic retinopathy as well as diabetic macular edema with vision loss—which is a two-line loss of vision with associated macular thickening. "Initiating therapy when patients reach those thresholds for diabetic macular edema and proliferative diabetic retinopathy is just as safe as treating early," he says.

Dr. Maturi is a consultant for Allegro, Allergan, Allgenesis, Eli Lilly, Dutch Ophthalmic, Novartis, neurotech and Jaeb Center for Health Research. He receives research support from Allergan, Genentech, Ophthea, Kalvista, Samsung Bioepies, Graybug, Santen, Thromobgenics, Gyroscope, Gemini, Boehringer Ingelheim, Allegro, Senju, Ribomic, NGM biopharmaceuticals, Unity, Graybug and Clearside. He's also the Safety Committee Chair of Aiviv.

1. Maturi RK, Glassman AR, Josic K, et al. Four-year visual outcomes in the Protocol W randomized trial of intravitreous aflibercept for prevention of vision-threatening complications of diabetic retinopathy. JAMA 2023;329:5:376-385.

Apellis' Syfovre Approved for Geographic Atrophy

Retina specialists will soon be able to treat patients with geographic atrophy in hopes of mitigating the loss of retinal cells and subsequent visual impairment that often develops in those with dry AMD. In February, the FDA approved the use of pegcetacoplan, a C3 inhibitor, from Apellis Pharmaceuticals for this indication. It will be marketed under the brand name Syfovre and will be priced at $2,190 per vial, the company announced.

In an investor call, Chief Medical Officer Caroline Baumal, MD, estimated that patients will need six to eight vials of Syfovre per year. A program called ApellisAssist will provide insurance support, financial assistance and disease education for eligible patients, the company said in the release.

Syfovre is approved for GA patients with or without subfoveal involvement and should be administered every 25 to 60 days, a flexible dosing schedule that should help patients and doctors alike maintain therapy over the long haul, the company noted.

Patients need to commit to an extended course of therapy to experience the drug's benefits. "This isn't a drug that flips the switch on day one," Apellis CEO Cedric Francois, MD, PhD, told Fierce Pharma in a recent interview. "It's a drug where you make an investment over many years, and where the longer you stick to the therapy, the better this drug is going to work for you."

In its FDA clinical trials (OAKS and DERBY), the drug "reduced the rate of GA lesion growth compared to sham and demonstrated increasing treatment effects over time, with the greatest benefit (up to 36 percent reduction in lesion growth with monthly treatment in DERBY) occurring between months 18 and 24," according to the press release. OAKS and DERBY subjects are currently participating in three-year extension trials to gauge the durability of treatment effect out to five years.

More than one million Americans have developed GA, Apellis says. The condition arises from the combined effects of genetic influencers, environmental stressors and the aging

(Continued on p. 16)

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*Low-dose OTC brimonidine. †Low-dose brimonidine is an α2-AR agonist that primarily constricts the venule. [1]McLaurin E, et. al. *Optom Vis Sci*. 2018;95(3):264-271. ‡In clinical trials, one case of rebound redness was reported. §In Home Use Test, March 2018. n=301.

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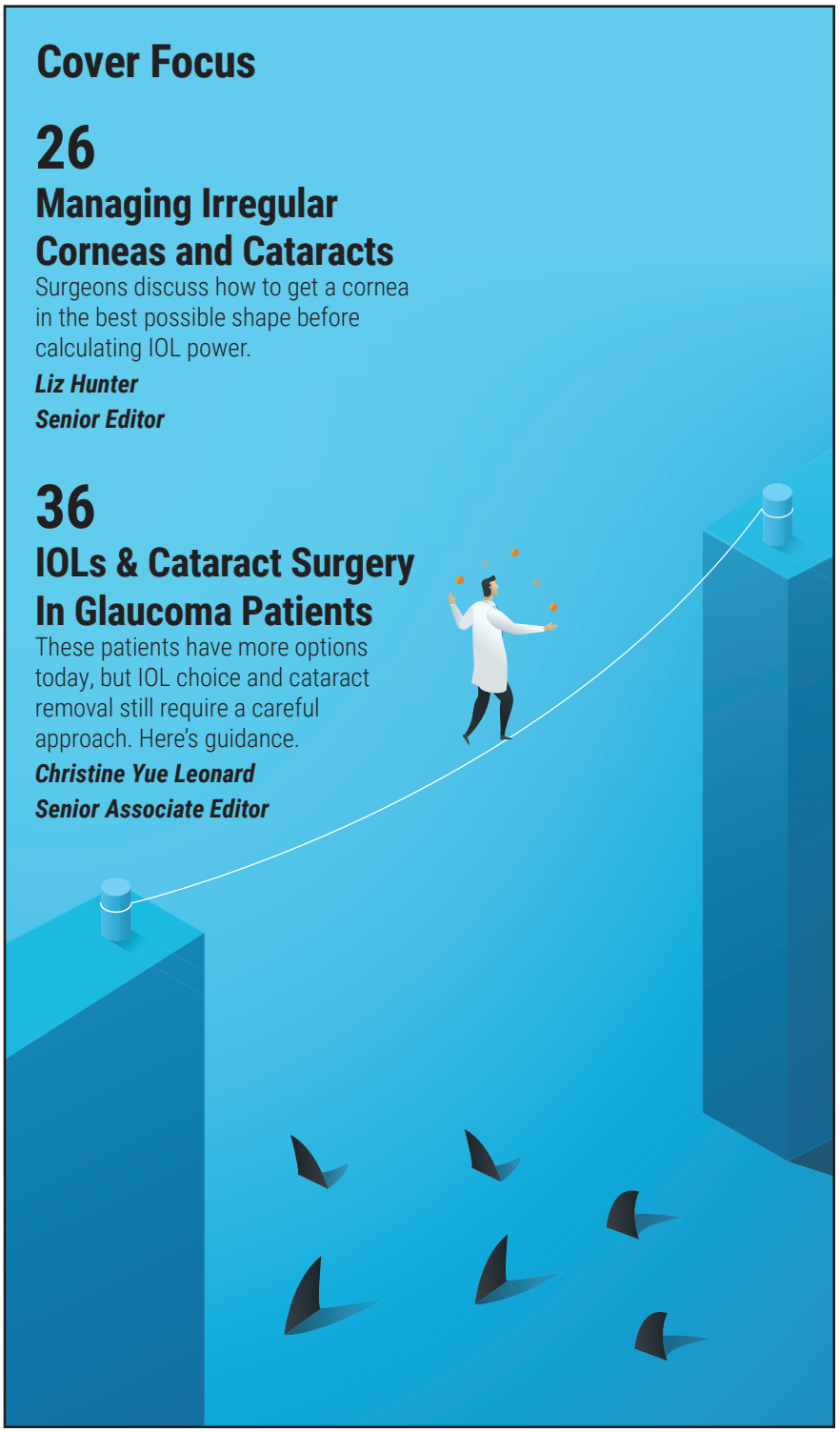

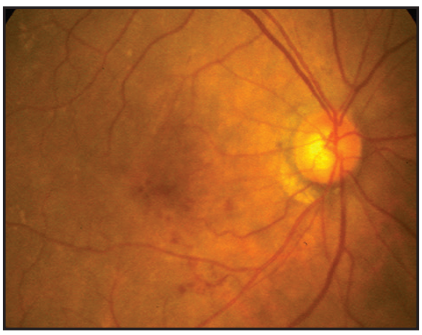

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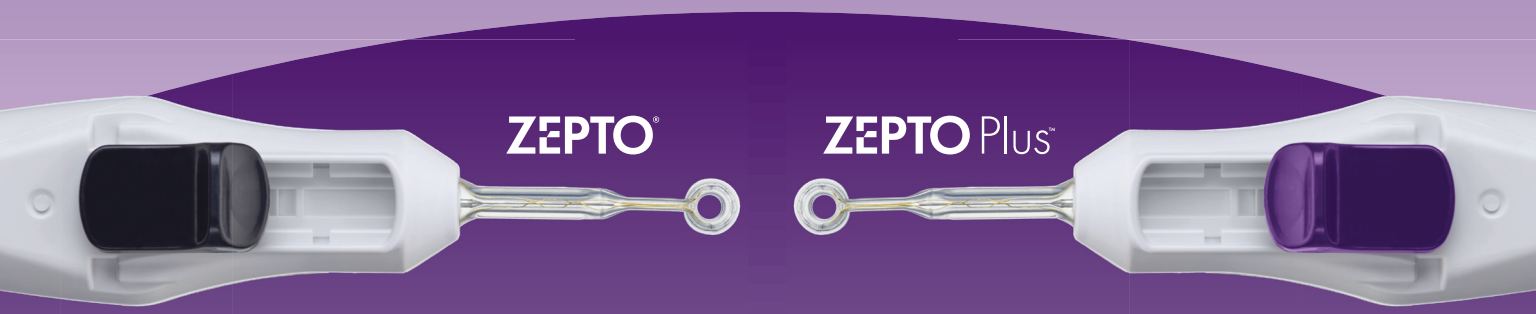

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EDITOR'S PAGE

Degree of Difficulty

Most people can manage a task when they're simply allowed to focus on the task itself, with no extenuating circumstances. For instance, for anyone who's done it for even just a couple of years, driving a car becomes an "overlearned" skill in which doing it precisely becomes almost second-nature (as anyone who's eaten a sandwich, changed the radio station and driven at the same time will tell you—not that I endorse such behavior).

However, change the driving environment from a sunny May day to an ice storm in January and suddenly the easy task of cruising down the boulevard becomes fraught with danger. You've now got multiple hazards to track: Limited visibility; other drivers; the road conditions. By some estimates, stopping distance can go from 60 feet on a dry road to as much as 600 feet when driving on ice. Your degree of difficulty just shot way up. (That sandwich can wait till you get home.)

Though much more complex than operating a car, cataract surgery is one of the most successful, effective surgeries known to medicine. Ophthalmologists have honed their skills to the point that both anatomical and visual results are uniformly excellent.

However, like driving on an icy road the addition of ocular co-morbidities can take a procedure that may have been routine and turn it into a much more challenging proposition. It's these challenging cases that surgeons discuss in two of our features this month.

In the first article (p. 26), both corneal specialists and expert cataract surgeons explain how to handle patients with co-existing corneal problems. These can range from the fairly garden-variety ocular surface disease to Fuchs' dystrophy and complex post-transplant eyes. The physicians provide valuable tips on such aspects as whether to proceed with sequential or simulataneous cornea and cataract procedures, and how to make sure you get the best IOL calculations in patients with irregular corneas.

In the other article exploring ocular co-morbidities and cataract surgery, experts tackle the question of how to get the best possible results—especially when it comes to selecting an intraocular lens—for patients with glaucoma. For surgeons who like to offer their patients the latest in presbyopia-correcting lenses, surgeons say the good news is that it's still possible, at least in some patients. "Patients who have ocular hypertension, glaucoma suspects or those with very mild, pre-perimetric glaucoma are going to be great candidates if they're also well-controlled and if their visual fields have very minimal peripheral defects," says Constance O. Okeke, MD, MSCE, of Norfolk, Virginia. "These are the patients you should consider pushing the envelope to offer them multifocals or extended depth of focus IOLs."

We hope the advice offered by the surgeons in this month's features helps you stay on course when the road gets rocky.

— Walter Bethke
Editor in Chief

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*Defined as modified Miyata grade 0, <25mv /mm^2 over 3 years (n=138), and over 9 years (n=20), respectively.

References: 1. Clareon® Vivity® Toric Directions for Use. **2**. Werner L, Thatthamla I, Ong M, et al. Evaluation of clarity characteristics in a new hydrophobic acrylic IOL. J Cataract Refract Surg. 2019;45:1490-1497. **3**. Oshika T, Fujita Y, Inamura M, Miyata K. Mid-term and long-term clinical assessments of a new 1-piece hydrophobic acrylic IOL with hydroxyethyl methacrylate. J Cataract Refract Surg. 2020 May;46(5):682-687. **4**. Maxwell A, Suryakumar R. Long-term effectiveness and safety of a three-piece acrylic hydrophobic intraocular lens modified with hydroxyethyl-methacrylate: an open-label, 3-year follow-up study. Clin Ophthalmol. 2018;12:2031-2037. **5**. Alcon Data on File, 2017. **6**. Lane S, Collins S, Das KK, Maass S, Thatthamla I, Schatz H, Van Noy S, Jain R. Evaluation of intraocular lens mechanical stability. J Cataract Refract Surg. 2019 Apr;45(4):501-506.

Alcon

REVIEW NEWS

(Continued from p. 8)

Syfovre Approved for GA

process. Central to the pathogenesis is the complement cascade, an immune response in which a protein compound called membrane attack complex is created, which then adheres to cells and causes lysis and cell death. Pegcetacoplan blocks the cleavage of complement protein C3 into C3a and C3b; the latter is an upstream precursor of membrane attack complex.

Apellis says that Syfovre availability will begin in March. For more information, visit https://syfovreecp.com.

Customized Cross-linking in Keratoconus

Upon evaluating the visual and tomographic results of customized crosslinking using excimer laser-assisted epithelium removal and topography-guided irradiation in the treatment of progressive keratoconus, researchers recently reported that one-year outcomes showed a significant improvement in visual acuity and stabilization of disease progression.

The prospective, non-randomized clinical trial enrolled 37 eyes of 32 patients with documented progressive keratoconus. Following de-epithelization with phototherapeutic keratectomy, customized UV irradiation was performed, designed as three concentric circular areas centered on the thinnest point. Energy exposure was 5.4 J/cm^2 in the outer circle and then increased centripetally to 7.2 J/cm^2 and 10 J/cm^2. Corrected distance visual acuity, refractive outcomes and Scheimpflug tomography were assessed at baseline and six and 12 months postoperatively.

Mean diameter for treated areas was 6.17 mm, 4.45 mm and 2.58 mm for the outer, medium and inner circle, respectively. At the one-year follow-up, mean CDVA improved significantly from 0.38 logMAR to 0.20 logMAR, with 92 percent of eyes retaining or improving CDVA. Mean preoperative minimum pachymetry decreased from 449.26 µm to 443.26 µm. The maximal curvature (Kmax) decreased significantly from 58.50 D to 57.05 D. After one year, 92 percent of eyes showed no signs of progression.

"The possibility to have a treatment alternative that's also capable of simultaneously improving the patient's vision provides us with a new therapeutic option and can help reduce the need for combined procedures for keratoconus," the study authors wrote in their paper. ◀

1. Gil JQ, Rosa AM, Costa AE, et al. Customized corneal crosslinking with excimer laser assisted epithelium removal for progressive keratoconus—one year results. J Cataract Refract Surg. February 13, 2023. [Epub ahead of print].

INDUSTRY NEWS

Alcon Settles Femto Litigation with J&J
Alcon entered into a settlement agreement with J&J Surgical Vision to resolve its pending legal proceedings relating to femtosecond laser-assisted cataract surgery devices. As part of the resolution, the parties exchanged cross-licenses of certain intellectual property and other mutually agreed upon covenants and releases, and Alcon will make a one-time payment to J&J Surgical Vision of $199 million for those rights and to resolve related worldwide intellectual property disputes.

FDA Accepts Ocuphire's New Drug Application
Ocuphire announced the FDA accepted the New Drug Application for Nyxol (phentolamine ophthalmic solution 0.75%) for the treatment of pharmacologically induced mydriasis.

Eylea Approved for ROP
Regeneron Pharmaceuticals received FDA approval of Eylea (aflibercept) Injection to treat preterm infants with retinopathy of prematurity.

We're willing to bet most eye care professionals don't realize just how prevalent *Demodex* blepharitis is.[1]

In fact, ~**25 million eye care** patients in the US may have *Demodex* blepharitis (DB).[2]

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References: 1. Data on file, Tarsus Pharmaceuticals, Inc. June 2022. **2.** O'Dell L et al. *Clin Ophthalmol.* 2022;16:2979-2987.

US--2200006 12/22

Tools to Lighten the Prior Authorization Load

Physicians and staff spend almost 13 hours per week on PAs, according to the AMA. Here are six tools that could help.

CHRISTINE YUE LEONARD
SENIOR ASSOCIATE EDITOR

Every practice has felt the strain of prior authorizations, from filing claims and fielding denials to waiting for approvals and negotiating with payers. According to the American Medical Association's 2021 physician survey, 93 percent of physicians reported care delays for their patients' treatments and 82 percent reported that prior authorization sometimes leads the patient to abandon their recommended treatment. These delays and complexities can have serious consequences: physicians also reported PA leading to serious adverse events, hospitalization, life-threatening events or permanent impairment, disability and congenital anomalies/birth defects or death.[1]

Both the AMA and the American Academy of Ophthalmology are working toward prior authorization reform in Medicare Advantage programs.[2-3] In the meantime, here are a few PA services and tools that may help to lift some of the burden from you and your practice.

What's Right for Your Practice?

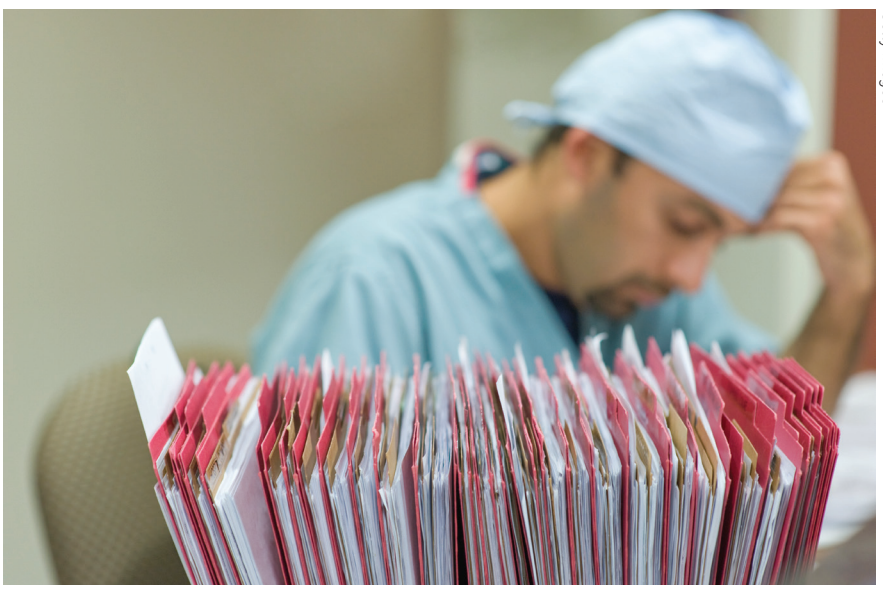
When each insurance company has its own definition of what's medically necessary or what counts toward step therapy, ensuring proper care for your patients can be a challenge. In some practices, it makes the most sense to assign a specific staff member or several to handle PAs. Many EHRs already have electronic PA filing systems, which can make this process simpler.

Other practices may want to look into outside help from PA tools or companies that specialize in PA. Many third-party outsourcing companies manage the PA process—reconciling different companies' requirements, forms, decisions; work with physicians and patients to obtain necessary information; and make appeals against denials.

As with any potential outsourced vendor, be sure to vet the company for security, transparency in reporting and good communication. Also be sure to find out what types of PA services they offer. Some are full-service and some are prescriptions-only, for example.

Prior Authorization Services

In many instances, outsourcing to companies that specialize in prior authorization can lead to



Getty Images

Prior authorization eats up a significant amount of time and money from a practice, in addition to sometimes delaying patient care. One option to alleviate this burden is to outsource the prior authorization process to a third-party company. Many full-service practice management companies take on the entire prior authorization process while some companies specialize in a single area, such as medications.

This article has no commercial sponsorship.

Dr. Colvard is a surgeon at the Colvard-Kandavel Eye Center in Los Angeles and a clinical professor of ophthalmology at the Keck School of Medicine of the University of Southern California. **Dr. Charles** is the founder of the Charles Retina Institute in Germantown, Tennessee.

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Here are a few companies that offer prior authorization services:

• ***Health Prime's Prime Authorization.*** This practice optimization company virtually obtains and processes PAs for the practice, with supplied documentation. Health Prime says its services reduce denials, save the practice time and money, minimize data errors and improve patient care. The company says it's HIPAA compliant and keeps up to date with changing government regulations to ensure compliance. For information, visit http://www.hpiinc.com.

• ***AthenaOne Authorization Management.*** Practice management company Athenahealth's PA specialists handle the PA process after the physician submits the order into the Athenahealth EHR. The company's Authorization Rules Engine checks all submitted orders against up-to-date payer requirements to determine whether PA is needed, and then begins the process when appropriate. The company says it provides clinical documentation submission, payer follow-up, end-to-end visibility and real-time processing. There's also a same- or next-day authorization option, where same-day authorizations are initiated within two hours of receipt. The company says 94 percent of urgent authorizations are completed within 48 hours. For information, visit http://www.athenahealth.com/solutions/authorization-management.

• ***Infinx.*** Infinx uses artificial intelligence and automation technology to speed up prior authorizations. The cloud-based software facilitates electronic requests. More complex requests and exceptions are handled by a team of specialists. The company provides real-time communication with automated follow-up bots that check requests under review for status change updates. Infinx says it provides complete coverage of PA requests with 98-percent accuracy and 99.5-percent adherence to turnaround times. Visit http://www.infinx.com/prior-authorization for more information.

Medication Prior Authorization

Timely medication prior authorization processing is an important aspect that can affect patient compliance.

Here are some companies that specialize in medication prior authorization:

> **In a 2021 AMA physician survey, 93 percent of physicians reported care delays for their patients' treatments and 82 reported that prior authorization sometimes leads patients to abandon their recommended treatment.**

• ***CoverMyMeds.*** This free online platform (part of McKesson) for physicians and pharmacists aids claims submissions using questions and prompts for filling out electronic PAs and guides practices and patients through automatic PA renewal. The tool is compliant with all ePA legislation and uses encrypted SSL technology to ensure data privacy. The platform is integrated with more than 500 EHRs and 72 percent of U.S. prescription insurance plans (including Medicaid and Medicare Part D). It's accessible from anywhere with an internet connection. Visit http://www.covermymeds.com for more information.

• ***SureScripts.*** SureScripts helps speed up the PA prescription process with streamlined ePA tools and electronic requests that the company says obviates the need for faxes, paper forms and phone calls. Documentation can be submitted through the portal. SureScripts narrows down only relevant patient-specific questions, pre-populates fields from the EHR, performs data validation and initiates benefit plan renewals. SureScripts is free and doesn't require an EHR (though it integrates with many); it also doesn't store or maintain information of portal transactions, though this means users need to retain their own copies. Visit http://www.surescripts.com for more information.

• ***Medly.*** Medly is a full-service pharmacy that manages PAs, including insurance validation and claim filing, applying financial assistance, coordinating medication delivery with the patient, and following-up with the patient to maintain adherence, address side effects, answer questions and process refills.

In the February issue of Review, Ramya N. Swamy, MD, MPH, of Baltimore, noted that outsourcing medication prior authorization to Medly made the process easier on her end since the company took care of everything once they received the online prescription. For more information, visit http://www.medly.com. ◀

1. The 2021 AMA prior authorization (PA) physician survey. American Medical Association. https://www.ama-assn.org/system/files/prior-authorization-survey.pdf. Accessed February 7, 2023.
2. Fixing prior authorization. American Medical Association. https://www.ama-assn.org/amaone/ama-recovery-plan-america-s-physicians-fixing-prior-authorization. Accessed February 15, 2023.
3. Prior authorization. American Academy of Ophthalmology. https://www.aao.org/advocacy/prior-authorization. Accessed February 15, 2023.

MARY PAT JOHNSON, COMT, CPC, CDE, CPMA

MEDICARE Q&A

2023 Update on Billing For Medications

Injectable drugs got some new rules and regulations in the new year. Here's what you need to know.

2023 brought changes to the rules for injectables used in both offices and ASCs. Here, we'll summarize some of them.

Q How does Medicare handle claims for Dextenza (dexamethasone), a drug eluting implant in the lacrimal canal used in conjunction with ophthalmic surgery?

A The passthrough status for Dextenza expired on 12/31/22. However, under CMS' regulation for non-opioid pain management drugs as surgical supplies, Dextenza still qualifies for separate ambulatory surgical center payment in 2023. Use HCPCS code J1096 (4 units).

That rule doesn't extend to hospital outpatient departments. In HOPDs, the payment for Dextenza is included in the facility fee for the concurrent procedure, not in addition to it.

The procedure for insertion of Dextenza is now identified using CPT code 68841, formerly 0356T. In 2023, this code was reassigned from APC5694 to APC5503, and the reimbursement changed. Payment will be made for a standalone, solitary procedure, but it's bundled with other concurrent procedures like cataract.

Q How does Medicare handle claims for Omidria (phenylephrine and ketorolac intraocular solution) used in conjunction with ophthalmic surgery?

A Since 2021, payment is made to an ASC for Omidria as a non-opioid pain management drug in addition to the ASC facility fee reimbursement for the associated procedure. That separate payment continues in 2023. Report HCPCS code J1097. As with Dextenza, the payment for the drug supply is not paid separately in the HOPD.

