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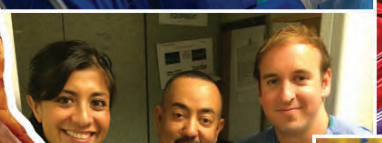

DIVERSITY AND INCLUSION IN RETINA

With guest editors Vivienne S. Hau, MD, PhD, and Basil K. Williams Jr, MD

RUNNING WITH RP: A GUIDE TO FOSTERING HOPE

DIVERSITY IN CLINICAL TRIALS

LGBTQ+ PEARLS FOR COLLEAGUES

XIPERE®
(triamcinolone acetonide
injectable suspension) 40 mg/mL

IN THE MANAGEMENT OF UVEITIC MACULAR EDEMA

XIPERE® DEMONSTRATED PROVEN EFFICACY THROUGH INNOVATIVE DRUG DELIVERY VIA THE SUPRACHOROIDAL SPACE[1-5]

SIGNIFICANT AND SUSTAINED BCVA IMPROVEMENTS[1-3*]

Improvement of ≥15 ETDRS letters from baseline at Week 24 in 47% of XIPERE® patients compared with 16% in the control group (n=96 and n=64, respectively; *P*<0.01) in the pivotal trial[2]

XIPERE DELIVERED DURABILITY[3†]

344 days was the median time to rescue for patients treated with XIPERE (n=28) in an observational extension study

Additionally, 50% of patients treated with XIPERE completed the study by reaching the Week 48 visit without rescue medication

PROVEN SAFETY PROFILE

Assessed in 3 clinical studies: PEACHTREE, MAGNOLIA, and AZALEA[2,3,6]

SCAN TO DISCOVER MORE DATA AT
XIPERE.COM

J-CODE (J3299) NOW AVAILABLE FOR XIPERE®
EFFECTIVE JULY 1, 2022

*Phase 3 Study Design: 6-month, randomized, multicenter, double-masked, sham-controlled study in patients with macular edema associated with anterior-, intermediate-, posterior-, or pan-uveitis. After a 2-week screening period, eligible patients returned to the clinic for the baseline visit (Day 0) when they were randomly assigned in a 3:2 ratio to treatment or control. The control group underwent a sham procedure to maintain masking. Patients were treated at baseline and week 12. The primary efficacy endpoint was the proportion of patients in whom best corrected visual acuity (BCVA) had improved by ≥ 15 letters from baseline after 24 weeks of follow-up.[2]

†24-Week Extension Study Design: Multicenter, non-interventional, 6-month extension study for patients who successfully completed the Phase 3 study without requiring rescue treatment. The final visit of the Phase 3 study was the crossover visit (Day 0) of this study with follow-up visits conducted every 6 weeks.[3]

Indication

XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use is a corticosteroid indicated for the treatment of macular edema associated with uveitis.

Important Safety Information

Patients should be monitored following injection for elevated intraocular pressure. See Dosage and Administration instructions in full Prescribing Information.

- XIPERE is contraindicated in patients with **active or suspected ocular or periocular infections** including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and fungal diseases.
- XIPERE is contraindicated in patients with known **hypersensitivity to triamcinolone acetonide** or any other components of this product.
- Use of corticosteroids may produce cataracts, increased intraocular pressure, and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses, and should be used cautiously in patients with a history of ocular herpes simplex.
- Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and hyperglycemia can occur following administration of a corticosteroid. Monitor patients for these conditions with chronic use.
- In controlled studies, the most common ocular adverse reactions were increased ocular pressure, non-acute (14%), eye pain, non-acute (12%), cataract (7%), increased intraocular pressure, acute (6%), vitreous detachment (5%), injection site pain (4%), conjunctival hemorrhage (4%), visual acuity reduced (4%), dry eye (3%), eye pain, acute (3%), photophobia (3%), and vitreous floaters (3%), and in 2% of patients: uveitis, conjunctival hyperaemia, punctate keratitis, conjunctival oedema, meibomianitis, anterior capsule contraction, chalazion, eye irritation, eye pruritus, eyelid ptosis, photopsia, and vision blurred.

  The most common non-ocular adverse event was headache (5%).
- Corticosteroids should be used during pregnancy