Q How does Medicare handle claims for Dexycu (dexamethasone intraocular suspension) used in conjunction with ophthalmic surgery?

A Like Dextenza, the passthrough status for Dexycu expired last year. Unlike Dextenza, Dexycu doesn't qualify as a non-opioid pain management drug, so there's no separate ASC payment for it in 2023, in either ASC or HOPDs.

Note: the payment indicators in the Medicare fee schedule identify the payment status for medications.

- ASC Indicator K2—Drugs and biologicals paid separately when provided integral to a surgical procedure on ASC list; payment based on OPPS rate
- ASC Indicator N1—Packaged service/item; no separate payment made
- HOPD Indicator N—Packaged service/item

Q In 2023, what's changed in reporting for discarded amounts of medications?

A CMS is finalizing requirements for the use of the JW modifier, for reporting discarded amounts of drugs, and a new modifier, JZ, for attesting that there were no discarded amounts. Providers will be required to report the JW modifier beginning January 1, 2023, and the JZ modifier no later than July 1, 2023 in all outpatient settings.[1]

MACs are instructed to deny claims submitted without the right modifier. This will heavily impact retina practices, since most claims for intravitreal medications could require either JW or JZ. Await instructions from the MAC before reporting the JZ modifier. Reporting before their systems are ready to handle the modifier could result in denials.

CMS has issued an FAQ about modifiers JW and JZ.[2] It says, in part, "Effective July 1, 2023, providers and suppliers are required to report the JZ modifier on all claims that bill for drugs from single-dose containers that are separately payable under Medicare Part B when there are no discarded amounts." However, the FAQ also says that the modifiers aren't used with vials of drugs with "overfill," which we take to mean drugs like Eylea and Lucentis.

Staying apprised of the rules for medications requires administrators to watch for claims instructions for new drugs, as well as changing guidelines for existing drugs. The CMS website and your local MAC can be useful sources of information. ■

1. https://www.cms.gov/newsroom/fact-sheets/calendar-year-cy-2023-medicare-physician-fee-schedule-final-rule.
2. https://www.cms.gov/medicare/medicare-fee-for-service-payment/hospitaloutpatientpps/downloads/.jw-modifier-faqs.pdf

This article has no commercial sponsorship.

Mary Pat Johnson is a senior consultant at the Corcoran Consulting Group and is based in North Carolina. She can be reached at mpjohnson@corcoranccg.com.

When Selecting a Prescription Dry Eye Treatment

DON'T MAKE HER WAIT.

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Indication

Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of signs and symptoms of dry eye disease (DED).

Important Safety Information

- Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients.
- In clinical trials, the most common adverse reactions reported in 5-25% of patients were instillation site irritation, dysgeusia and reduced visual acuity. Other adverse reactions reported in 1% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.
- To avoid the potential for eye injury or contamination of the solution, patients should not touch the tip of the single-use container to their eye or to any surface.

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East Hanover, New Jersey 07936-1080

xiidra® (lifitegrast ophthalmic solution)5%

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Because lasting symptom relief can start as early as

2 WEEKS[1*]

Access to Xiidra is better than ever[2]

*Xiidra reduced symptoms of eye dryness at 2 weeks (based on Eye Dryness Score compared to vehicle) in 2 out of 4 studies, with improvements observed at 6 and 12 weeks in all 4 studies.[1†]

Important Safety Information (cont)

- Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.
- Safety and efficacy in pediatric patients below the age of 17 years have not been established.

Please see Brief Summary of Important Product Information on adjacent page.

†Pivotal trial data

The safety and efficacy of Xiidra were assessed in four 12-week, randomized, multicenter, double-masked, vehicle-controlled studies (N=2133). Patients were dosed twice daily. **Use of artificial tears was not allowed during the studies.** The study end points included assessment of signs (based on Inferior fluorescein Corneal Staining Score [ICSS] on a scale of 0-4) and symptoms (based on patient-reported Eye Dryness Score [EDS] on a visual analogue scale of 0-100).[1]

Effects on symptoms of dry eye disease: A larger reduction in EDS favoring Xiidra was observed in all studies at day 42 and day 84. Xiidra reduced symptoms of eye dryness at 2 weeks (based on EDS) compared to vehicle in 2 out of 4 clinical trials.[1]

Effects on signs of dry eye disease: At day 84, a larger reduction in ICSS favoring Xiidra was observed in 3 of the 4 studies.[1]

References: 1. Xiidra [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp. **2.** Data on file. DRF Fingertip Formulary® Novartis Pharmaceuticals Corp; July 2022.

XIIDRA® (lifitegrast ophthalmic solution), for topical ophthalmic use
Initial U.S. Approval: 2016

BRIEF SUMMARY: Please see package insert for full prescribing information.

1 INDICATIONS AND USAGE

Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

4 CONTRAINDICATIONS

Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients in the formulation *[see Adverse Reactions (6.2)]*.

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:

- Hypersensitivity *[see Contraindications (4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In five clinical trials of DED conducted with lifitegrast ophthalmic solution, 1401 patients received at least one dose of lifitegrast (1287 of which received lifitegrast 5%). The majority of patients (84%) had less than or equal to 3 months of treatment exposure. One hundred-seventy patients were exposed to lifitegrast for approximately 12 months. The majority of the treated patients were female (77%). The most common adverse reactions reported in 5%-25% of patients were instillation-site irritation, dysgeusia, and reduced visual acuity.

Other adverse reactions reported in 1%-5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus, and sinusitis.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Xiidra. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Rare serious cases of hypersensitivity, including anaphylactic reaction, bronchospasm, respiratory distress, pharyngeal edema, swollen tongue, urticaria, allergic conjunctivitis, dyspnea, angioedema, and allergic dermatitis have been reported. Eye swelling and rash have also been reported *[see Contraindications (4)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on Xiidra use in pregnant women to inform any drug-associated risks. Intravenous (IV) administration of lifitegrast to pregnant rats, from premating through gestation day 17, did not produce teratogenicity at clinically relevant systemic exposures. Intravenous administration of lifitegrast to pregnant rabbits during organogenesis produced an increased incidence of omphalocele at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the recommended human ophthalmic dose [RHOD], based on the area under the curve [AUC] level). Since human systemic exposure to lifitegrast following ocular administration of Xiidra at the RHOD is low, the applicability of animal findings to the risk of Xiidra use in humans during pregnancy is unclear *[see Clinical Pharmacology (12.3) in the full prescribing information]*.

Data

Animal Data

Lifitegrast administered daily by IV injection to rats, from premating through gestation day 17, caused an increase in mean pre-implantation loss and an increased incidence of several minor skeletal anomalies at 30 mg/kg/day, representing 5,400-fold the human plasma exposure at the RHOD of Xiidra, based on AUC. No teratogenicity was observed in the rat at 10 mg/kg/day (460-fold the human plasma exposure at the RHOD, based on AUC). In the rabbit, an increased incidence of omphalocele was observed at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the RHOD, based on AUC), when administered by IV injection daily from gestation days 7 through 19. A fetal no observed adverse effect level (NOAEL) was not identified in the rabbit.

8.2 Lactation

Risk Summary

There are no data on the presence of lifitegrast in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lifitegrast from ocular administration is low *[see Clinical Pharmacology (12.3) in the full prescribing information]*. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for Xiidra and any potential adverse effects on the breastfed child from Xiidra.

8.4 Pediatric Use

Safety and efficacy in pediatric patients below the age of 17 years have not been established.

8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger adult patients.

Distributed by:
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T2020-87

Zombies

Musings on life, medicine and the practice of ophthalmology.

MARK H. BLECHER
CHIEF MEDICAL EDITOR

As I struggle to convince myself of the worth of humans as a species, it seems I'm constantly bombarded with evidence to the contrary. Many of you have read my rants and depressive monologues on the failures past and present of *Homo sapiens*, all made more apparent in our current society with unlimited and instant ability to push out every individual's thoughts and actions, no matter how dysfunctional. In recent conversations with friends, they were enthusiastic about a new HBO series. It was "interesting," it was "cutting-edge," it was "heartbreaking." I thought maybe this would be useful as a good diversion from the daily grind of negativity. I neglected to ask what it was about.

So, the other night I settled in with the TV and started to watch "The Last of Us." Big mistake. It's a zombie show. I hate zombie movies. I hate horror films. I hate movies about Armageddon and its aftermath. I have no idea why anybody would be attracted to any of these genres—they're scary and depressing. And they engender, at least in me, a profound hopelessness. However, they're all very popular. Very. Which led me to ask why. What is it that seems to draw people to zombie films? Since I couldn't find the answer internally, I turned to Dr. Google. And not surprisingly there are lots of answers.

There are a number of excellent psychological treatises on the subject which I'll try not to plagiarize too much. I will also be disagreeing with many of them. The original zombies were a creation, in myth and fact, of voodoo practices altering living humans with toxins and hallucinogens. The more modern version arose from the horror film industry with "Night of the Living Dead," and presented

Getty

us with reanimated corpses that were slow moving and pointless. Of course, that wasn't lurid enough for our modern culture, so the living zombie, created through biological disaster and driven to consume the non-infected, arose in the TV show "The Walking Dead."

For those of you who've seen TWD, it's intense, and it brings out intense responses from those struggling to not become infected. What drives us to want to watch? I'll refer you to an excellent summary referenced below.[1] It reviews a number of motivations, but the one I found most compelling was morbid curiosity. The same thing that causes us to drive slowly by a car accident. It's really horrible, and, more important, we're glad it's not us. This morbid curiosity has an evolutionary underpinning, too: The fear of predation and disease, and the idea of the survival of the fittest. It doesn't get more basic than that. And all three are central to any good modern zombie series. Other authors suggest we crave the fight or flight exhilaration it engenders, although I would find that too temporary and exhausting to want to re-engage weekly or even for a two-hour movie.

A more mundane reason for audiences' fascination with zombies is our fear of death. Or, more pointedly, fear of the near-death existence of these "humans" devoid of pleasure, excitement and connection. Watching the fight to escape such a life is a metaphor for fighting to escape the slow death of modern society, to summon the humanity to survive against all odds, and to infuse our days with real meaning. No matter how you dress up the reason people seem to be drawn to zombie movies, I still find it profoundly disturbing, depressing and, ultimately, pointless. The struggle seems unwinnable, and a particularly gruesome way to go. So, I'll continue to avoid these films like the plague (pun intended) and remain less than impressed with our superiority as a life form. ◀

1. Axelrod E.M. The psychology of zombies: Why are zombies so infectious? In: Zombies, divorce, & the internet: A collection of psychological disquisitions. Denver: APSG, 2014. https://traumathreatandpublicsafetypsychology.com/blog/psychology-of-zombies. Accessed February 14, 2023.

This article has no commercial sponsorship. **Dr. Blecher** is an attending surgeon at Wills Eye Hospital.

MANAGING IRREGULAR CORNEAS AND CATARACTS

Surgeons discuss how to get a cornea in the best possible shape before calculating IOL power.

LIZ HUNTER
SENIOR EDITOR

When a patient is referred for cataract surgery, that might not be the only issue the cataract surgeon has to address. Quite often, corneal irregularities will reveal themselves in preop testing, unbeknownst to the patient, and subsequently alter the treatment approach. We spoke with cornea and cataract specialists who recommend careful assessments of individual patients to exclude any corneal irregularities, and if found, say you should determine whether to address them medically or surgically prior to cataract removal. Here's their guidance on treatment and managing patient expectations.

Preop Testing

This phase of evaluation shouldn't be rushed to ensure nothing is missed, but top-of-the-line technology, while helpful, isn't always necessary.

It's important to discuss what tests are covered by patients' insurance, advises Kevin M. Miller, MD, who is the Kolokotrones Chair in Ophthalmology at the David Geffen School of Medicine at UCLA. "If they're planning cataract surgery, we put most of our patients through some sort of corneal mapping. We primarily use Scheimpflug devices, such as the Pentacam or the Galilei. You can also use a regular corneal topographer and pick up a lot of irregularities, and there are newer OCT devices that can also map out a cornea," he says. "The thing is, you can't just throw these screening tests at patients because insurance won't pay for them. You have to make sure to let the patient know what will be covered and what will be out of pocket. Sometimes patients won't opt for the extra testing and will just take their chances."

Other times, it comes down to the basics. "For assessing the tear film, there are many helpful technological components to the dry-eye assessment these days but these can sometimes be prohibitively expensive to the smaller ophthalmic practices or to the patient," says Tanya Trinh, MBBS, FRANZCO, who is a specialist in cornea, cataract and refractive surgery at Mosman Eye Centre and George Street Eye Centre in Australia, and a fellow of the World College of Refractive Surgery and Vision Sciences.

"A high-quality dry eye assessment is still very much in the hands of the surgeon with their ears primed for the patient's clinical symptoms, their eyes focused at the slit lamp and the humble fluorescein strip in their hands. Tear breakup time and surface staining are incredibly useful as well as visually and functionally assessing the eyelids and their meibomian gland integrity at the slit lamp," she continues.

"I teach all my residents and fellows to adhere to a systematic assessment of the tear film, corneal layers and ocular surface before moving beyond to other intraocular structures," says Dr. Trinh. "I then encourage them to match up their clinical findings with topography and/or tomography as well as their biometric measurements to ensure that all of it makes sense. It's not uncommon that something is missed on the clinical

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Dr. Koch consults for Alcon, Bausch + Lomb, Johnson & Johnson and Zeiss. **Dr. Miller** is a consultant for Alcon, BVI, Johnson & Johnson Surgical Vision, Long Bridge Medical and Oculus USA. **Dr. Rocha, Dr. Terry** and **Dr. Trinh** report no relevant disclosures for this topic.

ESTABLISHING THE NEXT LEVEL OF EYECARE

Bringing Together Technology to Better Monitor Pathology and Intraocular Pressures

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In today's busy eyecare practice, having the right tools to quickly and reliably assess ocular pressures and pathology is the first step to making the best clinical decisions for patients. Pairing innovative imaging devices, perimeters, and handheld rebound tonometers with clinical expertise can move providers from uncertainty to greater certainty on critical issues concerning patient ophthalmic disease status.

Retinal imaging using confocal-based technology can illuminate subtle structural issues of concern, while TrueColor imaging offers exceptionally high image quality and complexity for more confidence in what providers are viewing.

Perimetry has long played a crucial part in the diagnosis and monitoring of glaucoma and retinal diseases. Now, combining visual field tests with real-time retinal tracking and confocal fundus imaging opens the door to a reliable correlation between a patient's visual function and retinal structure.

In a busy clinic, being able to measure patient intraocular pressure with 200 degrees of positional freedom whether the patient is sitting, reclined, or in a supine position overcomes a host of anatomic and logistic challenges. At the same time, rebound tonometry requiring no anesthetic drops, air, or specialized skills simplifies the measurement process, adds to patient comfort, and is available for patients to use at home.

All of these capabilities are now available through iCare—a pioneer in handheld rebound tonometry that has expanded its offerings to address other core needs in eyecare. The result has been a high level of satisfaction from a cross-section of eyecare leaders.

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For better perception

GLAUCOMA TRACKING & CORNEAL EVALUATION

DR. AHMED: Please discuss how the iCare tonometer has advanced your practice.

DR. WIROSTKO: We use the IC100 in the clinic and as an alternative to dye-based application for routine exams. It requires little training, as opposed to the advanced training required for GAT, is easy to use, and is accurate. We also have found the iCare tonometer is less subjective than GAT, with less of a user "influence." Acquiring IOP in children along with people who squint or have other issues at the slit lamp is challenging with GAT. These and other patients who have trouble fitting into a slit lamp may be better candidates for the iCare tonometer.

DR. SARKISIAN: When I was in a university setting, I advocated for introducing the iCare tonometer at all of the clinics because of its clear superiority over the Tono-Pen, which we used frequently for pre- and post-retina/glaucoma laser patients, postoperative patients, and pediatric patients. A single-use sterile probe was mandatory, and many of us were frustrated by the constant need to calibrate the instrument. The iCare tonometer enables less experienced technicians who are not as skilled at GAT to provide more accurate pressure readings. Since going into private practice four years ago, I now own two iCare tonometers. The ability to capture data to 1/10th of a mmHg has been particularly helpful, and the ability to use supine is beneficial for certain patients.

"We use the iCare tonometer as a screening tool. Our technicians measure pressures with the device when they first see patients, which helps us identify individuals with high IOP that need to be seen more urgently by the doctor."

—Ike Ahmed, MD

DR. TYSON: I was actually standoffish about adding the iCare tonometer. My optometrist came to me and asked me about it, and I put it off for about a year or so. Then I brought in a cornea specialist who wanted the device for his corneal transplant and DSAEK/DMEK patients, and for irregular corneas that weren't going to yield good Kaplan-Meiers analysis. After we bought our first iCare tonometer for our cornea department, I kept hearing back from my technicians how much they liked it and how it

A New Era In Clinical Tonometry

With 200 degrees of positional freedom, the iCare IC200 tonometer measures intraocular pressure whether the patient is supine, reclined, or in a seated position. The tonometer is based on a rebound measuring principle requiring no anesthetic drops, air, or specialized skills for use.

An intuitive user interface maximizes efficiency. A green indicator light on the probe confirms tonometer positioning before measurement. The tonometer accepts only measurements taken in the correct way—perpendicularly from the center of the cornea—with individual readings displayed to one-decimal mmHg resolution, ensuring more reliable and accurate results.

Research On iCare HOME Tonometer

By Ike Ahmed, MD

Our group published a paper discussing the benefits of the iCare HOME tonometer and cases for which it may be most clinically useful.[1]

We concluded the iCare HOME tonometer "demonstrated excellent potential to transform the traditional approach to glaucoma diagnosis and management" and that it "is reasonably similar to GAT measurements, easy to use, and well accepted by patients."[1]

We determined the device was most useful for patients presenting with reasonable in-office IOP but whose disease may not be controlled due to significant visual field progression, optic nerve head and retinal nerve fiber layer changes, or other issues raising suspicion.[1]

Certain types of glaucoma patients—particularly those with pigment dispersion glaucoma, and suspects of angle-closure glaucoma and normal-tension glaucoma—were found to be especially well-suited to the home tonometer.

We also reported the iCare HOME tonometer was useful in monitoring postoperative IOP control and progress of patients after surgical interventions.[1]

1. Liu J, De Francesco T, Schlenker M, Ahmed II. Icare Home tonometer: a review of characteristics and clinical utility. Clin Ophthalmol. 2020 Nov 23;14:4031-45.

was speeding up the patient workup. I talked to my cornea specialist, and he felt that it was more than accurate so we bought several devices and started using them throughout our practice with seven locations.

The iCare tonometer has been a nice little workhorse; it speeds up our workup and adds a reliability factor because it removes some of the technical training necessary with other devices to get good readings. Overall, its ease of use and patient acceptance have been enormously valuable.

DR. AHMED: We use the iCare tonometer as a screening tool. Our technicians measure pressures with the device when they first see patients, which helps us identify individuals with high IOP that need to be seen more urgently by the doctor. With uncooperative patients or children, it enables us to get good IOP estimates. The device is easy to use, and instructions on the display as well as clear error messages help the technicians perform measurements correctly.

DR. AHMED: The iCare HOME2 tonometer, FDA-cleared in January 2022, includes a number of upgrades from its predecessor [e.g., measurements in supine position, patient mobile app, private patient cloud account, etc.) How has home tonometry improved short- and long-term patient care?

DR. WIROSTKO: With the iCare HOME2 tonometer, patient care continues to excel. The device

A Modern Approach To Diurnal IOP Monitoring

With the iCare HOME2 tonometer, patients can take IOP measurements throughout the day, at night, and when lying down. Measurement results are uploaded to a cloud database where they are accessible to the doctor and patient for accurate real-world IOP data to support treatment decisions.

iCare HOME2 tonometer

directly and immediately enables the doctor to alter treatment decisions to help slow disease progression and preserve patients' sight. We have many examples of catching IOP spikes outside of clinic hours with real-time information from the device, and have published numerous case reports on how these insights have informed medical and surgical treatment.[1] The newest home tonometer, HOME2, also empowers our patients to better understand their IOPs and fluctuations, and become more involved as a partner in their care decisions.

DR. SARKISIAN: The iCare HOME2 tonometer has captured critical data for our patients. I believe many patients are misdiagnosed as having low- or normal-tension glaucoma when in fact they simply have broad diurnal curve fluctuations. With this home tonometer, we can capture morning and late-evening IOPs. Not only does this make diagnosis more precise, but it provides more data to reassure the patient that we are in fact improving IOP fluctuation by doing treatments such as SLT or adding medications. Previously, we had to wait for a patient's glaucoma to progress before acting. In my practice, the device has also been helpful in monitoring patients after SLT to determine when repeat treatment is appropriate.

DR. AHMED: We provide (rent and sell) the iCare HOME and HOME2 tonometers to our patients and actually use it frequently in our clinic. After individual training, patients rent the device for a number of days to perform measurements and take notes about their activity. We often use the device for normal-tension or angle-closure glaucoma patients with intermittent eye pressure spikes. We find the SD analysis and the plotted graph for our patients particularly useful.

RETINAL IMAGING

DR. AHMED: Following the merger of iCare and CenterVue in 2019, iCare added retinal imaging products, including TrueColor Confocal Imaging Systems (EIDON, EIDON AF, EIDON FA, EIDON Ultra-Widefield Module, DRSplus). Please discuss the benefits of confocal imaging technology.

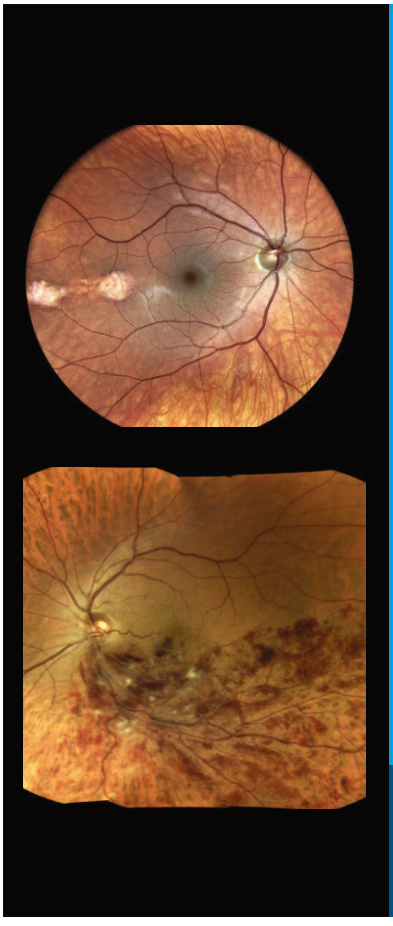
DR. WIROSTKO: Non-mydriatic confocal fundus imaging technology is almost always able to power through refractive errors, cataracts, or corneal issues and produce good images. EIDON's use of real light technology, and its ability to produce sharp, crisp, and real color images make it possible to easily detect abnormalities. I can have confidence that, if I'm not seeing serious issues such as choroidal nevi, etc., the findings likely aren't pathologic. Moreover, the "flicker" function, enabling side-by-side comparison of images taken at two different time points, helps me monitor subtle changes over time. What is particularly nice is the ability to share with the patient what I'm seeing, giving them a sense of involvement and empowerment in their management.

"Confocal imaging speeds up my workup because now I can get a very good view of the back of the eye at the beginning of the exam. Even if the patient is a poor dilator, I'm not held up waiting 30 or 40 minutes for the patient to dilate. "

—Farrell C. Tyson, MD, FACS

DR. SARKISIAN: I have found major benefits of the technology to be ease of use by my staff and the ability to capture high-quality images without dilation. In addition, the "flicker" function is uniquely beneficial for image comparison once a long series of images has been obtained. My EIDON fundus camera is an excellent value considering the amazing quality of images it produces and the growing need for fundus photography in a busy ophthalmic practice.

DR. TYSON: Our practice owned several CenterVue devices prior to iCare purchasing the company so we already had an EIDON and COMPASS. We really liked the fact that we were getting TrueColor im-



Harnessing The Power Of Confocal Imaging & TrueColor

Confocal imaging is considered superior to conventional fundus photography because it blocks the backscattered light of structures from the outside of the retina focal plane, increasing sharpness, optical resolution, and contrast.

Confocal imaging maintains strong image quality, even in the case of media opacities such as cataracts, and can work with pupils as small as 2.5mm without the need for dilation.

TrueColor imaging utilized in iCare devices employs white light LED for distortion-free, exceptional color fidelity. The retina appears as it does when directly observed due to the presence of the entire visible spectrum in the captured image.

iCare EIDON TrueColor technology can potentially improve the clinician's ability to diagnose and monitor retinal diseases. One study found iCare EIDON provided more balanced color images with a wider richness of color content than a conventional flash fundus camera.[1]

In addition, iCare EIDON's higher chromaticity offers the provider greater discriminative power and the opportunity for increased accuracy when diagnosing patients.

1. Sarao V, Veritti D, Borrelli E, Sadda SVR, Poletti E, Lanzetta P. A comparison between a white LED confocal imaging system and a conventional flash fundus camera using chromaticity analysis. BMC Ophthalmol. 2019 Nov 19;19(1):231.

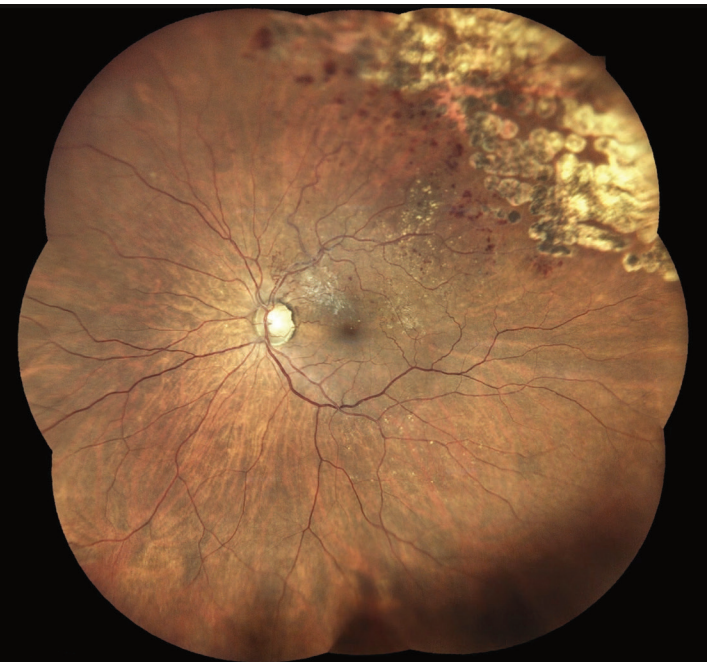
ages. The technology means you see what you normally see with the naked eye, but the confocal laser is able to go through a much smaller pupil, about a 2mm pupil, to produce a beautiful view of the back of the eye.

I'm primarily a cataract/refractive practice, and when I'm doing workups, the way the system takes the image makes epiretinal membranes practically glow at you so you really see them. With the 90-diopter slit lamp lens, you'd be much more challenged to pick them up. But when you're getting this comprehensive view and the epiretinal membrane is just shimmering on the image, it really makes you take notice and helps you to adjust your surgical plans.

Confocal imaging speeds up my workup because now I can get a very good view of the back of the eye at the beginning of the exam. Even if the patient is a poor dilator, I'm not held up waiting 30 or 40 minutes for the patient to dilate. I can go ahead and have a direct discussion with the patient about their eyes, their vision, and their pathology.

DR. AHMED: What is the importance of UWF's capability [up to 200˚ panoramic view] to illuminate early signs of ocular pathology in your patients, and how does this surpass standard field view?

DR. WIROSTKO: UWF's faster acquisition and wider field of view is vital for difficult imaging cases. Outlying areas are able to be imaged, giving the physician greater ability to more accurately diagnose and analyze normal vs. abnormal findings. UWF has far



iCare EIDON's ultra-widefield optics from 120° to 200° field of view allows imaging of the central retina as well as the periphery.

surpassed the original capture lens. Even if you are only able to get one picture of a patient, you can still acquire the most critical areas for diagnostic comparisons. This can be pivotal for catching diabetic retinopathies, BRVO, CRVO, etc., in the far periphery.

DR. TYSON: With UWF, you're not just getting from arcade to arcade, but you can see way out into the periphery. If you want to go even further, you can use Mosaic mode and see just about the whole back of the eye. This has helped us to confirm findings in the back of the eye and view certain pathologies more vividly.

DR. AHMED: iCare COMPASS combines visual field tests, fixation loss correction by a real-time retinal tracker, and ultra-high resolution confocal TrueColor fundus imaging for efficient assessment of function and structure, with reduction of motion artifacts. How does fundus-controlled perimetry aid you in assessing disease status?

"We have cases every day that are diagnosed, tracked, and followed more efficiently via the use of the EIDON. This is where normal fundus photography falls short or is cumbersome. "

—Barbara M. Wirostko, MD, FARVO

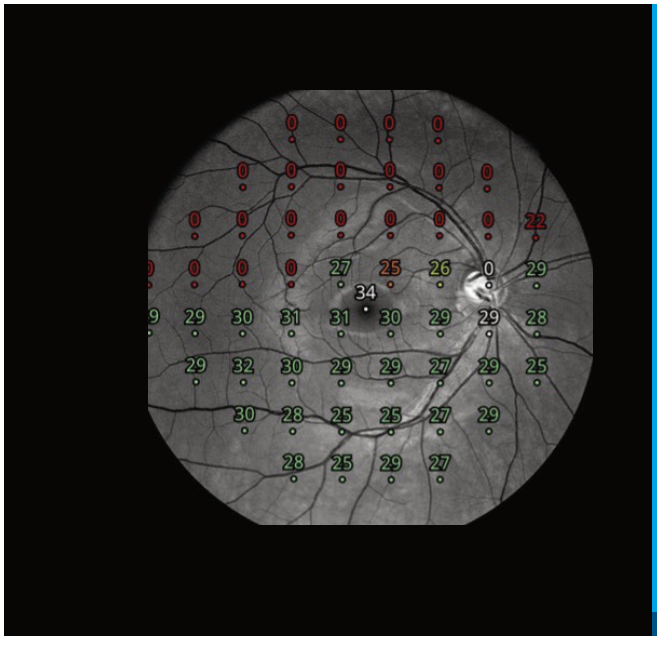
DR. TYSON: The beauty of the COMPASS is that the retina is being directly stimulated by the machine rather than indirectly off of a reflective perimetry bowl. The COMPASS knows where the nerve is, where the arcade is, which enables reproducibility. And the device can adjust for movement. With many machines, you have to do pupil tracking and see how well the patient is staying centered. We have found the COMPASS test is quicker, and more accurate and reproducible because the device knows where it is stimulating the retina and restimulates the same area from test to test.

DR. AHMED: We prefer the COMPASS visual fields over classic Humphrey fields for multiple reasons. The retinal tracker helps avoid errors caused by poor fixation and ensures accurate tracking of localized defects over multiple field tests. The high-resolution images of nerve and macula, as well as the retinal correspondence map aid us in deciding whether the field defects are glaucomatous in nature or potentially caused by retinal issues.

IMPROVING DISEASE MANAGEMENT AND PATIENT CARE

DR. AHMED: Do you have any cases to share that demonstrate how iCare technology helped you better identify or track disease, and care for patients?

DR. WIROSTKO: We have cases every day that are diagnosed, tracked, and followed more efficiently via the use of the EIDON. This is where normal fundus photography falls short or is cumbersome. The repeatable clear and sharp, colorful images that the EIDON can produce at the touch of a button are re-



Fundus-Controlled Perimetry Key Features

- Standard automated perimetry
- Active retinal tracking compensating for poor patient fixation in real-time
- Auto-focus—no trial lens needed
- Illustrative fixation analysis (fixation area and plot)
- High-resolution confocal TrueColor imaging of the retina
- The patient can blink freely and the test can be suspended at any time without data loss
- User friendly, requires minimal operator training

markable. The device makes physicians much more informed regarding treatment paths in a quick and effective manner. We use the iCare tonometer and EIDON on all of our patients with glaucomatous, retinal, and macular pathologies, and those who are pre- or post-surgery.

DR. TYSON: The COMPASS has given us the same quality as, if not better than, what we've been used to. It's not a compromise in the quality of the information we're receiving. We're getting better reproducibility and, therefore, can get fewer false positives and negatives. At the same time, we're gaining comfort from knowing the data is as accurate as what has been considered the Gold standard with Humphrey perimetry.

DR. AHMED: The iCare HOME tonometer has helped us discover high IOPs in dim lighting conditions in many of our angle-closure patients that would have otherwise been missed in the bright office. For our normal-tension glaucoma patients, minimal fluctuations are important and the iCare HOME results often lead to changes in medication (timing/frequency of drops, long- or short-lasting drugs) or indication for surgery.

"With the iCare product line, you have a range of diagnostics that touches all aspects of ophthalmology—from retina, to glaucoma, to general ophthalmology."

—Steven R. Sarkisian, Jr., MD

DR. AHMED: How can a comprehensive family of products such as the one iCare offers benefit practices across the eyecare spectrum?

DR. WIROSTKO: The iCare devices, with their diagnostic advantages, far exceed expectations and elevate patient care to ever higher levels. The ease and speed with which these devices collect accurate and vital information provides the clinician with the most up-to-date information at the touch of a button to direct specific and urgent, possibly sight-preserving changes of medical management. The iCare family delivers essential insights—from the retina to the optic nerve and cornea, offering the provider and patient the opportunity for superlative preventative care.

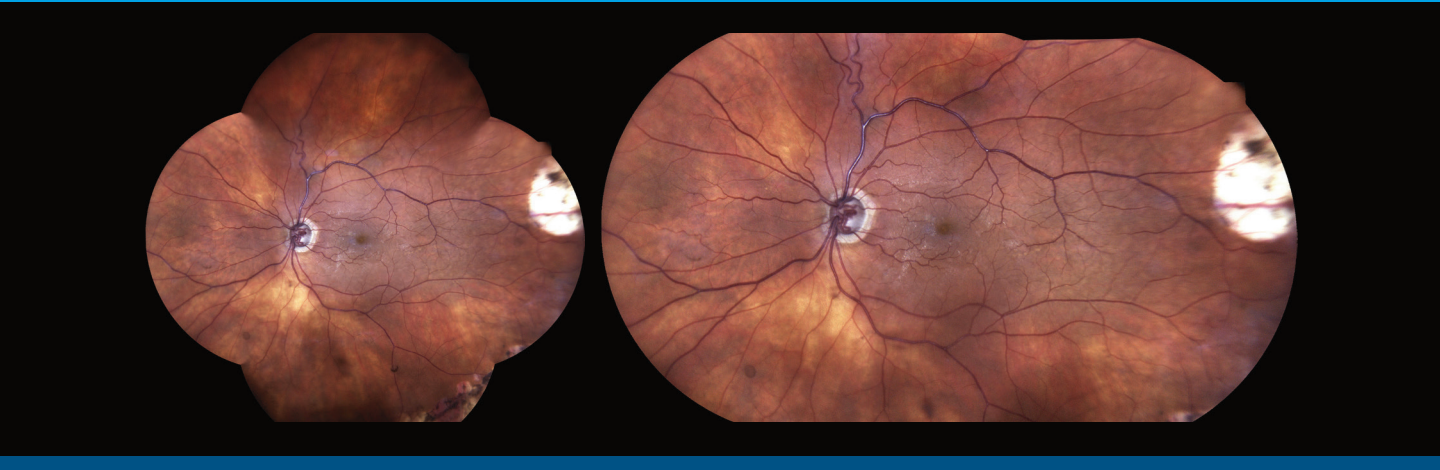
Case of Impending RVO

By Barbara M. Wirostko, MD

An 81-year-old male patient was followed for mild glaucoma damage for several years. His IOPs were well controlled, and he also had mild HTN, high cholesterol, and was a smoker.

On a routine dilated exam, he was discovered to have dilated and tortuous retinal venules in his left eye (OS) and was diagnosed as being at risk for an impending retinal vein occlusion on fluorescein angiography.

Carotids and systemic workup proved non-contributory. We made sure to control his HTN and IOP, and started him on a full aspirin a day.



EIDON widefield imaging helped illuminate a tortuous retinal venule in this patient's left eye (OS). Images: Barbara M. Wirostko, MD

DR. SARKISIAN: With the iCare product line, you have a range of diagnostics that touches all aspects of ophthalmology—from retina, to glaucoma, to general ophthalmology. As a glaucoma specialist, I would recommend all offices utilize the iCare tonometer for handheld tonometry due to its ease of use and accuracy.

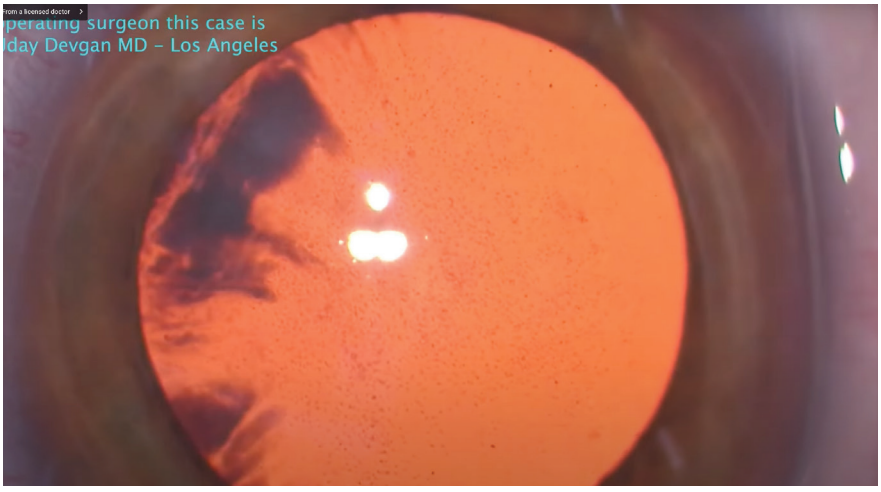
DR. TYSON: iCare is giving you top-shelf technology at a very reasonable price point, enabling practices of all sizes access to the best technology in their office. And at the same time, this family of products—whether it's EIDON, COMPASS, EIDON FA, the tonometers—offers the same ease of use. Once you get the techs trained on one device, it's very simple for them to move to the next one. It's clear by all of our iCare devices that the team designing them really has the technician in mind. This isn't a technological masterpiece that nobody can operate. These devices are really straightforward and easy-to-use, but you're getting unbelievable images and testing out of them.

DR. AHMED: By providing a seamless user experience between its products, and ideally by combining all results into one single software, iCare continues to improve efficiency in today's eyecare practice. ■

1. Levin AM, McGlumphy EJ, Chaya CJ, Wirostko BM, Johnson TV. The utility of home tonometry for peri-interventional decision-making in glaucoma surgery: case series. Am J Ophthalmol Case Rep. 2022 Sep 7;28:101689.

examination that the subsequent imaging is able to highlight and is useful for guiding any areas that you may need to take a second look at."

After making sure the acquisition of each modality is of robust quality, Dr. Trinh encourages residents and fellows not to forget the basics, such as patients' unaided and aided visual acuity, history of manifest refraction and stability, and assessment of the "match" between eyes in the same patient (keratometry, magnitude and axis of astigmatism, axial length matching between eyes and also with expected refractive status of the patient and more).



Uday Devgan, MD

The presence of guttae in the cornea could signify Fuchs' dystrophy. Although it may not appear as an irregular corneal surface, if it becomes more severe it can lead to severe irregular astigmatism and unreliable A-scan readings and IOL calculations. Depending on its severity, Fuchs' can often be treated simultaneously with cataract surgery.

The (Ir)regular Suspects

Corneal irregularities come in a broad range, from the ubiquitous dry eye to the more rare Fuchs' endothelial corneal dystrophy, and everything in between.

"The most common irregularity is dry eye, and then there are all kinds of corneal dystrophies, the most common being map-dot-fingerprint," says Dr. Miller. "Then there are ectatic conditions, like keratoconus, pellucid marginal degeneration and post-refractive surgery ectasia. Then there are eyes where you can't put a name on their condition but one or both corneas are irregular. Whenever I see someone for cataract surgery and they have a history of rigid contact lens wear, the radar goes off in my head because maybe they're in rigid contact lenses for the reason that they couldn't get good quality vision with glasses or soft contacts."

Mark A. Terry, director of Corneal Services at the Devers Eye Institute in Portland, Oregon, says corneal scarring is another category to look out for. "Included in this category would be the iatrogenic scarring from abnormal LASIK flaps, decentered PRK ablations, and radial keratotomy," he says. "Other common scars that can distort the corneal surface are pterygia, Salzmann's nodules, and of course traumatic lacerations."

Dr. Trinh says RK patients are becoming increasingly common as this patient group ages and develops cataracts, with special pre-, intra- and postoperative modifications required alongside careful preop counseling and extended close postop follow-up.

"The genetic/environmental disease of keratoconus is more commonly recognized today due to our improved diagnostic scanning devices such as the Pentacam," Dr. Terry says. "The ectasia that results from keratoconus gives a characteristic irregular astigmatism that's highly variable in amplitude and can be progressive. Identification of the presence of keratoconus is critical when considering surgery (such as cataract or refractive surgery) to avoid postop refractive surprises."

Dr. Trinh says subclinical keratoconus or pellucid corneal changes may cause irregular astigmatism, requiring additional diagnostics and approach to lens selection and expected outcomes. "Frank keratoconus or pellucid patients who exist comfortably in hard contact lenses may warrant a separate discussion as to their lens choice and postop contact lens wear approach," she says. "Patients who are post corneal grafting procedures also need special care as the risk of corneal graft rejection or failure needs to be pre-emptively monitored and managed.

If you're a transplant surgeon, penetrating keratoplasty or deep anterior lamellar keratoplasty are common causes of irregular astigmatism, says Dr. Terry. "It's rare for an eye following PK/DALK to not have some level of irregular astigmatism. While surgeons have tried various surgical solutions like suture technique variations and femtosecond laser-constructed complex wounds, the final topography after PK/DALK is largely determined by wound-healing dynamics, which the surgeon can't control."

There are some rare or unusual corneal irregularities that can be missed or that masquerade as dry eye.

"Epithelial basement membrane dystrophy is another common cause of differing or fluctuating corneal topographies," Dr. Trinh says. "Changes reminiscent of the classic map-dot-fingerprint types are easier to diagnose, but often can be missed if subclinical. Surgeons should specifically lift the upper eyelid and look at the superior mid-peripheral region of the cornea as well as assess for reverse fluorescein staining patterns which can highlight the presence of subclinical disease."

Salzmann's nodular degeneration, conjunctivochalasis, pterygium,

floppy eyelid syndrome, all can masquerade as dry-eye disease, says Karolinne M. Rocha, MD, PhD, associate professor of ophthalmology and director of the Cornea and Refractive Surgery Division at Medical University of South Carolina, Storm Eye Institute. "Neurotrophic keratitis stage one looks like dry eye," Dr. Rocha adds. "Checking for corneal sensitivity in the clinic is one way to test for that."

Dr. Terry says to be cognizant of Fuchs' corneal dystrophy, which causes progressive stromal edema. "This stromal swelling usually doesn't result in an irregular corneal surface, but if the endothelial dysfunction is severe enough, then epithelial edema and bullae can occur, causing severe irregular astigmatism and unreliable A-Scan readings and IOL calculations," he says.

Finally, post corneal refractive surgical patients are another expanding category, Dr. Trinh says. "Surgical scars may be minimally present or not present at all and patients will often 'forget' about these procedures and often will only reply in the affirmative when specifically prompted. It's very easy to miss these patients and all cataract surgeons need to actively screen for these by history, exam and diagnostics."

Cornea before Cataract?

Now that you have discovered an irregularity that may interfere with the patient's cataract plan, it's time to decide how to move forward.

"If the surgeon is considering cataract surgery, then the surgeon has to ask the following three questions: Is that corneal problem currently detrimental to vision? Will it make the A-scan calculations less reliable? Will it be a problem postoperatively?" says Dr. Terry. "If the answer to any of these questions is 'Yes', then the surgeon needs to perform sequential surgery: correct the corneal problem first, allow healing until the surface is stable, and then proceed with more accurate A-scan readings for the cataract surgery."

Patients may be thrown off by the fact that some other condition exists and may now delay their surgery.

"Some patients think that if they get their cataracts out, everything's going to be good," says Dr. Miller.

"But when you start doing some investigating and find irregularities, the question becomes: how much improvement will come from removing the cataract: 50 percent; 90 percent; or only 10 percent?" Dr. Miller continues. "If you think it's only going to be a 10-percent improvement, you should probably be dealing with the corneal problem first. If you think you're going to get a 90-percent improvement, then you can handle any symptomatic irregularity after."

However, Dr. Miller says he generally feels it's a bad idea to address corneal irregularity simultaneously with cataract surgery. "You either want to take care of it beforehand and regularize the cornea so you get the best lens power calculations, or you have a discussion with the patient about doing it after cataract surgery."

"I explain to patients that irregularities can affect the measurements for the IOL and I try to remind them that cataract surgery is a one-time surgery and the lens will last forever," says Dr. Rocha. "I make sure they understand how important the measurements are and that it's worth waiting a few weeks to treat their condition prior to cataract surgery. I usually show them the picture of their topography map, and I feel patients appreciate that we're not trying to rush."

Dr. Terry says there are only two exceptions he would consider for simultaneous cataract surgery.

"First, if the patient is monocular with a severe cataract and requires a corneal transplant to reduce the irregular astigmatism or bullous keratopathy, then simultaneous PK/DALK is warranted to get the patient usable vision as soon as possible. This is especially true if the patient is a prior successful scleral contact lens wearer," Dr. Terry says.

"Second, if the patient has endothelial dysfunction and there's no preoperative irregular astigmatism, then simultaneous DMEK with cataract surgery should be done to avoid two trips to the operating room for these two separate problems," he continues. "Our prior publications have shown that even toric IOLs can be used to accurately correct regular astigmatism in these Fuchs' dystrophy patients. For those few patients that are unhappy with their postop visual acuity without glasses, then LASIK or PRK can be done to resolve their minimal residual refractive error."

Dr. Trinh agrees, depending on the patient. "[Surgery to address] Fuchs' dystrophy can be combined with cataract surgery and the prevalence of this combined procedure should ideally be influenced by the severity of the cataract and the endothelial dysfunction at the time of surgery," she says. "Realistically however, these decisions can be further influenced by age and fitness for multiple surgical procedures if staged, as well as ease of access to the different healthcare systems and the local availability of corneal tissue for transplantation.

"In some cases, keratoconus or pellucid marginal degeneration may not require any treatment beforehand," Dr. Trinh continues. "If the patient is proven to have stable mild keratoconus or pellucid marginal degeneration, their manifest refraction, topography and tomography match in terms of axis and magnitude and they see well (20/40 or better), I would be more inclined to proceed straight to cataract surgery and place a toric lens with a capsular tension ring in situ," she says. "In cases where the cylinder component is less than 2 D, I may also be inclined to place a pinhole intraocular lens in the non-dominant eye and aim for a slightly minus refractive target to allow for some aided near vision."

All of the sources we spoke with agreed that dry-eye treatment should

begin prior to cataract surgery.

"It's critical to actively diagnose and treat dry eye before accepting the final measurements for cataract surgery," Dr. Trinh says. "In my practice, all patients receive a four-day course of fluorometholone and preservative-free tears prior to biometric measurements. Anyone with more moderate to severe dry-eye disease will be assessed and treated additionally preoperatively. This may even mean that their cataract surgery is delayed until the surface is adequately managed or at the best we can possibly rehabilitate.

"Because dry eye is often chronic, it's also imperative that patients understand that their lenses will always work best with a well-lubricated eye, and even that some lenses will perform at a degraded optical quality in the presence of untreated dry eye," she continues. "Severe dry-eye changes can also even be an automatic disqualifier for some types of lenses especially in the multifocal category, and patients must be counseled appropriately preoperatively about their expectations."

Dr. Rocha says she tackles dry eye and meibomian gland dysfunction prior to biometry measurements. "We can use Omega-3 EPA/DHA supplements, sometimes perform Lipiflow or iLux, and can start patients on medications such as lifitegrast or cyclosporine," she says. "Sometimes I like to use topical steroids for two weeks to really treat that inflammatory component right away since we know that lifitegrast and cyclosporine can take a few weeks to work."

In the treatment of EBMD and Salzmann's nodules, it's recommended to use superficial keratectomy before proceeding with cataract surgery. This can take approximately six weeks to heal before getting a normal surface topography, says Dr. Terry.

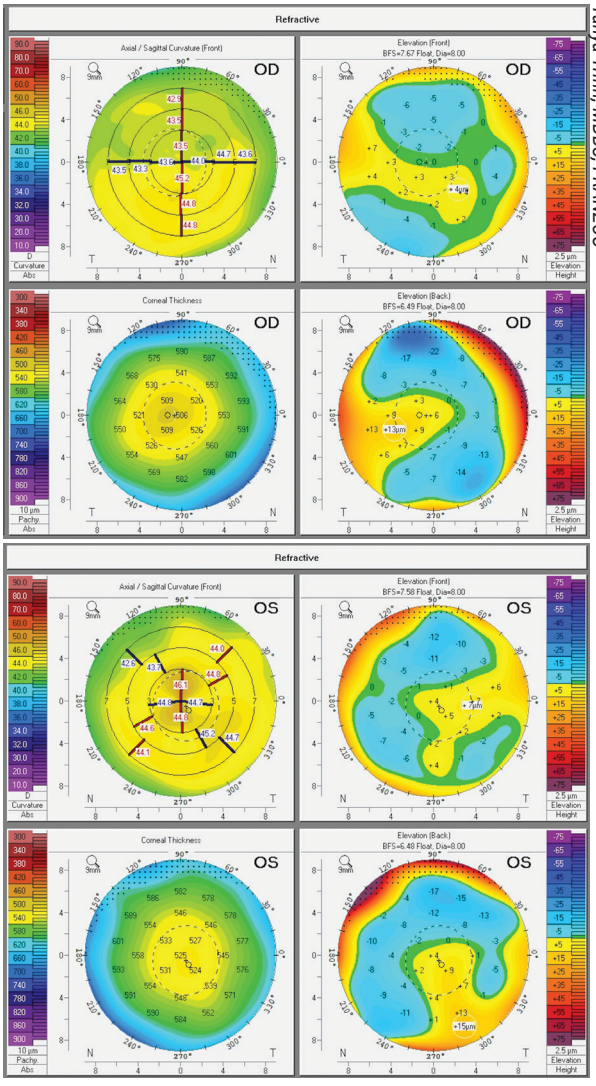
Dr. Trinh approaches Salzmann's nodules and pterygia similarly, asking three important questions: Does this patient have progressive disease? Is there concurrent dry-eye disease that requires treatment? Does this patient require surgical intervention to remove the pterygia or nodules prior to cataract surgery?

"In cases where the disease process is actively progressing, near the pupil or causing irregular astigmatism, I will remove the pterygium or SND beforehand and allow the eye to settle for a period of a few months before recommencing measurements for cataract surgery," says Dr. Trinh. "During the entire period, I will also ensure that ocular surface inflammation and dry eye is aggressively treated as standard; this will assist in minimizing chances of recurrence as well as optimizing the surface for future lens calculations."

After superficial keratectomy (or another surface surgery), Dr. Trinh says she typically waits three months on average before cataract surgery. "However, the actual endpoint is seeing the stability of topographic changes," she says. "So long as there's not a concurrent rapid change in cataract progression, the manifest refraction may also assist as a guide alongside topographic evaluation."

For the irregular astigmatism of corneal scarring, prior refractive surgery, and keratoconus, the decision of whether to fix the corneal problem first depends upon the level of distortion of the surface, says Dr. Terry. "If severe irregular astigmatism, and the patient can't tolerate a scleral contact lens, then a corneal transplant (PK or DALK) may be warranted before the cataract surgery," he says. "If the distortion isn't severe or the patient has success with scleral contact lens wear and the cataract is the main cause of visual loss, then cataract surgery alone is reasonable. For the irregular astigmatism after corneal transplantation (PK or DALK), the astigmatism may be reduced with relaxing incisions and/or PRK prior to cataract surgery."

Douglas D. Koch, MD, a professor and Allen, Mosbacher and Law Chair in Ophthalmology at Baylor College of Medicine in Houston, says he



Tanya Trinh, MBBS, FRANZCO

(Top) Right eye of patient demonstrating changes consistent with keratoconus with inferior asymmetrical steepening, decreased corresponding pachymetry and evolving elevated posterior float. (Bottom) Left eye of same patient demonstrating changes consistent with the irregular tomographic changes of epithelial basement membrane dystrophy.

would consider a scleral contact lens if the patient wasn't eager to undergo a surgery to address the cornea irregularity. "I would tailor my discussion with the patient about getting close with a lens implant and then finish it off with a scleral lens, and I might have them fit for the scleral lens or see what it's like before the surgery in order to be sure that's a reasonable option," he says.

IOL Calculations and Options

Our experts offered some insight into the factors that would influence their decision on IOL choice.

First, in power calculations, Dr. Miller says it's tough with any irregular cornea to figure out the true corneal power in the central 3 mm optical zone. "I think it's helpful to have some sort of corneal map and look at not just simulated K readings, but also look at the numbers that you see in the central 3 mm and maybe come up with an average number for the corneal power," he says.

Dr. Koch looks at the central 3 to 4 mm and the power across various meridians opposite 180 degrees. "If the power is fairly the same, say 39 on one side and 40 on the other, then I'm more comfortable proposing a Symfony lens or maybe even a trifocal if it's really uniform," he says. "On the other hand, if it's 39 on one side and 35 on the other, then I know there's a lot of irregular astigmatism and that guides me toward a monofocal IOL."

He adds that he does use the IOL calculations from the ASCRS website for corneas pertaining to post-RK or post-LASIK, for example.

As Dr. Terry says, every surgeon has their own preferred calculation formula. "Two of the most common are the Barrett and the Barrett Universal formula and I think those are excellent," he says. "I think the hardest situation for these formulas to be accurate is in cases of radial keratotomy eyes and eyes with highly irregular astigmatism from other forms of corneal scars. But RK has always been one that has been difficult for any of the formulas to show the degree of accuracy they do with other forms of irregular astigmatism. I use the Barrett formulas for determining most of my IOL choices."

Post-refractive surgery patients will also require differences in preoperative evaluation, says Dr. Trinh. "Higher order aberrations induced by some forms of refractive surgery may cause unexpected and undesirable visual phenomena postoperatively and limit the choices of lens technologies available to them," she says. "The challenges with IOL power predictions also require reflection and adjustment with biometric formulas designed for these subgroups. Generally, traditional lens formulas will result in a hyperopic surprise when applied to patients with past myopic correction and a myopic surprise in patients who have had past hyperopic correction."

Some surgeons have strong opinions about placing toric IOLs in patients with irregular corneas.

"I think that one of the biggest choices that surgeons have is whether or not to put a toric IOL inside the eye to correct astigmatism," says Dr. Terry. "The more regular the astigmatism is, the more I'm in favor of toric lenses and the more irregular the astigmatism is, the less I'm in favor of them. So there's a very black-and-white area on both sides and there's a gray area in the middle.

"For instance: I would place a toric IOL into a keratoconus or PK eye that has mild irregular astigmatism that's stable and has no prospects of a corneal transplant or scleral contact lens use in the future," Dr. Terry continues. "I wouldn't place a toric IOL in a keratoconus or PK eye that has highly irregular astigmatism, with shifting axis and with successful scleral contact lens use in the past. Therefore, placement of a toric IOL is something that has to be really individualized to the patient's circumstances."

Dr. Miller says he is hesitant to use toric lenses in any eye with corneal irregularity. "Too often I see papers published with great one-year results after a toric lens goes into an eye with a corneal transplant," he says, "then 10 years later the astigmatism has completely changed and now the toric lens isn't helping them. I might even be hurting them. Be cautious about putting toric lenses into eyes with irregular corneas."

Like most surgeons, Dr. Terry doesn't recommend multifocal IOLs in any eye with irregular astigmatism. "Multifocal IOLs require minimal to no astigmatism postoperatively to be effective and acceptable to the high standards of patients receiving these lenses," he says.

In general, Dr. Koch is conservative and tends to go with a monofocal IOL. "I've had some good luck with the Symfony and its new Opti-blue version in post-LASIK patients, but if there's much irregularity in the cornea I avoid multifocal or EDOF lenses," he says.

Dr. Koch and others are particularly excited about the Apthera IC-8 and how that will change conversations with patients. "I think, as an off-label use, this lens will be a very useful tool for getting these patients better quality vision and more accurate refractive outcomes," he says.

Dr. Rocha, who is also looking forward to possibly using the Apthera IC-8, feels that after these patients' ocular surface has been treated, they're in fact candidates for EDOF, trifocal or hybrid multifocal EDOF lenses, depending on the case.

"You have to consider, is their irregularity a condition that you can treat and then the patient is good, or is it a progressive disease?" she says. "Will the cornea continue to change shape? Yes, in some conditions, for example progressive keratoconus. In those cases, you need to be conservative and consider monofocal IOLs. But if someone had a small scar or nodule and you did a PTK with laser and now the cornea looks regular, that patient can benefit from some of the presbyopia-correcting lenses or

(Continued on page 63)

CATARACT SURGEONS LOOK AT NEW APPROACHES

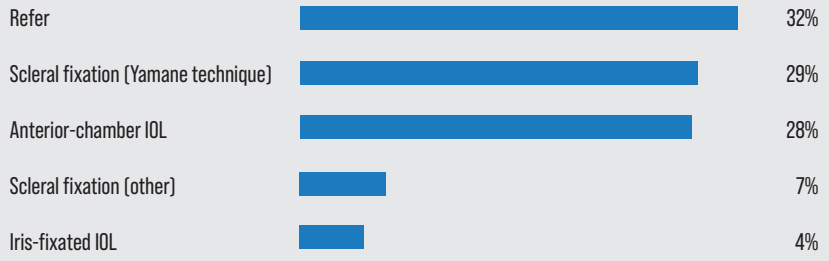
Cataract surgeons share their thoughts on the go-to techniques for everything from managing astigmatism and breaking up the nucleus to managing postop inflammation.

WALTER BETHKE
EDITOR IN CHIEF

If this year's survey on cataract-surgery techniques is any indication, surgeons appear to be warming up to different techniques—some new-ish, some more established but gaining a following. For instance, usage of horizontal phaco chop went up by almost 12 percentage points compared to last year's survey, and the percentage of surgeons who use either the femtosecond or the Zepto for some aspect of their cataract procedures increased by about 5 percentage points. More surgeons have taken a liking to the Yamane IOL fixation technique, with the percentage who say they prefer to use it increasing by 13 percentage points compared to last year.

These are just some of the findings on this year's survey on cataract surgery technique. This year, 4,159 of the 10,442 surgeons receiving the survey opened it (40 percent open rate), and 73 completed the survey. To see how your favorite surgical techniques and maneuvers compare with theirs, read on.

Surgeons' Preferred IOL Fixation Method in the Absence of Capsular Support



Suturing an IOL

When faced with an IOL that has little or no capsular support, a good number of surgeons (29 percent) turn to the Yamane technique. This is an increase of 13 percentage points compared to last year's survey. Twenty-eight percent of the respondents use an anterior-chamber IOL and 7 percent perform a form of scleral fixation other than Yamane. The rest of the results appear in the graph above.

"I like the Yamane technique because of its relative simplicity," says Robert Bullington Jr., MD, of Phoenix. "It's the least-invasive and gives very stable IOL fixation," says another surgeon. Jonathan Adler, MD, of Bradenton, Florida, notes, "[Yamane] places the lens in the best position and is stable." A surgeon from Montana agrees, saying, "The Yamane technique is predictable."

A surgeon from Virginia prefers to use an anterior-chamber IOL. "The outcomes are equal [to other methods] but it's done quicker for the patient (they can see sooner)," he says. Richard Wieder, MD, of Missouri also uses AC IOLs in these situations, because the procedure is "Quick and very straightforward." Mechanicsville, Virginia, surgeon D. Alan Chandler opines, "I would do an iris-fixated approach but sometimes it doesn't work well."

Managing Astigmatism

Surgeons also delved into the various ways they tackle a patient's

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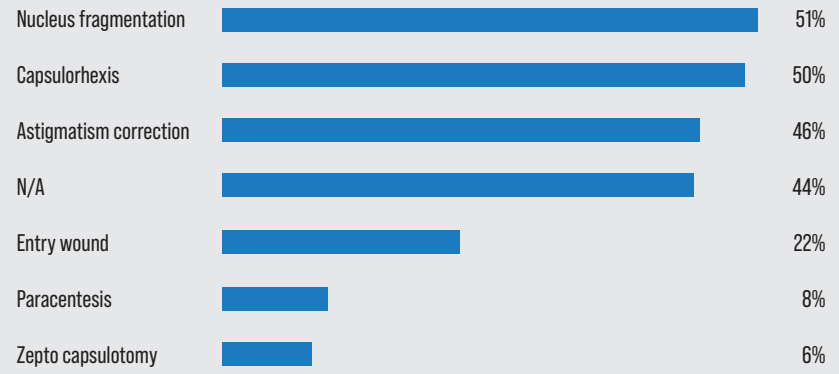
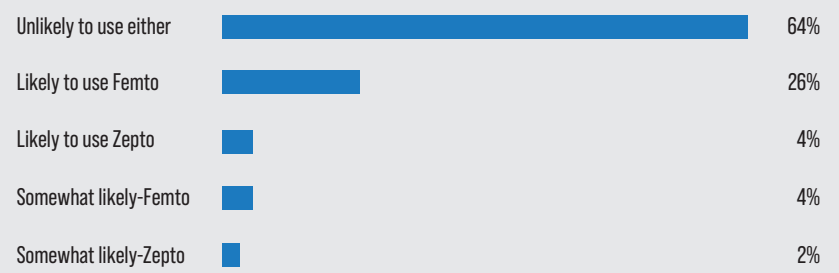
Surgeons' Use of Femto or Zepto for Cataract Surgery



Likelihood of Using Femto or Zepto in the Coming Year



How Surgeons Manage Pre-existing Astigmatism

existing astigmatism.

The most popular option is a toric IOL, chosen by 55 percent of the respondents. Combining a toric with placing the entry wound on the steep axis comes in second, with 12 percent, tied with combining a toric lens with femto astigmatic keratotomy. The rest of the options and their results appear in the graph above.

"Toric IOLs, when guided by intraoperative aberrometry, provide excellent astigmatism improvement," says Dr. Wieder. A surgeon from California feels similarly, saying, "[Toric IOLs] are reliable and don't weaken the cornea or require me to change my incision site."

"Using a toric IOL typically provides a more predictable and better postoperative outcome," Dr. Bullington says. "I'll also place my incision along the axis of astigmatism, depending upon the amount and axis of the astigmatism." Marc Michelson, MD, of Birmingham, Alabama, says he often goes the toric IOL route because, he says, it's a "one-step process and there's no alteration in the corneal architecture. Resort to postop refractive procedures as needed."

Ligaya Prystowsky, MD, of Nutley, New Jersey, uses a toric lens but combines it with an entry wound on the steep axis. She says, "I've used the femto when available but with toric IOLs at a higher power now, [the remaining astigmatism] is not as significant and I can add sutures for the last diopter if necessary."

Other Technology Options

Some surgeons rely on various technologies that they say enhance their results.

• ***Femtosecond laser and Zepto.*** On this year's survey, 56 percent of the surgeons say they use either the femtosecond laser or the Zepto in their cataract surgeries. Of these, 10 percent use the Zepto device for capsulotomy creation, the rest use a femtosecond laser for one or more stages of the procedure. The most popular use of the femto is to create the capsulorhexis (chosen by 50 percent of the surgeons), followed by nuclear fragmentation (48 percent). The surgeons could choose more than one answer for this question. The breakdown for the rest of the uses appears in the graph on the left.

William Lipsky, MD, of Houston, says he sees both pros and cons to using the femtosecond. "It definitely makes it easier to fragment a very hard lens," he says. "I use it for astigmatism. I didn't find the main incision or paracenteses [creation] helpful."

G. Peyton Neatrour, MD, of Virginia Beach, says he uses the Zepto for capsulotomies, and comments: "I like the precision, accuracy and safety that surpasses human hands."

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surgeons who don't use either the femto or the Zepto, 26 percent say they're "likely" to begin using the femtosecond for some aspect of the surgery in the coming year, and 4 percent say they're "somewhat likely" to do so. Four percent say they're "likely" to use the Zepto for capsulotomy creation, and 2 percent say they're "somewhat likely" to use it.

• ***Intraoperative wavefront aberrometry.*** On this year's survey, 47 percent of the surgeons use this technology (ORA System, Alcon) to help them place the appropriate IOL. Fifteen percent say it's "excellent," 21 percent think it's "good," 8 percent say it's "fair," and 3 percent deem it "poor."

"It's helpful to better determine the spherical power of the IOL in real time," says a Michigan surgeon. "It's also helpful with aligning toric IOLs." A surgeon from Montana says the technology is "good," but it's not foolproof, and you still need to be ready to do some surgical decision-making. "I've used it for more than eight years," he says. "Once an incision is made on the cornea and the incision is manipulated during phacoemulsification/use of instrumentation, the ORA measurements are affected… sometimes significantly. Like they say about bear spray, 'it's not brains in a can.'"

Opinions on Meds

Surgeons shared their perspective on maintaining an adequate pupil during surgery, as well as managing postop inflammation and preventing infection postop.

To promote a wide pupil during their procedures, the largest proportion of surgeons on the survey use an intracameral injection of epinephrine and lidocaine (49 percent). Twenty-three percent use Omidria (phenylephrine and ketorolac injection, Omeros), which is up from 17 percent on last year's survey. Seventeen percent use some sort of mechanical means, such as the Malyugin ring, the I-Ring, or a Kuglen hook/Beckert rotator combination.

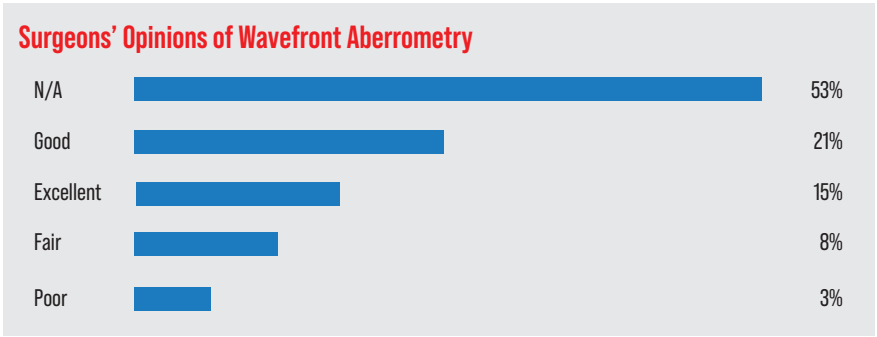
Topical is still tops when it comes to managing patients postop, say surgeons. Fifty-four percent of the respondents say they use separate topical anti-inflammatories and antibiotics postop. Jon S. Jacobson, MD, of Scottsdale, Arizona, says the all-topical route "is safe and effective."

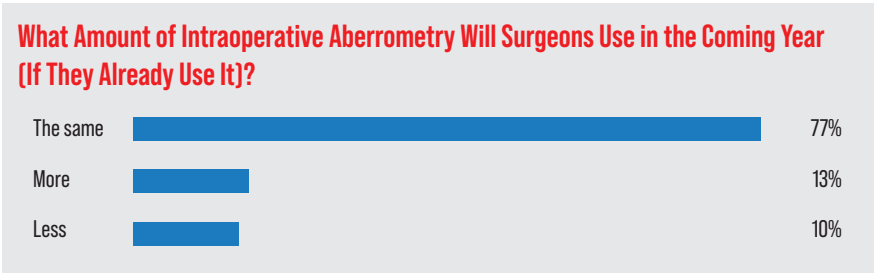
The percentage who use a combined topical mixture of these drugs was the next most popular option, chosen by 13 percent of surgeons. The breakdown of the popularity of the options appears in the graph above. Interestingly, an intraocular injection of combined antibiotic/steroid was more popular this year compared to last (9 percent vs 4 percent in 2022).

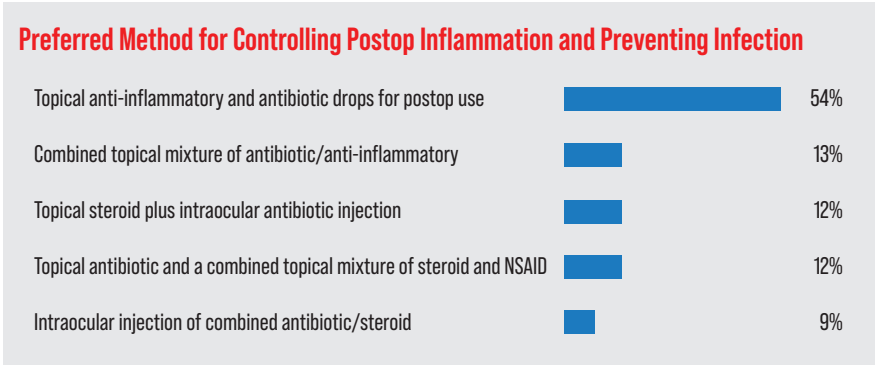
"The hospital forbids compounded drops," says New Jersey's Dr. Prystowsky. "The surgicenter where I operate allows intracameral Trimoxi."

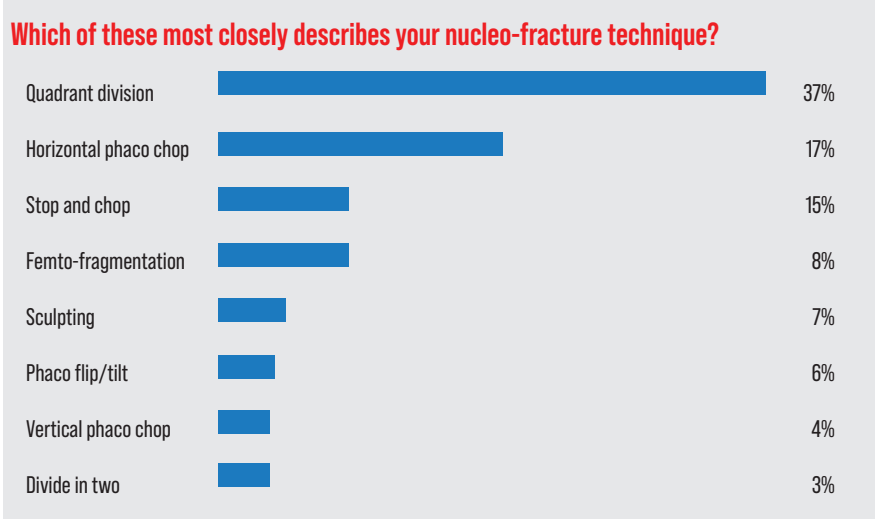
Breaking Up the Nucleus

Surgeons also shared their favorite methods for attacking









the nucleus.

Quadrant division led the way again this year, but not by as much as in years past; 37 percent of the surgeons chose it, compared to 46 percent last year. "I have the most comfort level [with quadrant division] after doing it for many years," says Dr. Prystowsky. "[I like its] safety, and the fact that it's dependent on instruments that are available in the facility, both at the hospital and in surgicenters."

Though it may take a year or so to say this is a true trend, horizontal phaco chop made a big jump in the rankings, going from just 5 percent of surgeons choosing it last year to 17 percent on this year's survey. "It's useful for any density nucleus," says Colorado Springs surgeon Steve Dewey. "It puts far less stress on the zonules than a technique involving trenching."

The next most popular approach is stop-and-chop, chosen by 15 percent of the respondents. The full results of surgeons' nucleo-fracture preferences appear in the graph to the left.

Pearls

Surgeons also shared their best pearls. Some of them include:

- Consider ECCE for rock hard nucleus cases.
- If there's even minimal wound leakage at the end of the case, put in a 10-0 Vicryl suture. It'll dissolve in four to six weeks, and any induced cylinder will resolve without further treatment.
- Adapt your technique to each case. One size does NOT fit all.
- No premium intraocular lenses in super high anxiety/Type-A personality patients!
- Anchor your hands on the patient's face so you can move in sync with him.
- Be prepared by knowing the AXL, ACD, CCT and lens thickness. It'll guide your phaco settings and make surgery safer, barring zonular dehiscence, which you'll feel during the capsulorhexis.
- Make sure nuclear hydrodisection is performed adequately to make the remaining surgery much more straightforward.
- Use dispersive viscoelastic to prevent PC tears. Re-inject frequently, especially in the later stages of nucleus removal.
- Be patient.
- Keep it simple. ◀

IOLS & CATARACT SURGERY IN GLAUCOMA PATIENTS

These patients have more options today, but IOL choice and cataract removal still require a careful approach. Here's guidance.

CHRISTINE YUE LEONARD
SENIOR ASSOCIATE EDITOR

Cataract surgery is a valuable adjunctive treatment for glaucoma. Alone, it's been shown to reduce intraocular pressures in patients with glaucoma and ocular hypertension, and it opens up the possibility of combining cataract removal with a minimally invasive glaucoma surgical procedure in mild to moderate cases. However, selecting a lens implant and performing cataract surgery in glaucoma patients may be less straightforward than in those with healthy eyes.

Here, cataract surgeons and glaucoma specialists discuss considerations for these patients undergoing cataract extraction, share surgical pearls and tips for choosing lens implants and offer advice on postoperative steroid management.

Less (Disease) is More

In general, the less glaucoma a patient has, the better. "You'll get a better outcome in milder cases because you're not competing with other levels of impairment," says Constance O. Okeke, MD, MSCE, of Virginia Eye Consultants in Norfolk. "So, patients who have ocular hypertension, glaucoma suspects or those with very mild, pre-perimetric glaucoma are going to be great candidates if they're also well-controlled and if their visual fields have very minimal peripheral defects. These are the patients you should consider pushing the envelope to offer them multifocals or extended-depth-of-focus IOLs."

"Poor candidates may include patients with advanced disease, any kind of central visual field defect, poorly controlled disease or at high risk for progression," she says. "These patients may need a trabeculectomy or tube shunt and won't do well with advanced-technology lenses because of the astigmatism these procedures can create."

As with any cataract or refractive procedure, addressing ocular surface issues is important for achieving good measurements and good outcomes. However, if the patient is on a heavy medication load, it may be difficult to get their ocular surface under control, Dr. Okeke points out. "We have to do what we can to improve patients' ocular surfaces, whether that's by using artificial tears, medications such as Restasis or Xiidra, removing excess lid debris or treating the meibomian glands.

"I use a number of different treatments for meibomian gland rehabilitation such as iLux, LipiFlow and BlephEx," she says. "I offer these in addition to recommending vitamins and warm compresses for long-term care. It's important to address all aspects of ocular surface disease prior to surgery and then also let the patient know they may be dealing with some of these issues after the surgery as well."

Set Expectations

For those who are candidates, Dr. Okeke says that setting expectations before surgery in a way that's understandable by the patient is vital. "I always have a visual field that's at least three months old or from that day to show the patient where they are with their glaucoma," she says. "I explain to them in pictorial form what a normal visual

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Dr. Okeke discloses consultant, researcher and/or speaker relationships with Alcon, Allergan, New World Medical, Sight Sciences, Santen, Nova Eye Medical and Glaukos. **Drs. Frenkel** and **Grayson** have no related financial disclosures.

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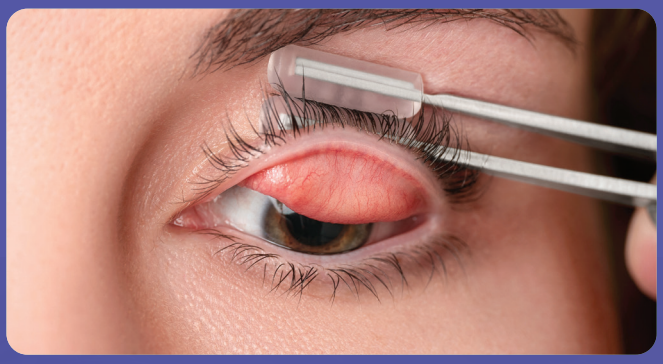

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field looks like, and then I show them what their visual field looks like. I explain to them where their blind spot is naturally and where the blind spots are from glaucoma.

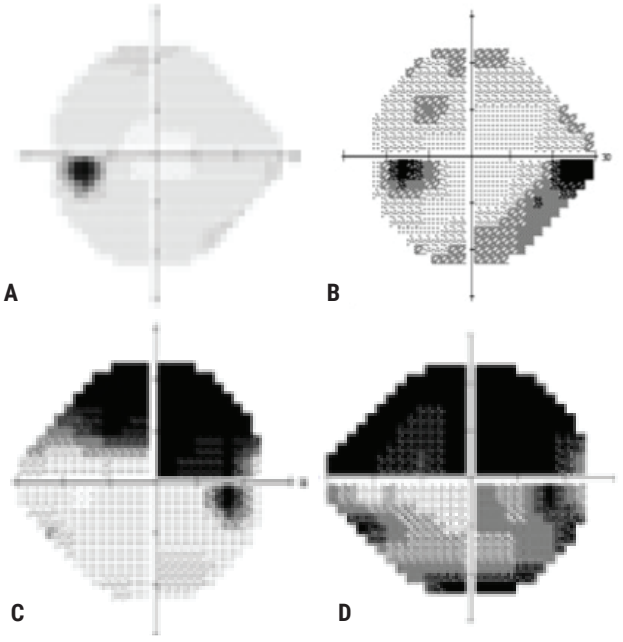
"Then, I put my hand over the visual field and say, 'A cataract is like a film on top of this. When I move the cataract away, what's left are the areas that can be enhanced. So, a light gray area on the visual field is where you can expect to have enhanced vision. Any dark gray to black areas are permanently damaged spots from glaucoma.' Patients need to have an understanding of where their glaucoma is so they can understand that after the surgery, when the cataract is gone, what's left is their glaucoma," she says. "Now, that's the set expectation as opposed to having them wonder why they're not seeing better and thinking the surgery was supposed to cure their glaucoma."

For patients with moderate to advanced glaucoma, Dr. Okeke says a frank discussion about visual fields is also needed. "If they have central fixation loss, then it's really important to let the patient know that you feel premium lenses may not be as beneficial to them and may actually make their vision worse, in terms of contrast sensitivity and vision quality. For patients who aren't candidates for extended-depth-of-focus or multifocal lenses, adding a presbyopia drop as a secondary solution to a monofocal IOL set for distance may offer some advantage."

Which Lenses Can You Offer?

When trying to choose a lens implant for a glaucoma patient, experts say they consider the patient's age, the severity of their disease, the number of medications they're on and the state of their ocular surface (*Figure 1*). "If I saw two patients with mild glaucoma—one younger and one older," says Joshua Frenkel, MD, of Evergreen Eye Center in Auburn, Washington, "I may be more cautious in the younger patient, who has greater potential for future vision loss, than the older patient who's farther along in age and perhaps less likely to progress."

If patients want less dependence on glasses, there are trade-offs, Dr. Okeke points out. "Patients who have glaucoma already have reduced contrast sensitivity and may be sensitive to glare, so certain premium options may be off the table," she says.



Constance O. Okeke, MD

Figure 1 A-D. (A) Patient is a candidate for a multifocal, an EDOF or a toric lens. (B) Patient is a candidate for an EDOF or toric lens. (C) Patient is a toric candidate. (D) Defer from advanced-technology IOLs.

Monofocals are the safest choice for patients with preexisting ocular pathology since they don't split light, but not all glaucoma patients are limited to the standard lens. Dr. Frenkel says, "Though multifocals can be used in patients with mild glaucoma, I tend to be a bit on the conservative side, in the sense that I'd probably recommend an extended-depth-of-focus lens, such as Vivity or Symfony, if a mild glaucoma patient desired a little more range of vision.

"For a moderate to severe patient, you're certainly going to lean toward recommending a monofocal," he continues. "Once the patient has a certain amount of loss of contrast sensitivity, they'll be more likely to notice any drop-off in vision with a premium lens."

He says Eyhance or the Light Adjustable Lens are appropriate options for glaucoma patients. "The LAL is a monofocal, but you can induce some extended depth of focus, though I wouldn't induce a large amount in an advanced glaucoma patient," he adds. "The LAL also does well with blended vision, so you can give patients something similar to the premium result they're looking for with good accuracy for their glaucoma."

Dr. Okeke cautions that monovision may not be a good option in certain glaucoma patients. "I tend to dissuade patients from monovision who have moderate to advanced glaucoma in one eye and very mild glaucoma in the other eye because they'll be putting all the 'weight' of vision on one eye," she says. "If you have significant glaucoma in one eye, it's likely that there will be greater risk for progression in that eye, so at some point, they won't be able to use that eye well for monovision function and they'll be back in glasses."

Toric lenses are another strong option for glaucoma patients who wish to have their astigmatism corrected. Since these IOLs don't split light, they enable a glaucoma patient to see a specific focal point with their best vision, Dr. Okeke explains. "There are a number of premium toric options including the Tecnis toric, Eyhance, AcrySof IQ toric and EnVista toric," she says.

To treat ocular inflammation and pain following ophthalmic surgery or ocular itching associated with allergic conjunctivitis.

DEXTENZA KEEPS PATIENTS COMPLIANT AND SATISFIED[1-3*]

A hands-free advancement in ophthalmic steroid treatment.[1,4]
Easy-to-insert[†] and preservative-free intracanalicular DEXTENZA offers patients a satisfying post-op experience—providing up to 30 days of sustained steroid coverage.[1-5]

INDICATIONS

DEXTENZA is a corticosteroid indicated for:

- The treatment of ocular inflammation and pain following ophthalmic surgery.
- The treatment of ocular itching associated with allergic conjunctivitis.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DEXTENZA is contraindicated in patients with active corneal, conjunctival or canalicular infections, including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella; mycobacterial infections; fungal diseases of the eye, and dacryocystitis.

WARNINGS AND PRECAUTIONS

Intraocular Pressure Increase - Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. Intraocular pressure should be monitored during treatment.

Bacterial Infections - Corticosteroids may suppress the host response and thus increase the hazard for secondary ocular infections. In acute purulent conditions, steroids may mask infection and enhance existing infection.

Viral Infections - Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).

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Delayed Healing - Use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation.

Other Potential Corticosteroid Complications - The initial prescription and renewal of the medication order of DEXTENZA should be made by a physician only after examination of the patient with the aid of magnification, such as slit lamp biomicroscopy, and, where appropriate, fluorescein staining. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.

ADVERSE REACTIONS

Ocular Inflammation and Pain Following Ophthalmic Surgery

The most common ocular adverse reactions that occurred in patients treated with DEXTENZA were: anterior chamber inflammation including iritis and iridocyclitis (10%), intraocular pressure increased (6%), visual acuity reduced (2%), cystoid macular edema (1%), corneal edema (1%), eye pain (1%), and conjunctival hyperemia (1%). The most common non-ocular adverse reaction was headache (1%).

Itching Associated with Allergic Conjunctivitis

The most common ocular adverse reactions that occurred in patients treated with DEXTENZA were: intraocular pressure increased (3%), lacrimation increased (1%), eye discharge (1%), and visual acuity reduced (1%). The most common non-ocular adverse reaction was headache (1%).

Please see adjacent Brief Summary of full Prescribing Information.

*93% (187/201) DEXTENZA patients were satisfied with the insert in the Phase 3 Study for the treatment of ocular inflammation and pain following ophthalmic surgery.[3]

†73.6% of physicians in Study 1, 76.4% in Study 2, and 79.6% in Study 3, for the treatment of ocular inflammation and pain following ophthalmic surgery, rated DEXTENZA as easy to insert.[2,5]

References: 1. DEXTENZA [package insert]. Bedford, MA: Ocular Therapeutix, Inc; 2021. **2.** Tyson SL, et al. *J Cataract Refract Surg*. 2019;45(2):204-212 [erratum in: 2019;45(6):895]. **3.** Data on File 00837. Ocular Therapeutix, Inc. **4.** Sawhney AS, Inventors, et al. Incept, LLC, Assignee. Drug Delivery Through Hydrogel Plugs. US Patent 8,409,606 B2. April 2, 2013. **5.** Walters T, et al. *J Clin Exp Ophthalmol*. 2016;7(4):1-11.

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"Eyhance is a newer lens that has a continuous change in power from the outside in, which allows for both strong distance and enhanced intermediate vision."

One thing to consider with toric lenses is that glaucomatous eyes often have small pupils. "You may need to use pupil expanders in these eyes," Dr. Okeke says. "Afterwards, when removing the pupil expander, the pupil can come down, and this can sometimes limit your view of the toric markings, so you have to be able to manipulate the eye to ensure the lens is appropriately aligned.

"Also, be cognizant of zonular weakness," she adds. "You may have a patient with pseudoexfoliation who shows no signs of zonular dehiscence at the time of surgery, but it's still a good idea to prevent that from happening and use a capsular tension ring for extra stabilization.

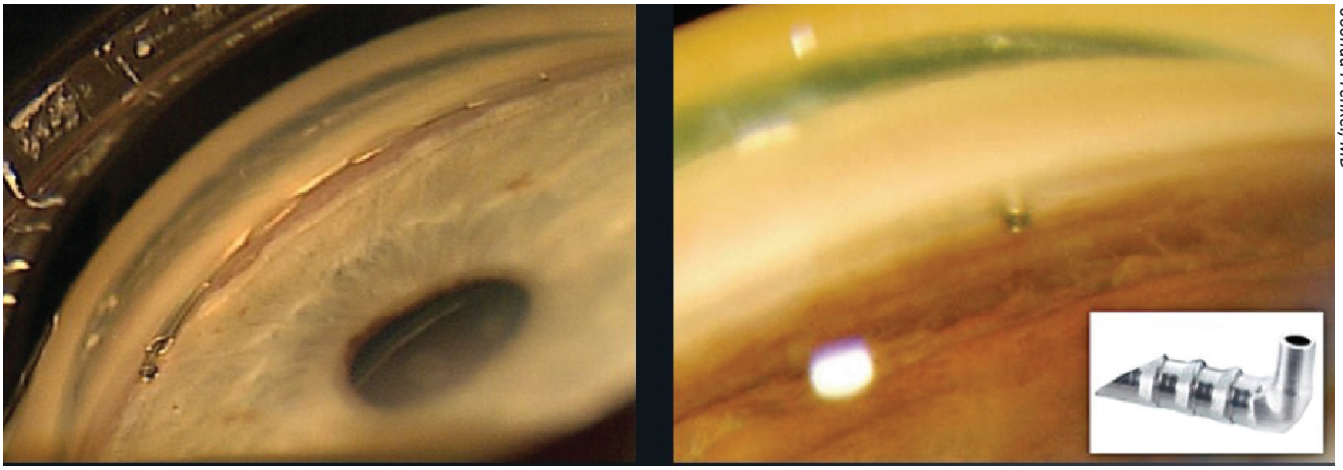
"I don't combine toric IOLs with trabeculectomies or tube shunts because of the inconsistency of the outcomes and the potential development of astigmatism afterwards," Dr. Okeke notes. "I'd give the patient at least six months or more to have a stable refraction and then do the cataract surgery, with the expectation of a good outcome if they have a good field of central vision."

Douglas K. Grayson, MD, of Omni Eye Services in the New York Metro Area, points out that postoperative glaucoma bleb patients will benefit from a toric lens if their bleb-induced astigmatic error is stable. "These patients have to be followed for a while," he says. "If the bleb is overgrowing onto the cornea, you may one day have to revise it by physically minimizing its intrusion. Then, whether you want to use a toric lens or not depends on how true the toricity induced in the cornea is."

He says multifocal and extended-depth-of-focus IOLs can be used successfully in glaucoma patients, with certain caveats. "We've been successfully using multifocal lenses in glaucoma patients—mild, moderate and borderline-severe—depending upon where the defect is," he explains. "Now, if a patient has advanced field loss with a central island, they've had so much loss of contrast sensitivity already from their glaucoma that using a multifocal lens wouldn't be a good idea. In patients with superior arcuate defects and clear inferior hemifields, however, we've had success using Symfony and PanOptix.

"The hedge for most of my team is to use something like Symfony rather than PanOptix because the EDOF lens tends to be a little more forgiving of power fluctuations," he continues. "Whether you're off by half a diopter plus or minus, patients still seem to do very well, as opposed to the trifocal where precision calculation is particularly important."

He adds that implanting a PanOptix lens in a patient with a filtering bleb and a low pressure can be problematic. "A patient with a filtering bleb and a pressure of 6



Joshua Frenkel, MD

Figure 2. A Hydrus and a first-generation iStent in the angle. Dr. Frenkel demonstrates a Hydrus implantation in a video available in the online version of this article at reviewofophthalmology.com.

mmHg will have their axial length affected," he says. "If they have cataract surgery and their bleb tends to fail, the pressure could go back up to 25 mmHg and that would change the size and contour of their eye and alter the refraction. We've been successful using multifocals in patients who've had filtering operations, so we don't think that's a contraindication, but in more severe cases, it's an individual discussion and judgment call with the patient."

Multifocal lenses can lead to OCT artifacts, and the reduced contrast sensitivity can decrease one's ability to monitor visual fields, Dr. Okeke notes. "It's important to keep this in mind," she says. "However, it seems that patients who have mild, pre-perimetric glaucoma and glaucoma suspects can do well with multifocals. If reduced visual field encroaches anywhere close to fixation, multifocals aren't ideal."

She says that Vivity is a good option for certain glaucoma patients. "The lack of diffractive rings means there's less visual disturbance and fewer halos," she explains. "The fact that Vivity doesn't split light helps with the issue of contrast sensitivity. It's enabled more glaucoma patients to be premium IOL candidates."

Dr. Grayson says that some normal-tension glaucoma patients can also receive premium lenses. "Normal-tension glaucoma's effects tend to be near fixation and these patients tend to be younger and need lower pressures," he says. "In terms of doing the cataract surgery, they're still going to have a MIGS. Depending upon how severe their visual field loss is, I'd still do a multifocal lens if they had even some damage around fixation, as long as it wasn't too extensive."

Dr. Frenkel says that depending on the level of visual field changes, he'd treat normal-tension glaucoma patients similarly to those with primary open-angle glaucoma. "Anecdotally, (n= a few), I've noticed that some normal-tension glaucoma patients who have cecocentral scotoma tend to have more significant glare," he notes. "So, for some of them, I'd consider a lens that has a very low amount of glare such as the LI60AO from Bausch + Lomb, optic-captured in the sulcus.

"I once had a normal-tension glaucoma patient who complained of some glare before," he continues. "We thought it was due to cataract, but after we took his cataract out, his glare intensified. He had a monofocal and a great result, but we wound up exchanging it for a three-piece lens that we put in the sulcus with optic capture to reduce glare, which did help some. So, it seems some patients with visual field deficits close to fixation may be more sensitive to glare."

MIGS and Cataract Surgery

Experts say it's more or less become standard practice to perform a MIGS procedure in someone who's on multiple glaucoma medications and is undergoing cataract surgery, in order to try to restore vision, minimize medication burden and control intraocular pressures.

"With a few exceptions, I'd consider doing a combined procedure in almost any patient who has glaucoma with an angle that can be treated and a cataract that's significant," Dr. Frenkel says. "You can combine many of the MIGS procedures with cataract surgery, including goniotomy procedures such as Trabectome and the Kahook Dual Blade; gonioscopy-assisted transluminal trabeculectomy; stents such as iStent, iStent Infinite and Hydrus (*Figure 2*); canaloplasty such as ABiC with iTrack or Visco360; subconjunctival such as Xen; and the combined Omni."

(To view a video of Dr. Okeke performing femtosecond laser combined cataract and MIGS surgery, go to https://youtu.be/evvQ6ZrJtVo.)

Dr. Grayson's MIGS procedure of choice is goniotomy using a

Kahook Dual Blade (*Figure 3*). "The procedure doesn't involve implanting any material that can be obscured by peripheral anterior synechiae, which is especially useful in the chronic angle closure patients who will always tend to form PAS at a higher rate," he says. "I find that removing the anterior wall of Schlemm's canal is a safe, effective and minimally traumatic approach. Stents, on the other hand, may be difficult to implant in a chronic angle-closure patient due to synechiae, and canaloplasty induces more trauma to the trabecular meshwork which may result in a higher rate of hyphema and regression to higher pressures."

Dr. Grayson says he considers Xen procedures somewhere between trabeculectomy and MIGS procedures. "Any of the Xen procedures are done in combination with mitomycin," he explains. "If you don't get mitomycin, the Xen is destined to fail. And once you start doing cataract surgery and giving mitomycin subconjunctivally, you're really entering the realm of true glaucoma-specialist surgery and that's not typically something that the comprehensive ophthalmologist wants to deal with. Mitomycin has a higher risk of inducing hypotony. That's why I don't really consider Xen as a MIGS. To me, the goniotomy and stent groups have a risk profile that's roughly zero, whereas with Xen, the risk profile is somewhat higher than zero and thus becomes a true glaucoma procedure."

When should a comprehensive ophthalmologist think about referring the case? Dr. Grayson says that if a patient has severe glaucoma with pressures that aren't adequately controlled, "certainly the comfort level of doing trabeculectomy or Xen is up to that individual comprehensive ophthalmologist. If they perform a combined MIGS (e.g., goniotomy) and cataract surgery, then it's important for the patient to be aware that there's a real chance their glaucoma could still go out of control, in which case they'd be referred to a glaucoma specialist. It's important for comprehensive ophthalmologists to have relationships with glaucoma specialists if they're doing a lot of MIGS procedures."

Dr. Okeke notes that if you're considering adding a MIGS procedure, ensure your patient has at least 180 degrees of viable angle tissue to perform the MIGS and has controlled IOP. "An eye with an open angle, mild to moderate glaucoma and with one to three medications is an ideal candidate for MIGS," she says.

What about using a femtosecond laser to perform the cataract surgery? Experts say using femto for cataract surgery in glaucoma patients is an excellent option, particularly for addressing astigmatism. "It's good for low levels of astigmatism correction and for premium lenses, which benefit from the consistent capsulorhexis size and location a femtosecond laser can create," Dr. Frenkel says. "Some doctors aren't fans of FLACS in general and, theoretically, the IOP does rise for 15 to 25 seconds,

but the pressure isn't going to be much higher than it is at times during cataract surgery, so I don't believe the risk is much higher. The benefits of femto in glaucoma patients are similar to those in non-glaucoma patients."

"It's a matter of how much phaco energy you need to break up the cataract, and there's always less energy needed with femto, so I really have no contraindication to using femto in glaucoma patients," Dr. Grayson says, who uses the Catalys laser. "Femto also offers a more stable capsulotomy. In patients with pseudoexfoliation and zonular compromise where there's a question of lens stability, it's beneficial to have a perfectly circular capsulotomy cut by femto in case you need to use capsular hooks to support the capsule during the phaco procedure. It's a nice added benefit of femto, because very frequently, capsular hooks are needed to stabilize these patients."

When it comes to cataract surgery, there are several potential anatomical considerations in glaucomatous eyes. "Glaucoma patients often have small pupils, as a result of certain drops they may be using such as pilocarpine, or they may have uveitis as a component of their glaucoma, creating synechiae formation," says Dr. Okeke.

"Anterior capsule contraction and posterior capsule opacification are also potential concerns, as well as zonular instability in certain subtypes of glaucoma such as pseudoexfoliation glaucoma," she says. "In these eyes, you'll have to consider the lens position decades out from when the procedure was done. In a combined cataract and trabeculectomy procedure, there may be issues related to postoperative astigmatism creating a refractive error, which will need correction."

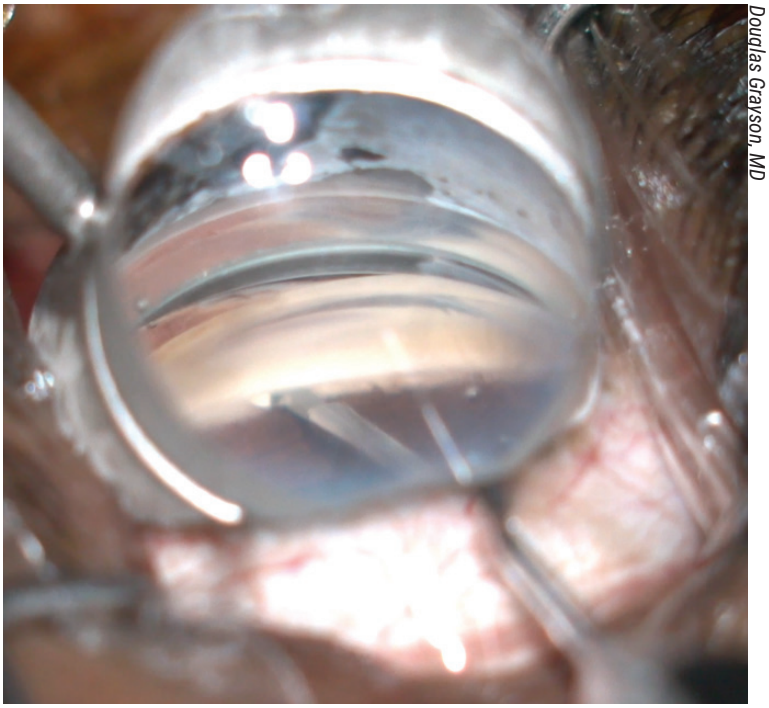
"Cataract surgery works well in patients with pseudoexfoliation glaucoma because the infusion for doing the surgery scatters the pseudoexfoliation material obstructing the trabecular meshwork, usually resulting in a lower pressure," notes Dr. Grayson. "We see a similar effect in pigmentary-dispersion glaucoma. However, in this subtype, patients often have elevated pressures again, whereas the narrower angle or angle-closure patients usually have longer, sustained reductions."

In certain patients with angle-closure glaucoma, cataract extraction may be warranted even if the cataract isn't visually significant. "The EAGLE study confirmed that some patients had a significant lens-induced secondary glaucoma mechanism from a cataract," Dr. Grayson explains. "Cataracts grow thicker, and in someone who's predisposed to narrow angles, the progression of a cataract can actually obstruct the angle. And so, if someone had elevated pressure, a narrow angle and a cataract, cataract surgery alone would lower the pressure.

"Our threshold to take out a cataract went much lower after the EAGLE study came out in 2016," he continues. "A patient may or may not be visually symptomatic

from cataract, but if, for example, they're unresponsive to medications or to iridotomy and clearly have a lens-induced secondary angle-closure mechanism, you may then have an indication to do a lensectomy in someone who's not truly visually symptomatic from the cataract."

Importantly, he adds that the patients included in the EAGLE study had difficulty using their medications or had pressures that were uncontrolled. "Simply having narrow angles and a cataract isn't an appropriate criterion for lensectomy," he says. "I believe that this is a subgroup in which an iridotomy wouldn't be beneficial. It was shown not to benefit the patient, in addition to being less cost-effective than clear lens extraction."



Douglas Grayson, MD

Figure 3A. Douglas K. Grayson, MD, performs the goniotomy after capsulotomy and before phacoemulsification. He says, "Visibility is best with a clear cornea. If there's any hyphema caused by the goniotomy, it won't obscure the creation of the capsulorhexis. The hyphema usually resolves by the end of the case."

Here, the goniotomy blade is used to unroof the anterior wall of the trabecular meshwork with minimal trauma to the canal of Schlemm. A single forehand pass with the KDB Glide engaging the trabecular meshwork, maintaining mild anterior traction and continuing for three to four clock hours results in a clean excisional goniotomy.

Pearls

Here are some pearls for successful cataract surgery in glaucoma patients:

• ***Consider performing the MIGS procedure at the beginning of the case.*** "Most people tend to do their MIGS procedure at the end of the case," Dr. Frenkel says. "For several years, I did it at the end of the case but then at the suggestion of someone, I tried doing the MIGS at the beginning. I found I liked that because the cataract was still in there, maintaining good chamber stability. The amount of bleeding is very minimal after most of these procedures, so it doesn't really obscure the view. I also use less viscoelastic when I do the MIGS at the beginning because I've already filled the chamber with Viscoat at the start of the case.

"I prefer to do the MIGS procedure at the beginning of the cataract surgery now, but it can be done either way," he continues. "It's really a personal preference. For younger surgeons in training, it can be nice because it ensures them a clear view and good opportunity to do the MIGS procedure. Also, if they're just starting out and have a hard time getting [the MIGS done] at the beginning, it gives them a second shot at the end of the case as well when they can try again."

• ***Clear PAS using an iris stretching technique.*** Chronic angle closure patients frequently have PAS that need to be cleared. Dr. Grayson says he prefers a stretching technique for the iris, but if that's insufficient, then he turns to iris hooks. "I don't use Malyugin rings because I feel that they compromise maneuverability in the eye, especially in a hyperope with a shallow chamber with chronic angle closure," he says. "Using iris hooks is a precise way to get pupillary dilation and have more maneuverability in the eye. Plus, if you do need more capsular support, you already have iris hooks in the eye. Those hooks can be moved slightly to engage the capsular bag to give you more stability. If you have a Malyugin ring in place, it can be difficult to get all the additional hooks over the ring to then support the capsular bag. Sometimes you may even take out the ring and put in a clip, which is a lot of maneuvers inside the eye."

• ***Add goniosynechialysis to cataract surgery in angle-closure patients.*** Performing goniosynechialysis in conjunction with cataract surgery is a valuable adjunct in the chronic angle-closure patient, according to Dr. Grayson. "Very frequently, the pressures will come down and stay down and much of the synechiae won't re-form if you clear out the angle and allow better access of the trabecular meshwork to the aqueous," he explains. "Occasionally, I'll do an additional Miostat infusion to keep the pupil down after goniosynechialysis for a few days to allow better aqueous access to the trabecular meshwork."

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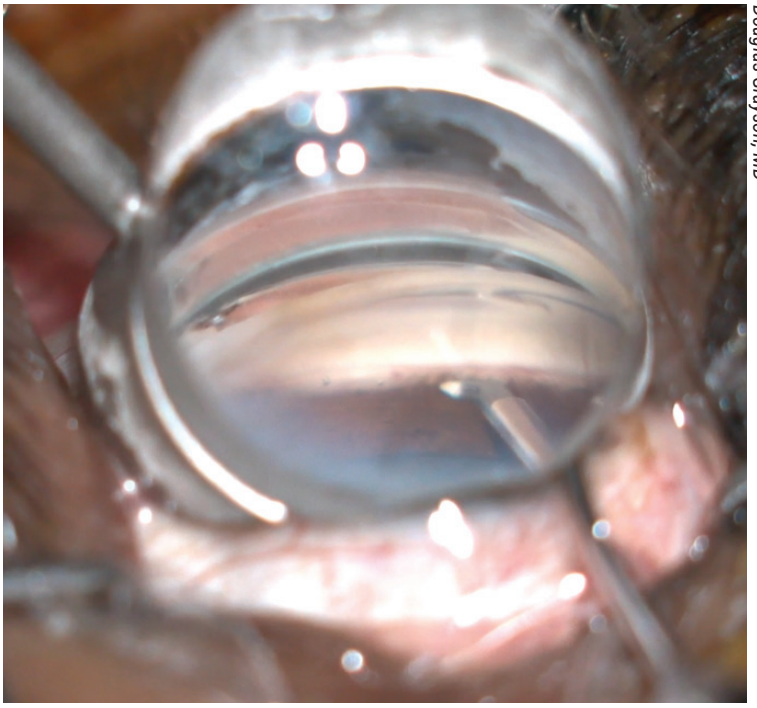
"If a pseudoexfoliation patient has zonular issues, you have to be much more careful disassembling the nucleus," Dr. Grayson says. "I prefer a supracapsular tilt procedure where the nucleus is tilted approximately one-third of the iris plane and the remainder is in the capsular bag. However, this tilt maneuver sometimes places stress on the zonules, which may be compromised, so if I feel there's too much mobility, I'd defer to a quadrantic cracking technique in the capsular bag, which is going to be a little bit less traumatic to the zonules.



Douglas Grayson, MD

Figure 3B. Continuing from Figure 3A, the bunt edge of the KDB Glide can be used for goniosynechialysis and to further open the canal of Schlemm to access anterior chamber aqueous after the anterior wall of trabecular meshwork is removed.

• ***Leave the eye firm in a patient with a previous trabeculectomy.*** These patients may be prone to postoperative hypotony. "If the trabeculectomy is working, you could consider leaving the eye a little firmer, so the pressure doesn't get too low," Dr. Frenkel advises. "I usually recommend leaving the eye very firm at the end of the case to reduce the risk of hyphema. Leaving the firm helps tamponade any bleeding or at least reduces the risk of it. Obviously, you don't want to leave the eye so firm that the pressure makes it so the patient can't see anything. There's a test where you ask the patient if they can see the lights, and if they can't then their pressure is too high.

"Find a balance between leaving the eye firm enough that it's going to reduce the risk of bleeding but don't leave it so high that the patient has really high pressure overnight. You may also consider tapering steroids more slowly if you're worried about the inflammation causing trab or tube failure, though this should be done on a case-by-case basis."

• ***Consider shortening a tube shunt if it's an issue.*** Dr. Okeke says, "If the tube is in contact with the cornea or cataract, you can shorten it using intraocular scissors and Utrata forceps to remove it from the eye; a Sinskey hook through a paracentesis will stabilize the tube as you perform this maneuver. Be sure to use Viscoat to protect the endothelium and reapply as needed during the procedure."

• ***Use a higher steroid regimen in a filtering bleb patient.*** Patients with filtering blebs usually require more aggressive postop steroid treatment to control inflammation. "If you're operating on a cataract in a patient who already has a filtering bleb, you want to ensure you're using a higher postop steroid regimen, such as every two hours, preferably with something like Durezol. Pred Forte and its generics aren't quite as potent. We'll also combine a goniotomy in a patient who's had a filtering bleb if they're on additional medications if their filtering bleb isn't functioning at 100-percent efficiency. So, for someone who's on two medications along with a filtering bleb, we'll do cataract along with goniotomy."

Postoperative Steroids

Monitoring patients' pressures is important. For certain patients, it may be necessary to check them more frequently in the postoperative period to make sure that their pressure hasn't spiked. "Sometimes, after a goniotomy, we'll keep the patients on pilocarpine for a month or so since pilocarpine drops reduce the risk of PAS developing," Dr. Frenkel explains. "I also counsel patients to continue their glaucoma medication while in the immediate postop period, because of the risk of high pressure the day after surgery and the risk of steroid response within the postoperative period. Many glaucoma patients tend to be steroid responders. I tend to say, "Keep on your medications while you're on your steroids, and then we'll reassess after that.' "

Dr. Grayson says that patients who already have glaucoma or patients who are predisposed to developing glaucoma may exhibit steroid response, where using steroids, especially a potent one like Durezol, could cause an elevation of pressure. "These patients need steroids after their cataract surgery to decrease inflammation, so you have to follow them closely," he says. "For example, if a patient had a combined cataract-goniotomy

(Continued on page 62)

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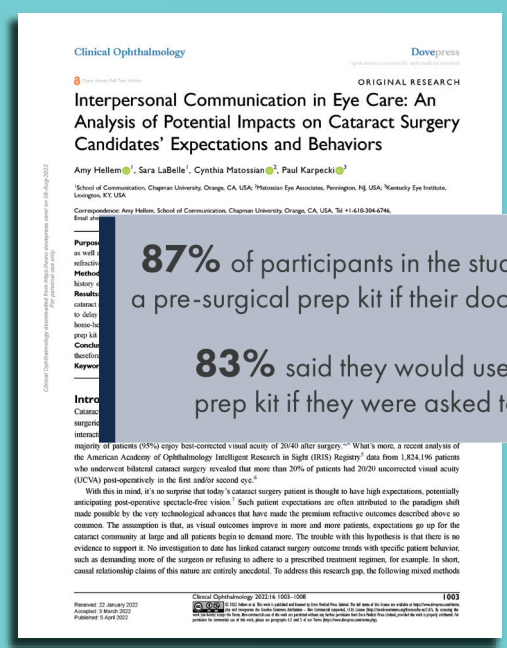

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TREATING DIFFICULT CASES OF WET AMD

New options may turn the tide against tough-to-treat neovascular AMD cases.

MICHELLE STEPHENSON
CONTRIBUTING EDITOR

Retina specialists have been treating neovascular age-related macular degeneration with anti-vascular endothelial growth factor therapies for years. Though it's been remarkably successful for many patients, there are still those few who don't respond to their initial anti-VEGF treatment and need something more. Here, retina specialists discuss how they handle recalcitrant wet AMD.

Starting Treatment

The goal of managing any case of neovascular AMD is to preserve macular function, in particular, at the foveal center. "Typically, that means trying to control the exudation," says New York's K. Bailey Freund, MD. "If we're not having success after a typical monthly loading phase, most retinal specialists, including myself, might try switching agents."

Carl Regillo, MD, in practice at Wills Eye Hospital in Philadelphia, says that he starts treatment with one of the first-generation anti-VEGFs, which include bevacizumab, ranibizumab or aflibercept. "We now have more treatment choices than ever before, but the reality is that most insurance companies mandate bevacizumab first," he says. "It's not by choice, but we usually end up starting with that. If I'm not getting an adequate response, meaning the macula is not completely, or nearly completely, drying within the first three treatments, I'll then switch to on-label ranibizumab or aflibercept and treat a few more times. If the macula is optimally responding, then I'll stick with one of those two drugs. If there's persistent, significant exudation or the patient needs a very frequent treatment regimen to have optimal disease control, I'll think about switching to faricimab next."

He adds that faricimab (Vabysmo, Genentech) has better durability than the first-generation drugs, and it may also achieve better drying in select patients. He is not using much brolucizumab at this time because of the ocular safety issues. "Before faricimab was FDA-approved, I did opt for brolucizumab as the next step in suboptimal responders, but the safety profile's not as good as other anti-VEGFs," Dr. Regillo says.

Dr. Freund agrees. "I haven't been using brolucizumab since the safety issue of occlusive vasculitis emerged; however, during the brief period I used the drug, it seemed that eyes that couldn't be controlled with the other agents responded more robustly to brolucizumab," he says. "The safety issue was very unfortunate, and, in my opinion, this risk usually outweighs the drug's potential benefit, even in patients who aren't optimally controlled."

Physicians will sometimes consider switching from bevacizumab or ranibizumab to aflibercept in tough cases. In one retrospective study, researchers included 282 and 359 eyes "non-switch" (i.e., staying on ranibizumab) and "switch" (switched to aflibercept) cohorts, respectively. The researchers say the cohorts were well-balanced. Though visual

This article has no commercial sponsorship.

Dr. Csaky is a consultant/advisor to Abbvie, Adverum Biotechnologies, Merck & Co, Inc, Ocular Therapeutix, Regeneron, and Ribomic. He is a consultant/advisor to and receives grant support from Genentech/Roche and Novartis Pharma AG. He is a consultant/advisor and receives equity from EyeBio. **Dr. Regillo** is a consultant to 4DMT, Adverum, Aldeyra, Allergan, Annexon, Apellis, Aviceda, Genentech, Iveric, Kodiak, Merck, NGM Biopharmaceuticals, Notal Vision, Novartis, Ocugen, Opthea, Ray, Regenxbio, Regeneron, Stealth Biotherapeutics, Takeda, Thea and Zeiss. **Dr. Freund** is a consultant to Bayer, Genentech, Novartis and Regeneron.

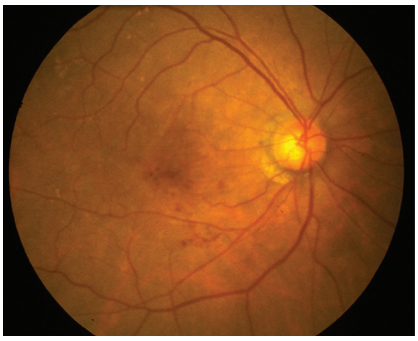
acuity remained stable during the observation period in both cohorts of eyes, the researchers say that optical coherence tomography images demonstrated lower prevalence of intraretinal and subretinal fluid as well as pigment epithelial detachment at 12 months in eyes subjected to switch of anti-VEGF agent compared to the non-switch eyes.[1]

In another study, researchers analyzed 164 eyes (101 were switched from bevacizumab to aflibercept (group 1) and 63 from ranibizumab to aflibercept (group 2). One year after the switch, there was an overall nonsignificant mean decrease of two ETDRS letters in BCVA. Three years after switching, there was an overall mean decrease of seven ETDRS letters, which was statistically significant. However, they noted a significant improvement in the mean central retinal thickness was found at one, two and three years. They say that aflibercept can be useful in the management of refractory neovascular AMD, with a good morphological response. However, in the long-term, it didn't achieve BCVA stabilization.[2]

Vabysmo

Looking at relatively newer arrivals on the AMD scene, according to Karl Csaky, MD, PhD, in practice in Dallas, many retina specialists who treat tougher cases of AMD are now considering Vabysmo [faricimab-svoa, Genentech], with some saying they might even use it for initial therapy.

"There hasn't been anything new for wet AMD since aflibercept was approved over a decade ago, until the recent introduction of Vabysmo," Dr. Csaky says. "Many of us are considering Vabysmo now that there are more real-world data to suggest that it's safe and that we're not seeing anything that's of concern. Some of my colleagues are even starting to consider Vabysmo as an initial therapy, and I think that's completely reasonable given the clinical data. In many cases, Vabysmo may be a very good alternative to other therapies. We're in a transition zone to fully appreciate what the full impact of Vabysmo will be on real-world utilization."



Agents that act on different forms of VEGF, come in higher doses or use sustained-delivery may help in tough AMD cases.

Vabysmo is the first FDA-approved treatment designed to block both VEGF-A and Ang-2 in wet AMD. It's been shown to improve and maintain vision with treatments from one to four months apart in the first year following four initial monthly doses. Based on positive results across four Phase III studies in wet AMD and DME, it was approved by the FDA in January 2022. The studies consistently showed that patients treated with Vabysmo given at intervals of up to four months achieved non-inferior vision gains compared to aflibercept (Eylea, Regeneron) given every two months in the first year. It was well-tolerated in all four studies, with a favorable benefit-to-risk profile. The most common adverse reaction was conjunctival hemorrhage, which was reported in 7 percent of patients.[3]

According to Dr. Csaky, Vabysmo is following the aflibercept model. "If we look at what happened 10 years ago when Eylea came out, we went right into using Eylea for the refractory cases and trying to understand its full impact," he says. "We were beginning to feel comfortable that the safety profile was good, and then it was just a question of determining the full potential of the drug. We had refractory cases of patients on Lucentis who then did very well on Eylea."

The real question with any new AMD drug is its durability. "Vabysmo was approved just over a year ago, and some practices are just starting to feel comfortable enough to use it," Dr. Csaky explains. "I don't think we have the full stamp of approval yet, but it's now clearly a nice alternative to consider once you've gone through the typical switching and looking to try to treat and extend. There are still questions about whether it needs to be loaded, or whether we can treat and extend right away."

Dr. Freund adds that faricimab appears to be a bit more robust in its ability to dry and possibly extend the duration between injections than the other agents, excluding brolucizumab. "I was cautious in starting to use faricimab after I saw a patient develop occlusive vasculitis with brolucizumab," he says. "My impression of faricimab is that I'm not seeing as big of a benefit as I saw with brolucizumab compared to the other anti-VEGFs. But, it does seem to help control exudation better than the other agents in some of these refractory cases. Although I might be able to reduce or resolve fluid in some of those incomplete responders, I haven't been able to extend the injection interval more than a week or two. I think we have to manage expectations because, in the clinical trials, there were patients who could go to these very long treatment intervals of 12 to 16 weeks. If an eye already can't be controlled or extended with the current agents beyond a month, it's unrealistic to think that switching to faricimab will be able to both get rid of the exudation and also extend to a very long interval. Patients who can be extended are more likely going to be treatment-naive cases, which tend to respond more robustly after the first injection."

PCV Patients

Polypoidal choroidal vasculopathy is often considered more refractory to anti-VEGF therapy than other neovascular AMD cases, according to Dr. Freund. "That may be because there are dilated vascular elements

within the neovascular lesion," he says. "Also, these eyes often have choroidal features that overlap with CSR and indicate choroidal venous congestion that may drive fluid into the subretinal and intraretinal spaces. So, in those cases, it might be desirable to initiate treatment with one of the more potent agents, such as aflibercept or faricimab."

He adds that high-dose aflibercept, currently under FDA review, might be an effective alternative to use in eyes that might benefit from a more aggressive therapy to get them under control. "Rarely, I also will use photodynamic therapy in PCV cases," he says. "But, unlike some colleagues, I feel that using combination therapy at the initiation of therapy isn't an effective long-term strategy for PCV. PCV patients typically present 10 years younger than our typical age-related macular degeneration patients of Western European ancestry. While combination therapy may seem effective for several years, recurrences occur because the treatment targets just the polypoidal lesions and not the larger neovascular complex referred to as a 'branching vascular network.' New polyps typically occur, and visual outcomes for eyes receiving multiple PDT treatments are often poor. I've learned through experience that this reactive strategy often fails due to these unpredictable recurrences."

Dr. Regillo also occasionally uses verteporfin photodynamic therapy in these patients with PCV. "It's the only photosensitizing drug that's FDA-approved for photodynamic therapy," he notes. "The chances of me needing photodynamic therapy is really rare. In fact, less than 1 percent of neovascular AMD ever gets photodynamic therapy nowadays."

Other Treatments

Dr. Freund says that he will occasionally use off-label strategies, such as treating more than monthly if a patient is really not being controlled. "If a patient continues to have hemorrhage or is losing vision, I might give an additional injection between monthly injections," he says. "In those situations, I often use a sample. In some patients, you just need to treat more aggressively at the initiation of therapy."

He also occasionally uses aqueous suppressants to extend the duration of anti-VEGF injections. "Glaucoma agents reduce the production of aqueous and may slow the clearance of drugs, which may extend the duration just a little bit," Dr. Freund explains. "In some patients, we may not be making progress because the drug may only last for say three-and-a-half weeks, and we're only injecting monthly. By the time we give the next injection, we're back to where we started, not building on the success of the first injection. But, if you could extend that just a few extra days, then you could potentially continue to dry the macula. In some of my patients, just adding a topical timolol-brinzolamide combination seems to help get them under control. I might try this strategy if there's no contraindication to using those drugs, but to prove whether that's an effective strategy would require a formal randomized trial with placebo."

The Future

Physicians say there are therapies on the horizon, such as gene therapy and high-dose aflibercept, that hold out the hope for more effective treatments for recalcitrant cases.

Dr. Freund notes that gene therapy looks promising if the safety issues related to intraocular inflammation can be overcome. Dr. Regillo adds that other agents in the pipeline hold promise, as well. "There's a high likelihood that high-dose aflibercept will be FDA-approved and in our hands within the next year or so," he says. "It met its primary endpoint in the Phase III neovascular AMD study, so it's pending FDA approval. That drug looks more durable than the older drugs we've been using. There is also still the possibility that KSI-301 could get FDA-approved for wet AMD."

Other agents currently in the pipeline include OPT-302, which is a fusion protein that binds VEGF-C/D. "It's in Phase III clinical trials, and is being used as a combination therapy with a VEGF-A blocker (ranibizumab or aflibercept)," Dr. Regillo explains. "It's being used in combination in hopes of getting improved visual acuity outcomes. It'll probably be another couple of years before we know the study results. Then, there are a whole host of therapeutics in the pipeline, mostly aiming at greater anti-VEGF durability, many of which are sustained release of an anti-VEGF-A or an anti-VEGF-like agent. And that includes the port-delivery system [Susvimo, Genentech], which was FDA-approved over a year ago, but implementation of the device is on hold because of an issue with the septum of the device that has to be rectified. But patients would undoubtedly benefit from highly effective sustained delivery and choose it."

Also being examined is a class of therapeutics called tyrosine kinase inhibitors. "These are small molecules that have to be packaged in polymer-like sustained delivery platforms, injected intravitreally, or in a suspension injected suprachoroidally aiming to get an anti-VEGF-like effect for four, six or eight or so months," he adds. "Those are all in the sustained-delivery category. It'll provide an effect like we get now, but for more than just three or four months, which is about the limit to the drugs that we're using. Lastly, there are several more gene therapy approaches being tested aiming for very long-lasting, potentially even indefinite, anti-VEGF therapy." ◀

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In Defense of Trabeculectomy

Why trabeculectomy needs to survive and how we can ensure its future.

AN INTERVIEW WITH SECTION EDITOR KULDEV SINGH, MD, MPH, BY SENIOR ASSOCIATE EDITOR CHRISTINE LEONARD
PALO ALTO, CALIF.

Trabeculectomy remains the gold standard procedure for patients with advanced or rapidly progressing glaucoma who need very low intraocular pressures. When successful, the procedure offers long-term IOP control without an implanted device and the opportunity to titrate filtration to achieve a desired goal. For many with severe disease, a trabeculectomy is the best and only reasonable option. However, with the decreasing number of trabeculectomies performed in training programs, there's a concern that this surgery could fall by the wayside if the next generation of glaucoma specialists is not adequately trained in the performance and perioperative management associated with this procedure.

There are a number of reasons for this—some within our control and others outside of it—but one thing is certain: The population is aging, and the prevalence of glaucoma is increasing. As patients live longer with glaucoma, there will be many more who need trabeculectomy to prevent blindness in their lifetimes.

Tortoises and Hares

The majority of patients who are diagnosed as having glaucoma and treated with IOP lowering therapy have slowly progressive disease. Many such patients tend to experience very little visual field loss over their lifetime, and their disease can usually be managed using topical medications, lasers or minimally invasive glaucoma surgery. With few visual symptoms, especially in early stages, many such individuals are completely unaware that they have glaucoma. Major trials such as the United Kingdom Glaucoma Treatment Study and the Early Manifest Glaucoma Trial have shown that approximately 66 percent and 33 percent of patients receiving placebo or no therapy do not show progression of glaucomatous disease respectively.[1-2]

Only a small subset of patients are fast or catastrophic progressors as demonstrated by a Canadian analysis of 2,324 patients in clinical care, where 4.3 percent displayed fast progression (defined as mean deviation <-1 to -2 dB/year) and 1.5 percent showed "catastrophic" progression (MD <-2 dB/year).[3] Though the proportion of fast and catastrophic progressors is small, the rate increases with advancing age.

A Vanishing Act

As the population ages, we can expect an increase in the number of glaucoma patients in their 80s and 90s along with a corresponding increase in the absolute number of cases with advanced glaucoma.[4] Some of these older patients will require more aggressive pressure lowering, with IOP goals in the single digits—a feat unlikely to be accomplished without trabeculectomy, which remains the only glaucoma procedure associated with a high likelihood of achieving IOPs in this low of a range.

Despite the sizable projected public health need for trabeculectomy in the next couple of decades, there's a very real risk that trabeculectomy could disappear from our armamentarium. So, why aren't doctors offering trabeculectomy to patients with severe disease? There may be a number of reasons. Here are a few:

- They didn't adequately learn trabeculectomy in their training so they either don't feel comfortable performing the procedure or get poor results.
- They choose not to perform trabeculectomy for other reasons such as perioperative effort or insufficient reimbursement.
- They're not aware of the data showing the benefits of trabeculectomy in glaucoma patients with potentially blinding disease, as such data isn't commonly presented at contemporary meetings. This reason is particularly problematic because it may preclude patients being offered the opportunity to see other practitioners who are adequately trained and available to provide vision saving trabeculectomy. As one of my mentors once said: You don't know what you don't know.

Trabeculectomy is taught less than in the past because there are so many newer surgeries and devices to choose from, such as tube shunts

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and MIGS. In U.S. glaucoma fellowship training, the median number of trabeculectomy or Ex-Press shunt procedures performed with fellows as the primary or assisting surgeon decreased from 49 to 32 over a five-year period (2014 to 2019) whereas over that same period, the number of aqueous shunt procedures remained roughly the same at 55 and 57 procedures, respectively. The median number of trabeculectomy and aqueous-shunt revision surgeries remained reasonably stable as well (ranges for both: 9 to 14), but the number of primary surgeon *ab interno* angle procedures increased from zero to 12.[5]

Many of the surgeons experienced in the art of trabeculectomy—particularly the early postoperative manipulation required for a successful procedure—are retiring or nearing retirement. As they leave the field it can become difficult to find a doctor in many parts of the United States who can perform or teach this procedure with high success and a low risk of complications. If trabeculectomy needs to be repeated, then there are additional risks such as scarring and bleb failure as well as lower success rates, so the best shot you get with trabeculectomy is usually as the first conjunctival incisional procedure.

If young surgeons don't receive sufficient training, they won't get good results. This will undoubtedly make them hesitant to perform trabeculectomy because they lack confidence in the procedure. This in turn causes a vicious cycle where fewer trabeculectomies leads to less trabeculectomy training, which leads to fewer surgeons performing trabeculectomy.

Even some glaucoma specialists are shying away from trabeculectomy—sometimes perhaps for financial reasons. From a business standpoint, a MIGS practice may be more attractive to some due to MIGS' relative simplicity, low complication rates and higher reimbursement per time spent. Trabeculectomy has a steep learning curve and, in addition to intraoperative complexity, good results generally require multiple postoperative visits in the weeks following surgery, with timely interventions to safely titrate IOP to desired goals. Such interventions include digital massage, lysing or releasing scleral flap sutures, as well as administration of subconjunctival antifibrotic agents such as 5-fluorouracil. Many clinics either can't provide or don't want to provide such postoperative care.

> **The number of trabeculectomies is going down at a time when . . . the number of patients needing trabeculectomy is likely going up.**

Based upon Medicare data, the number of trabeculectomies is going down at a time when, based upon our population demographics, the number of patients needing trabeculectomy is likely going up. These dynamics have the potential to lead to a public health crisis. This is a tough area to study, but my clinical impression is that there are more glaucoma patients going blind today because they didn't get a timely trabeculectomy relative to a decade ago, often because their doctor didn't offer this as an option or, alternatively, refer them to another physician who was adequately trained and willing to perform the procedure.

Who Needs a Trab?

Glaucoma surgery can be divided into broad categories: procedures that increase outflow by enhancing the eye's natural drainage pathways (e.g., implantable MIGS devices); by creating a new drainage system (e.g., filtration and shunt surgeries); or procedures that decrease inflow, such as cyclophotocoagulation.

When choosing a glaucoma procedure, consider the following factors:

- glaucoma risk (age, severity, progression);
- lens status;
- IOP goals for the procedure;
- medication tolerance/acceptance; and
- preserving future options.

Patients with mild to moderate glaucoma who are taking IOP-lowering medications are candidates for implantable MIGS devices combined with cataract surgery, an approach that has been well-studied in several major clinical trials as a way to decrease dependence on such medications. Choice of MIGS depends on surgeon comfort or preference as well as individual ocular anatomy and pressure-lowering needs.

Most people who get MIGS today are unlikely to be destined to noticeably lose sight in their lifetimes. Most won't go on to have vision loss resulting in an inability to read, drive or watch TV. In contrast, patients who are candidates for trabeculectomy generally have more advanced and/or rapidly progressive disease and are thus likely to have these hurdles in their future. So, it's possible that because of the increasing popularity of and preference for MIGS, and the corresponding decrease in the number of trabeculectomies performed, that we may see more glaucoma-related blindness in the years to come, despite having these newer surgeries. It would be most unfortunate if the revolution in novel glaucoma surgical procedures, by leading doctors away from trabeculectomy, results in greater glaucoma-related blindness in fee-for-service populations such as in the United States.

Trabs' Track Record

We can't let trabeculectomy fall by the wayside. Trabeculectomy has a long history of success, yielding sustained low pressures and slowing of disease progression. Postoperative titration is possible, and it's also been shown that the procedure can improve visual function.[6]

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A study of normal-tension glaucoma patients reported a mean IOP decrease from 15.7 to 10.3 mmHg and a decreased VF progression rate from 0.70 to 0.25 dB/year five years after trabeculectomy.[7] Another study reported pre-trabeculectomy VF progression decreased from 1.1 dB/year (mean IOP 13.5 mmHg) to 0.25 dB/year (8.5 mmHg) six years after surgery.[8]

In the Tube Versus Trabeculectomy study, similar mean pressures were achieved but fewer medications were needed by the group that received trabeculectomy for the first few years after surgery but not at five years (14.4 ±6.9 mmHg in the tube group vs. 12.6 ±5.9 mmHg in the trabeculectomy group; p=0.12; 1.4 ±1.3 medications in the tube group vs. 1.2 ±1.5 medications in the trabeculectomy group; p=0.23).[9] While the mean IOPs were similar, the proportion of eyes with very low pressures was greater in the trabeculectomy group. Patients with advanced disease may sometimes require single digit IOPs to adequately slow disease progression.

When performed with 5-fluorouracil or mitomycin-C, trabeculectomy has been found to produce safe and effective pressure reduction. In a prospective, randomized, multicenter trial, 113 patients were randomized to receive 5-FU (50 mg/ml for five minutes) or MMC (0.4 mg/ml for two minutes). A total of 108 patients were analyzed (n=54 for each group). In the MMC group, 89 percent reached the predefined target IOP <18 mmHg after surgery vs. 83 in the 5-FU group; 70 vs. 73 percent reached IOP <15 mmHg; and 53 vs. 38 percent reached IOP <12 mmHg, respectively (no significant difference).[10]

Importantly, a paper by Joseph Caprioli, MD, and colleagues demonstrated that trabeculectomy can slow the rate of perimetric decay and may improve long-term visual function in glaucoma.[6] In the retrospective, longitudinal study, 74 eyes of 64 OAG patients underwent trabeculectomy with MMC. A control group of 71 unoperated eyes of 65 patients with similar baseline characteristics was included. The authors reported that the mean rate of change for all VF locations slowed after surgery, from -2.5 ±9.3 percent/year before surgery to -0.10 ±13.1 percent/year after surgery (p<0.001). In the trabeculectomy group, they observed that 70 percent of locations decayed before surgery versus 56 percent of locations after surgery; they also observed improvement in 30 percent of locations before surgery and in 44 percent after surgery (p<0.0001). IOP reduction was associated with the excess number of VF locations showing long-term improvement (p=0.009). In the trabeculectomy group, 57 percent of eyes showed improvement in 10 or more VF locations postoperatively.

What Can We Do?

More people will need trabeculectomy in the next 20 to 30 years, but with fewer doctors well-versed in the procedure, lack of training, declining reimbursement and insufficient knowledge about what trabeculectomy can do, we may find ourselves with a public health crisis on our hands.[11]

Here are some steps to ensure we're ready to meet the needs of our patients:

1. Ensure that the training programs and physicians who have the ability to teach trabeculectomy continue to do so. Teaching the art and science of trabeculectomy will be vital for the survival of the procedure. One of the most valuable training techniques for trabeculectomy is direct mentoring with an experienced glaucoma surgeon, in addition to postoperatively following a number of cases.

2. Physicians who perform trabeculectomy should get adequately reimbursed for their effort. This isn't directly in our hands, but advocacy measures may help raise awareness. Currently, some doctors may have a disincentive to do trabeculectomy because reimbursement is too low for the complexity and amount of time devoted to the procedure and postoperative care. Surgeons' payment should be similar to what they're doing in other areas of practice—if a trabeculectomy takes twice as much effort as another procedure, pay twice as much, and that includes postoperative care.

3. We need more traditional glaucoma doctors to ensure that we can meet the needs of people with glaucoma. Some and perhaps many fellowship-trained glaucoma specialists are developing cataract/MIGS practices and don't want to bother taking care of patients with severe or high-risk glaucoma.

If we create a culture that recognizes trabeculectomy's place in glaucoma management, we can better equip ourselves and the next generation of surgeons to learn and practice the art and science of trabeculectomy. ◂

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Managing Retinal Complications of KPro

The device that solves problems in the front of the eye can sometimes cause other problems in the back.

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Permanent keratoprosthesis (KPro) has restored vision in many patients with anterior segment diseases, however, it may lead to vision-threatening posterior segment complications. In this article, we'll review the retinal complications that can occur with these devices and how to manage them.

Background

KPro is an implantable device that serves to replace a native cornea with an artificial one, for patients with advanced corneal disease who aren't candidates for traditional penetrating keratoplasty.[1] The most common KPro in the United States is the Boston type I KPro, developed by Claes H. Dohlman, MD, and associates. The Boston KPro consists of a front plate with an optical stem, a back plate, a donut of donor cornea in between, which is sutured to the host cornea, and a titanium locking ring that holds the structure together.[2] The design has undergone several adaptations, and now includes holes in the backplate, which enable the flow of nutrients from the aqueous humor.[3]

The type I design is by far the most frequently implanted model and is used for patients with non-autoimmune graft failure with good tear and lid function. The type II KPro is often used for patients with severe cicatricial corneal disease with deficient or absent tear function such as in Stevens Johnson Syndrome (SJS), Ocular Cicatricial Pemphigoid (OCP) or severe chemical burns. This device is similar, requires a permanent tarsorrhaphy, and has an extra 2-mm long anterior optical nub attached to the collar button that protrudes through the upper eyelid.[4] Other permanent KPro devices include the AlphaCor (Addition Technology, Des Plaines, Ill.) and the Osteo-odonto keratoprosthesis or OOKP (originated by Italian ophthalmic surgeon Professor Benedetto Strampelli, modified by Rome's Giancarlo Falcinelli, MD).

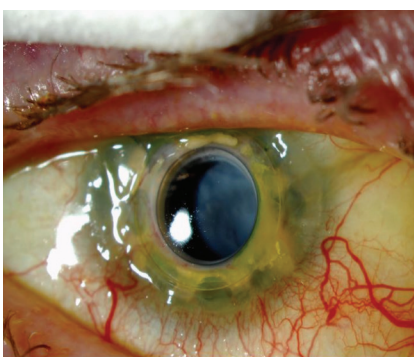

Figure 1. A retroprosthetic membrane post-KPro that required surgical removal.

Although KPros are an effective treatment for many complex corneal diseases, vitreoretinal complications following the procedure represent a significant cause of vision loss and ultimately, KPro failure.[5] Darin Goldman, MD, and colleagues showed that in eyes with posterior segment complications, 61 percent had 20/400 or worse visual acuity at most recent follow-up, while only 24 percent of eyes without complications ended up with such poor vision.[5] With the increasing use and long-term stability of KPro, it's important for ophthalmologists to be able to recognize and manage vitreoretinal complications to prevent unnecessary vision loss. Therefore, patients that undergo KPro implantation require long-term and close follow-up.

Indication for the Procedure

Indications for KPro include multiple graft failures or significant ocular surface disease caused by conditions such as SJS, OCP, autoimmune diseases, limbal stem cell deficiency, ocular burns, aniridia, herpetic keratitis, pediatric corneal opacities or silicone oil keratopathy.[2,5] In addition, KPro has favorable vision outcomes and decreased risk of glaucoma complications when compared to repeat PK.[6]

Surgical Procedure

Following is a brief discussion of the steps of the KPro procedure, and how surgeons can avoid potential complications at each juncture:

- ***Patient selection.*** From a retina perspective, it's crucial for patients to undergo a thorough eye exam,

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Dr. Regillo is the director of the Retina Service of Wills Eye Hospital, a professor of ophthalmology at Thomas Jefferson University School of Medicine and the principle investigator for numerous major international clinical trials.
Dr. Yonekawa is an assistant professor of ophthalmology at Sidney Kimmel Medical College at Thomas Jefferson University. He serves on the Education Committee of the American Society of Retina Specialists and on the Executive Committee for the Vit Buckle Society, where he is also the vice president for academic programming.

which often includes ultrasound to assess for the presence of vision limiting conditions such as retinal detachment, choroidal detachment or severe optic nerve disease. For the cornea surgeon, it's important to evaluate the status of the ocular surface as well as lid abnormalities in order to determine the most appropriate procedure for the patient. If the visual prognosis and posterior segment status cannot be evaluated preoperatively, an exploratory vitrectomy with endoscopy can be performed to determine whether there is posterior segment potential to proceed with K-Pro implantation.[2]

• ***Advantage of pars plana vitrectomy and lens removal.*** At the time of KPro surgery, we often perform vitrectomy and lens removal at our institute, Weill Cornell Medical College (WCMC). If the eye to be implanted is phakic, the crystalline lens is removed and the optical power of the KPro is adjusted for implantation in an aphakic eye. If the eye is pseudophakic, we consider a similar approach and perform IOL removal at implantation in most cases, except for those with well-positioned IOLs and strictly corneal abnormality requiring KPro. The combination of vitrectomy and rendering most eyes aphakic at the time of implantation offers certain advantages to decrease the risk of future complications.

The advantage of lens removal is that it prevents future cataract formation (if phakic) or retro-IOL membranes, which wouldn't only limit a patient's vision, but the view to the retina as well, making it difficult to follow these patients in the future. It's much more difficult to remove a RPM in a pseudophakic eye. Vitrectomy enables the surgeon to assess the visual potential of the eye (particularly the retinal and optic nerve status) and remove any inflammatory materials and debris; many pseudophakic eyes harbor substantial, and potentially inflammatory, residual lens material in the capsular periphery.[1,7] Vitrectomy is typically performed with a 25- or 27- gauge system in a typical transconjunctival technique.[2,8] We avoid doing maneuvers in the open eye as much as possible. For example, vitreous hemorrhage can occur during KPro placement and is often secondary to drop-down bleeding from the wound while the eye is open; effective treatment requires prompt eye closure and subsequent vitrectomy in a closed system.[2] When indicated, a glaucoma drainage device is placed at the time of KPro surgery at WCMC. The reason is that it's often difficult to accurately measure IOP in these patients, and many already have or will develop subsequent glaucoma.

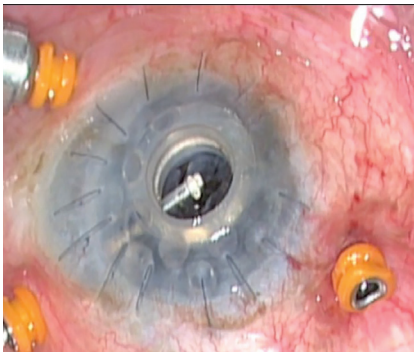

Figure 2. When removing an RPM, avoid creating unnecessary retinal traction and possible subsequent retinal detachment.

Postoperative Management

Patients should be advised that KPro surgery requires frequent follow-up visits and life-long use of topical medications following surgery.[1] Coordinated care with corneal surgeons, retinal specialists and glaucoma specialists is also crucial to manage these complex cases and potential future complications.[7] Antibiotic prophylaxis regimens typically include topical vancomycin and a fourth-generation fluoroquinolone in the initial postoperative period, while dual-agent coverage should be continued for patients who are monocular or have autoimmune disease. Patients at lower risk of endophthalmitis are often treated with a topical fluoroquinolone or polymyxin B/trimethoprim for antibiotic prophylaxis. The placement of a bandage contact lens ensures ocular surface hydration, reduces the risk of stromal melt, dellen formation and necrosis; and improves patient comfort. However, care must be taken with close follow-up, as chronic bandage contact lens use can increase the risk of infections. Lastly, while topical steroids are recommended in patients with KPro to prevent inflammation, it's important to closely monitor patients for side effects such as IOP elevation.[9]

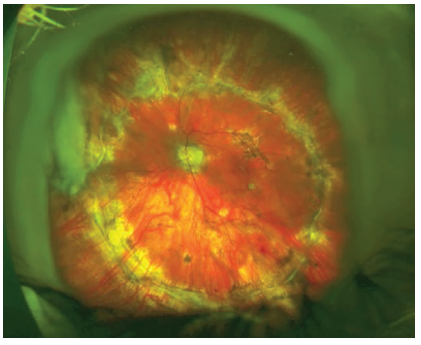

Figure 3. This eye underwent KPro implantation followed by PPV for retinal detachment with PVR.

Managing Vitreoretinal Complications

Though many KPro procedures proceed without issues, if a vitreoretinal complication occurs, the following guidelines and treatment approaches can help you treat them successfully.

• ***General principles.*** Challenges to performing surgery in patients with KPro include achieving adequate surgical exposure, visualization and hemostasis. Attention should be made to avoid causing damage to the back plate, as iatrogenic manipulations can affect visual prognosis. Most importantly, maintenance of a firm eye and a closed system is critical.[8] When a patient requires a pars plana vitrectomy after KPro implantation, sclerotomy placement should be made around 9 mm from the center of the KPro as the limbus

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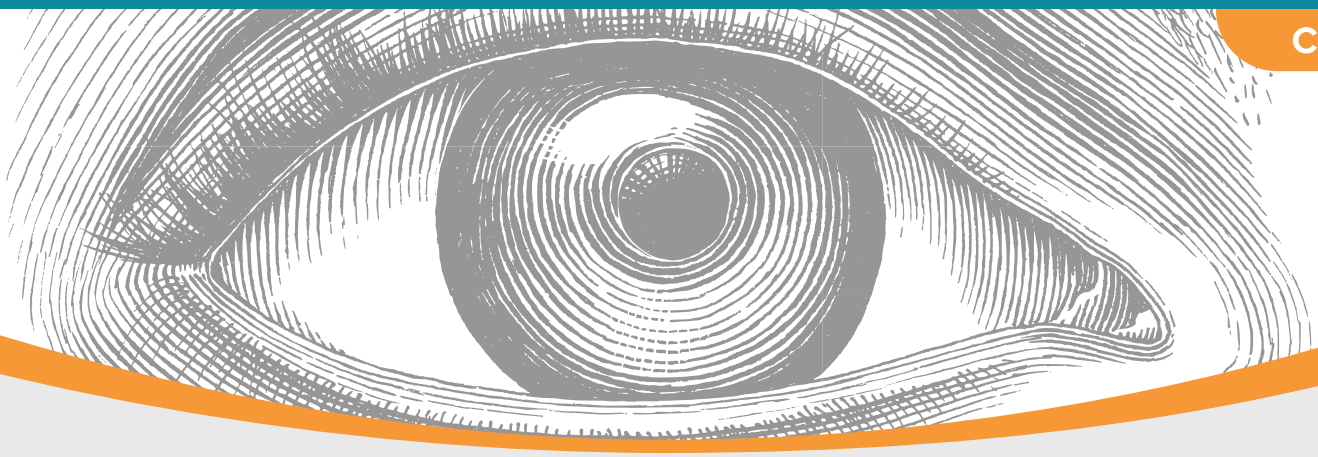

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is often not well defined.

• ***Retroprosthetic membane (RPM).*** Retroprosthetic membrane is the most common complication after KPro surgery, affecting approximately one-third to half of patients.[1,3,7,8,10,11] The membrane is thought to originate from the host's corneal stroma, grow through gaps in Descemet's membrane, migrate to the posterior surface of the KPro backplate and then can adhere to the anterior iris surface. An RPM can appear weeks to months after initial KPro surgery, and has been seen as early as a week postop and as late as four years after surgery.[1]

Risk factors for RPM include postoperative inflammation, retinal detachment, infectious keratitis and aniridia, and is potentially more severe in younger patients.[1] They can become visually significant and limit both vision and your view of the retina, which can impede accurate follow-up. In addition, RPM can be associated with development of chronic hypotony (possibly secondary to traction on the ciliary body) can be a risk factor for future retinal detachment and sterile keratolysis.[1,12] Figure 1 demonstrates a patient who required the surgical removal of an RPM following KPro placement. Figure 2 shows RPM removal. *(Videos of RPM removal and KPro implantation followed by pars plana vitrectomy for retinal detachment with proliferative vitreoretinopathy appear with the online version of the article.)*

Once an RPM becomes visually significant, initial treatment can include laser membranectomy with an Nd:YAG technique, although this can increase the risk of future retinal detachment.[1,8] Thick RPMs are treated surgically. Pay careful attention to avoid creating unnecessary retinal traction and possible subsequent retinal detachment. During surgical repair, it's important to minimize excess inflammation and hemorrhage, which can increase the risk of membrane recurrence.[8]

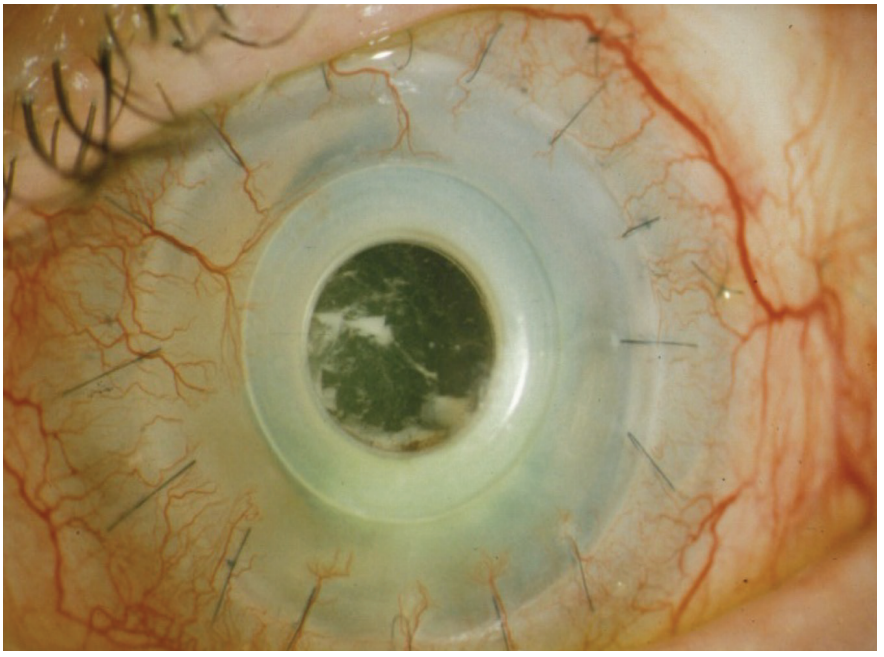

Figure 4. Infectious endophthalmitis from a coagulase-negative staphylococcus following KPro implantation.

Despite surgical treatment, many RPMs can recur with rates of approximately 65 percent.[1] In eyes that are left pseudophakic, it's more difficult to remove a retro-K-Pro membrane, as there's a risk of displacing the IOL or damaging the prosthesis; therefore, the IOL may need to be removed in order to clean the KPro.[2,7] As previously discussed, we remove lenses and IOLs at the initial KPro surgery to decrease these issues.

• ***Retinal detachment.*** Retinal detachment is the second most common complication in patients with KPros, and can be potentially blinding. They can occur months to years following the initial KPro surgery. Retinal detachment has been reported in 2 to 17.6 percent of cases.[3,5,8,10,11] Dr. Goldman's study found that 16.9 percent of eyes (14 of 83) developed retinal detachment at a median time of 10.4 months after KPro implantation.[5] Clemence Bonnet, MD, of the Corneal Biology Lab at UCLA, reported that among 224 Boston Type I keratoprosthesis surgeries performed, 28 (15.2 percent) developed retinal detachment at a mean of 10.9 months. Among these cases, they evaluated 21 retinal detachments surgeries, and identified vitreoretinal proliferation in 18 eyes (85.7 percent) and anatomic success following repair was achieved in 18 (85.7 percent) eyes.[11]

Retinal detachments can be either tractional or rhegmatogenous and can be caused by retinal breaks or proliferative vitreoretinopathy in the setting of chronic inflammation.[1,8] These cases tend to be complex, many of which present with proliferative vitreoretinopathy due to the degree of intraocular inflammation. Patients may initially not be very symptomatic, as many already have limited vison secondary to other conditions such as advanced glaucoma or prior posterior segment disease. Therefore, patients should be followed routinely to detect detachment early. Given that the view of the peripheral retina in patients with KPro may be limited, B scan ultrasonography and ultra-widefield color fundus imaging is often recommended.[11] At follow-up visits, all of our patients obtain a complete anterior and posterior segment exam, along with UWF imaging, and a B scan when indicated.

The surgical approach to repair retinal detachments in KPro cases is done via pars plana vitrectomy, with a low threshold for silicone-oil tamponade. Scleral buckling is often avoided due to the altered scleral and anterior segment anatomy in these patients. Advancements in surgical instrumentation, including smaller-gauge surgery, along with improvements in wide-angle viewing systems, allow for good peripheral visualization and safer PPV repair through the KPro. Silicone oil is often our tamponade agent of choice due to the need for a longer tamponade in these complex cases. In addition, some patients are monocular and require immediate postoperative functional vision.[5] These patients should be co-managed with our glaucoma colleagues, as many have glaucoma filtering devices that need to be removed or ligated prior to oil placement. Perfluoro-n-octane may also be used as a temporary tamponade but should only be used for a short period of time due to its inflammatory qualities.[7] For patients with KPros who require vitreoretinal surgery, the sclerotomy placement should be altered as described above, due to difficulty in locating a clear limbal landmark.

• ***Infectious endophthalmitis.*** Endophthalmitis is a potentially devastating complication, and can occur in 1 to 19 percent of KPro cases. Patients who've received KPros are at a higher risk of endophthalmitis, as there's a conduit between the ocular surface and anterior chamber. Specific endophthalmitis risk factors include preoperative conditions such as autoimmune disease and poor dental hygiene.[1] Since the advent of topical antibiotic prophylaxis, however, the incidence of endophthalmitis from gram-positive infections after KPro surgery has decreased from 12 to 5 percent.[4] Bandage contact lenses can also lower the incidence of tissue melt, scleral thinning and breakdown of the KPro/host interface. Jay Chhablani, MD, of the University of Pittsburgh Eye Center, and his co-authors reported that among 136 eyes that received a Boston Type I KPro between 1999 and 2012, five cases (3.67 percent) of exogenous endophthalmitis occurred.[13] In another study, University of California-Davis retina specialist Ala Moshiri and colleagues reported seven (19 percent) cases of endophthalmitis, all of which were salvaged with antibiotics and vitrectomy. Three of these cases developed retinal detachment.[3]

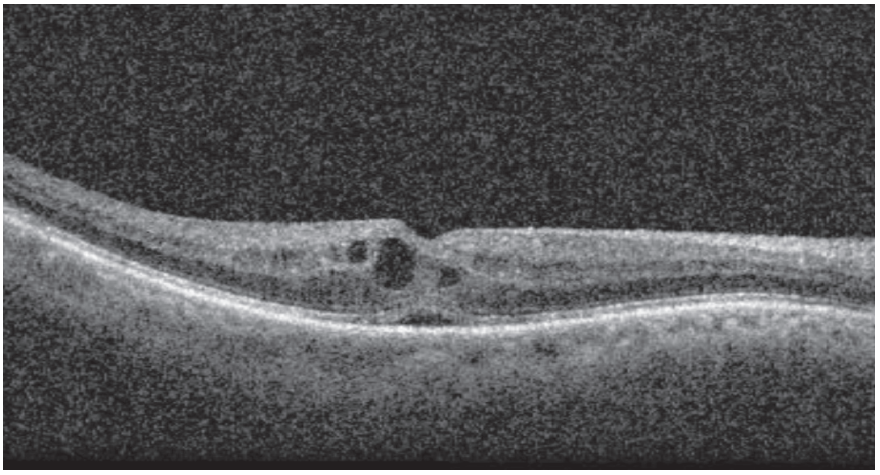

Figure 5. An OCT of a patient who developed CME following KPro implantation. He was subsequently treated with topical difluprednate with resolution of CME.

Endophthalmitis can present weeks to months and, rarely, years following KPro placement, once again highlighting the importance of close and long-term follow up. As discussed, prophylaxis with daily, broad-spectrum antimicrobial drops has significantly decreased the incidence of endophthalmitis. Historically, the most common organisms are gram-positive, although with vancomycin prophylaxis, fungal and gram-negative bacteria have become more common.[1]

Patients with bacterial infection present with sudden onset of eye pain, injection, decreased vision and intraocular inflammation, while fungal infections are typically more indolent and can start as keratitis in the KPro graft.[4] Of course, endophthalmitis always requires immediate intervention. If you suspect it, perform an intravitreal tap or a vitreous biopsy to aid with diagnosis and help target antimicrobial therapy. Treatment involves the intravitreal injection of antimicrobials (i.e., vancomycin, amphotericin and ceftazidime) with or without surgery.[1] A surgical vitrectomy has the advantage of removing enough specimen for analysis, can decrease organism load and remove vitreous scaffolding, which reduces the risk of subsequent vitreoretinal fibrosis and adhesions.[8] Endophthalmitis following KPro placement has a poor visual prognosis.[13]

• ***Sterile vitritis/isolated vitreous opacity.*** Sterile vitritis is an immune-mediated, non-infectious process that can be triggered either by the KPro or by corneal antigens released during tissue necrosis that travel through holes in the KPro back plate into the posterior chamber. It can occur in zero to 14.5 percent of cases.[1,5] Sterile vitritis presents as painless visual loss (without injection and tenderness), which can help differentiate it from infectious endophthalmitis. If it's unclear whether the findings are infectious or not, we recommend a vitreous tap with antimicrobial injections.

Sterile vitritis can occur months to years after surgery. While the eye appears white and quiet, patients develop vitritis that may appear as a "snowflake" pattern. Sterile vitritis can be managed with peribulbar (triamcinolone or dexamethasone)

or topical (prednisolone or difluprednate) steroid treatment depending on the severity. Patients typically can recover visual acuity after about two to 10 weeks of treatment.[1]

• ***Choroidal detachments/hypotony.*** Choroidal detachments occur in 1.7 to 16.9 percent of patients[1,5] and can occur shortly after surgery or years after implantation. They're often associated with inflammation and/or hypotony. Specifically, hypotony occurs in 1.8 to 11 percent of cases and is due to various causes, including corneal stromal necrosis with perforation, RPM or glaucoma device over-filtration. Small, stable choroidal detachments can be observed, while larger ones may require treatment. They can be managed with systemic or local steroids, while you address the cause of hypotony alongside your cornea and glaucoma colleagues. RPMs should be removed, particularly if they're significant and potentially associated with the hypotony. Choroidal drainage can be considered in cases of appositional ("kissing") choroidals to prevent subsequent vision loss and retinal detachment, though the underlying cause of hypotony should still be addressed.[1,5]

• ***Vitreous hemorrhage.*** Vitreous hemorrhage occurs postoperatively in 1.6 to 11 percent of eyes after KPro placement. VH can be secondary to intraocular bleeding from the trephinated cornea, lysis of iridocorneal adhesions or manipulation of other vascularized structures. Inflammation, intraoperative steroid use and diabetes are also associated with VH. B-scan ultrasonography should be performed when posterior segment view is inadequate, to rule out other pathology such as retinal or choroidal detachments. Though VH often resolves spontaneously, when it's persistent it can be managed with vitrectomy.[1] The Goldman study reported vitreous hemorrhage in 6 percent (5/83) after a median time of 0.3 months after K-Pro implantation. All cases were observed and ultimately resolved.[5]

• ***Cystoid macular edema.*** Post-surgical CME is another common complication following KPro surgery. Goldman et al., reported CME in 10.8 percent of cases (nine of 83) at a median time of 4.1 months following surgery. Five of the eyes were treated with either intravitreal bevacizumab or triamcinolone, and two eyes required multiple injections.[5] Optical coherence tomography is critical in diagnosing CME, while fluorescein angiography can be used in atypical cases to rule out other causes. CME can be managed with topical, periocular or intravitreal steroids; or intravitreal anti-VEGF medication, depending on the severity and response to treatment.

• ***Other complications.*** Other vitreoretinal complications that have been described include the development of epiretinal membrane or macular holes. Goldman et al., found ERM in 7.2 percent of eyes (six of 83) at a median time of 17.7 months after KPro placement,[5] while Moshiri et al., reported four (11 percent) cases of ERM and one case (3 percent) of macular hole.[3]

Visually significant ERMs or macular holes benefit from pars plana vitrectomy and membrane peeling. Modern day small-gauge vitrectomy and wide-angle viewing systems greatly help with the surgery.

In conclusion, postoperative retinal complications following implantation of a permanent keratoprosthesis are a significant cause of vision loss. Therefore, it's important for ophthalmologists to recognize these complications to make a prompt diagnosis and pursue the appropriate treatment. The most common retinal complications are retroprosthetic membrane, infectious endophthalmitis, sterile vitritis, retinal detachment and choroidal detachment. A retina specialist plays a crucial role in the preoperative evaluation, initial surgical implantation (when combined pars plana vitrectomy is performed) and in the postoperative care. Ultimately, close and long-term follow-up, along with coordinated care between cornea, retina and glaucoma specialists, are vital to managing vitreoretinal complications of KPros and preventing vision loss. ◀

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Glaucoma & Cataract

(Continued from page 46)

procedure, they'll probably end up on Durezol or Pred Forte four times a day. Instead of seeing that patient at the three-week postop, you may want to see them one day and then one or two weeks postop to make sure that they don't have a pressure spike to 30 mmHg.

"It just requires more attentiveness," he says. "You may have to then stop the steroid, switch to a non-steroidal, and then switch to a less potent steroid to regulate the pressure again—which is one of the reasons I don't use intracameral postop steroid injections. Should that patient have a steroid response, and they've got intracameral steroids, those aren't going anywhere. You may have a very hard time controlling their pressure because your only choices—especially with a glaucoma patient who's already on glaucoma medications—would be something like Diamox. These aren't patients in whom you can just add timolol and their pressure will go down. Odds are they're already on one or two glaucoma medications. So, I avoid intracameral steroid injections in pretty much all my patients but especially in those glaucoma patients."

Post-goniotomy patients with small hyphemas may also need more aggressive steroid treatment. Dr. Grayson notes that in any minimally invasive glaucoma procedure, there's a risk of bleeding from either the device or the trauma to the eye during the procedure. He says that even a small amount of blood in the anterior chamber can cause a significant decrease in vision and an elevated pressure.

"Generally speaking, more steroids help clear that blood and squash the inflammation faster," he says. "If there's a hyphema from goniotomy, patients will be concerned because they're not seeing that well, but if you want to increase their steroids, you have to follow these patients a little bit more closely, maybe every few days. We can't let them just coast with a one-day and then a three-week postoperative visit until you know exactly what their intraocular pressure status is. So, they've got to be monitored. They've got to be watched to make sure there isn't a steroid response. Especially with hyphema, which could in a matter of days lead to a spike to 40 mmHg, which could cause a significant amount of damage very fast. It's important to be more on top of those patients."

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CORNEAS AND CATARACTS

(Continued from page 30)

the small-aperture optics."

Patient expectations should be managed along the way, says Dr. Trinh. In someone with Fuchs' endothelial dystrophy, the surgeon should help the patient understand the natural pathophysiology of the disease, balancing the severity of the cataract against the severity of the endothelial disease. "Because there's a statistically higher chance of endothelial failure in this group of patients, the choice of lenses used may also be affected," she says. "For example, patients desiring spectacle independence may choose to avail themselves of monovision options rather than using multifocal technologies."

Dr. Trinh highlights another specific scenario for keratoconus or pellucid patients (or any patient with higher irregular astigmatism such as corneal grafts) who enjoy wearing their hard contact lenses and have the dexterity to continue doing so. In this situation, she'll generally place a non-toric IOL and allow the contact lens to address the irregularity of their astigmatism. "This will always give the best quality of result in terms of vision," she says.

Dr. Miller dreams of postop power adjustable lens technology that could be tweaked, not just for sphere and cylinder, but also higher-order aberrations. "This may be our best way of dealing with eyes that have irregular corneas," he says. "If you could counteract the distorted wavefront of the cornea by compensating with a counter-distorting wavefront on the lens, maybe we could get really good quality vision for these patients. One of the long-term problems with irregular corneas is they tend to change over time. So if you had such a technology, it would have to be continuously adjustable to be truly beneficial."

Parting Advice

The best way to prepare for these irregularities is to approach each patient with a suspicion for them, advises Dr. Miller. "They're very common and you can't always look through a slit lamp biomicroscope and see it," he says. "It helps if you have a way of mapping every person who comes through. When you only map the people who opt for premium lenses, that's where you're going to get burned. If you discover a problem after surgery, then you caused the problem—that's what the patient will think. You can't tell them it was probably irregular before surgery if you don't have a picture to prove it. You must have a system for detecting things systematically." ◀

Omega-3s and Diabetic Retinopathy

Inflammation is associated with diabetic retinopathy development and progression, and previous studies have demonstrated that omega-3 polyunsaturated fatty acids (PUFAs) have anti-inflammatory properties. Therefore, investigators say that the goal of their study was to determine if omega-3 PUFAs, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) were associated with decreased risk and severity of retinopathy in individuals with type 2 diabetes.

In a combined population of 1,356 individuals with type 2 diabetes from the Multi-Ethnic Study of Atherosclerosis (MESA) and Genetics of Latino Diabetic Retinopathy (GOLDR) cohorts, odds ratios using logistic regression were determined to assess the association between PUFAs and retinopathy.

Here are some of the findings:

- In 1,356 participants with type 2 diabetes, individuals in the fourth quartile of DHA were 17 percent less likely to have retinopathy compared to the first quartile (p=0.009; CI, 0.72 to 0.95).
- Secondary analysis revealed a 38 percent lower severity of retinopathy in individuals in the fourth compared to the first quartile of DHA (p=0.006; CI, 0.44 to 0.87) and EPA+DHA (p=0.004; CI, 0.44 to 0.85).
- No significant associations were observed between EPA and retinopathy.

Investigators found DHA was inversely associated with presence and severity of diabetic retinopathy. They suggested that increased intake of dietary sources of DHA may provide some protection against retinopathy in individuals with type 2 diabetes and warrants more research as a preventative option.

Retina 2023; Jan 30 [Epub ahead of print].

Weir NL, Guan W, Karger AB, et al.

Blood Pressure Associated With GCC Thinning

Researchers investigated the association of baseline blood pressure measures with rates of change of the macular ganglion cell complex in patients with central or moderate to advanced glaucoma damage at baseline.

This prospective cohort study, conducted from August 2021 to August 2022, used data from patients in the Advanced Glaucoma Progression Study at the University of California, Los Angeles. Participants were between 39 and 80 years of age and had more than four macular imaging tests, and two or more years of follow-up. They had a diagnosis of glaucoma with either central damage or a visual field mean deviation worse than -6 dB.

The main outcome was the association of blood pressure measures with ganglion cell complex rates of change. Macular ganglion cell complex thickness rates of change were estimated with a Bayesian hierarchical model. This model included relevant demographic and clinical factors. Blood pressure measures, intraocular pressure and interactions were added to the model to assess the association of baseline blood pressure measures with global ganglion cell complex rates of change.

The cohort included 105 eyes from 105 participants. The mean age was 66.9 ±8.5 years; 10-2 visual field mean deviation was -8.3 ±5.3 dB; follow-up time was 3.6 ±0.4 years; and 67 patients (63.8 percent) were female. The racial and ethnic makeup of the cohort was 55 white (52.4 percent), 23 Asian (21.9 percent),15 African American (14.3 percent) and 12 Hispanic (11.4 percent). Here are some of the findings:

- In multivariable analyses, female sex, history of taking blood-pressure medications, higher IOP, thicker central corneal thickness, shorter axial length, higher contrast sensitivity at 12 cycles per degree and higher baseline 10-2 visual field mean deviation were associated with faster ganglion cell complex thinning.
- Lower diastolic blood pressure was associated with faster rates of ganglion cell complex thinning at higher intraocular pressures.
- For IOPs of 8 and of 16 mmHg (10 and 90 percent quantiles, respectively), every 10 mmHg-lower increment of diastolic blood pressure was associated with 0.011 µm/y slower and -0.130 µm/y faster rates of ganglion cell complex thinning, respectively.

Researchers found a combination of lower diastolic blood pressure and higher intraocular pressure at baseline was associated with faster rates of ganglion cell complex thinning. The researchers say that these findings support consideration of evaluating and addressing

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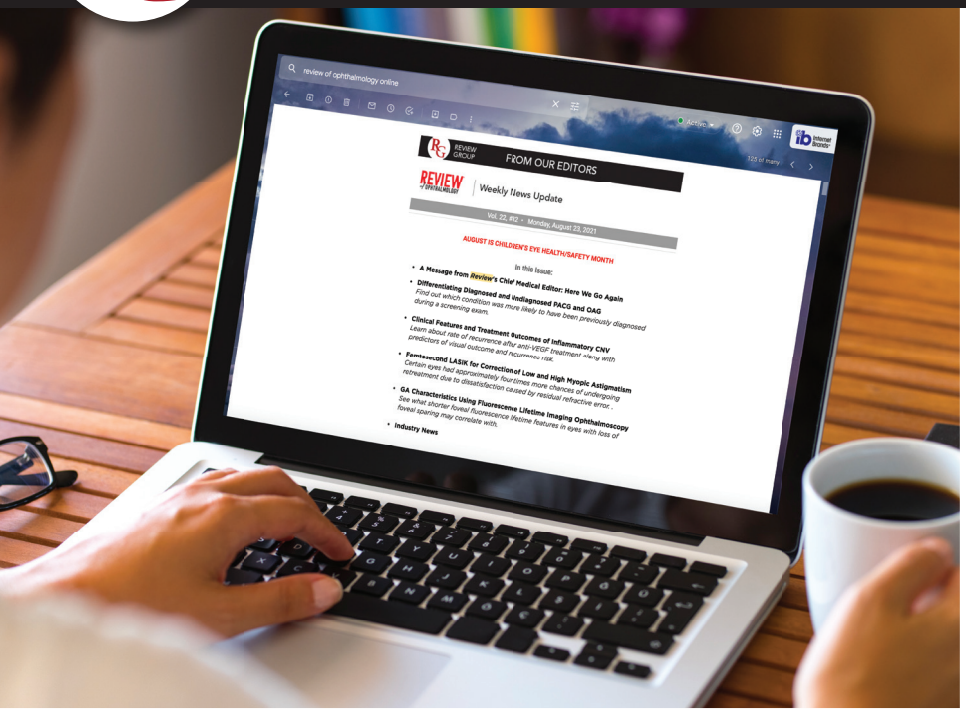

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REVIEW GROUP — FROM OUR EDITORS

REVIEW of OPHTHALMOLOGY | Weekly News Update

Vol. 22, #32 • Monday, August 23, 2021

AUGUST IS CHILDREN'S EYE HEALTH/SAFETY MONTH

In this Issue:

- **A Message from *Review*'s Chief Medical Editor: Here We Go Again**
- **Differentiating Diagnosed and Undiagnosed PACG and OAG**
  Find out which condition was more likely to have been previously diagnosed during a screening exam.
- **Clinical Features and Treatment Outcomes of Inflammatory CNV**
  Learn about rate of recurrence after anti-VEGF treatment along with predictors of visual outcome and recurrence risk.
- **Femtosecond LASIK for Correction of Low and High Myopic Astigmatism**
  Certain eyes had approximately four times more chances of undergoing retreatment due to dissatisfaction caused by residual refractive error.
- **GA Characteristics Using Fluorescence Lifetime Imaging Ophthalmoscopy**
  See what shorter foveal fluorescence lifetime features in eyes with loss of foveal sparing may correlate with.
- **Industry News**

A message from *Review*'s Chief Medical Editor, Mark H. Blecher, MD: Here We Go Again

I am, like most of you, totally over COVID. But as the cliché saying goes, "COVID isn't over us," which was mildly funny until it wasn't. We had a small happy window of normalcy this spring when marginally successful vaccinations caused the infection rate to plummet. The sun started to shine again ... and then it was gone. The smug satisfaction the vaccinated among us enjoyed was

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diastolic blood pressure as a therapeutic measure in patients with glaucoma if supported by appropriate clinical trials.

JAMA Ophthalmol 2023; Feb 9 [Epub ahead of print].
Mohammadzadeh V, Su E, Mohammadi M, et al.

DME Treatment Cost Analysis

Investigators wrote that the DRCR Retina Network Protocol AC showed no significant difference in visual acuity outcomes over two years between treatment with aflibercept monotherapy and initial bevacizumab followed by a switch to aflibercept for suboptimal response in treating diabetic macular edema. As such, they wrote that understanding the estimated cost and cost-effectiveness of these approaches is important.

The investigators evaluated the cost and cost-effectiveness of aflibercept monotherapy vs. bevacizumab-first strategies for DME treatment, as part of an economic evaluation/preplanned secondary analysis of a randomized clinical trial. Participants were ages 18 years or older, with center-involved DME and best-corrected visual acuity of 20/50 to 20/320, enrolled between December 15, 2017, and November 25, 2019.

Between February and July 2022, the incremental cost-effectiveness ratio (ICER) in cost per quality-adjusted life-year (QALY) over two years was assessed. Efficacy and resource utilization data from the randomized clinical trial were used with health utility mapping from the literature and Medicare unit costs.

The study included 228 participants. The median age was 62 (range: 34 to 91 years), 116 (51 percent) were female, 117 (51 percent) were white, 60 (26 percent) were Hispanic and 44 (19 percent) black, and with one study eye. The aflibercept monotherapy group included 116 participants, and the bevacizumab-first group included 112, of whom 62.5 percent were eventually switched to aflibercept. Here are some of the findings:

- Over two years, the cost of aflibercept monotherapy was $26,504 (CI, $24,796 to $28,212) vs. $13,929 (CI, $11,984 to $15,874) for the bevacizumab-first group, a difference of $12,575 (CI, $9,987 to $15,163).
- The aflibercept monotherapy group gained 0.015 (CI, -0.011 to 0.041) QALYs using the better-seeing eye and had an ICER of $837,077 per QALY gained compared with the bevacizumab-first group.
- Aflibercept could be cost-effective with an ICER of $100,000 per QALY if the price per dose were $305 or less, or the price of bevacizumab was $1,307 or more per dose.

Investigators wrote that, as always, variability in individual needs will influence clinician and patient decisions about how to treat specific eyes with DME. However, they found that the bevacizumab-first group costs averaged approximately $12,600 less over two years compared with aflibercept monotherapy, potentially conferring substantial cost savings without sacrificing visual acuity gains.

JAMA Ophthalmol 2023; Feb 2 [Epub ahead of print].
Hutton DW, Glassman AR, Liu D, et al.

OPT-303 Phase II Results

Researchers wrote that neovascular age-related macular degeneration is driven by vascular endothelial growth factors-A, -C and -D. They added that intravitreal injections of anti-VEGF-A drugs are the standard of care but don't inhibit VEGF-C and -D, which may explain why many patients fail to respond fully. This trial aimed to test the safety and efficacy of OPT-302 (Opthea, Princeton, N.J.), a biologic inhibitor of VEGF-C and -D, in combination with the anti-VEGF-A inhibitor ranibizumab.

The dose-ranging, Phase IIb, randomized, double-masked, sham-controlled trial enrolled participants with treatment-naïve nAMD from 109 sites across Europe, Israel and the United States.

Participants were randomized to six four-weekly intravitreal injections of 0.5-mg OPT-302, 2-mg OPT-302 or sham, plus intravitreal 0.5-mg ranibizumab.

The primary outcome was mean change in Early Treatment Diabetic Retinopathy Study best-corrected visual acuity at 24 weeks. Secondary outcomes (comparing baseline to week 24) were the proportion of participants gaining or losing ≥15 ETDRS BCVA letters; area under the ETDRS BCVA over time curve; change in spectral-domain optical coherence tomography central subfield thickness (CST); and change in intraretinal fluid and subretinal fluid on SD-OCT.

Of 366 participants recruited December 2017 to November 2018, 122, 123 and 121 were randomized to 0.5 mg OPT-302, 2.0 mg OPT-302 or sham, respectively. Here are some of the findings:

- Mean (± standard deviation) visual acuity gain in the 2-mg OPT-302 group was significantly superior to sham (+14.2 ±11.61 vs. +10.8 ± 11.52 letters; p=0.01).
- The 0.5-mg OPT-302 group wasn't significantly different to sham (+9.44 ±11.32 letters; p=0.83).
- Compared to sham, the secondary BCVA outcomes favored the 2-mg OPT-302 group, with structural outcomes favoring both OPT-302 dosage groups.
- Adverse events were similar across groups, with 16 (13.3 percent) participants in the lower dose, 7 (5.6 percent) participants in the higher dose and 10 (8.3 percent) participants in the sham group developing at least one serious adverse event.
- Two unrelated deaths both occurred in the sham arm.

Researchers concluded that significantly superior vision gain was observed with OPT-302 2-mg combination therapy vs. standard of care, with a favorable safety profile. ◀

Ophthalmology 2023; Feb 6 [Epub ahead of print].
Jackson TL, Slakter J, Buyse M, et al.


ENOUGH
IS ENOUGH
There's a better way.
Providing the best care and achieving professional fulfillment—that's what matters. We know these days it's hard. Between rising costs, declining reimbursements, staffing challenges, regulations, and billing complexity—seems like there's just not enough time. But the right technology can help. Imagine a single EHR and PM platform with mobile transcription, easier ophthalmic-specific workflows, and efficient billing. Plus, a better way to engage patients. All from a partner who'll be there for the long-haul.
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PROGRESSION IN GEOGRAPHIC ATROPHY IS RELENTLESS AND IRREVERSIBLE[1-4]

While GA progression may appear to move slowly, it can affect your patients faster than you think[1,4-6]

The consequences of Geographic Atrophy (GA) are too critical to be ignored[7-9]

IN A MEDIAN OF ONLY 2.5 YEARS,
GA lesions encroached on the fovea according to a prospective AREDS study (N=3640)[2*]

2 OUT OF 3 PATIENTS
lost the ability to drive in a median time of <2 years according to a retrospective study (n=523)[10†]

GA lesions can lead to visual impairment even before they reach the fovea[1,5,6]

See the effect of GA progression on your patients

*Data sourced from the Age-related Eye Disease Study (AREDS) Report #26—a long-term, multicenter, prospective study examining progression of GA area in a cohort of 3640 patients with signs of early and more advanced forms of AMD.

†A retrospective cohort analysis (N=1901) of a multicenter electronic medical record database examining disease burden and progression in patients in the United Kingdom with bilateral GA secondary to AMD.

BCVA=best-corrected visual acuity.

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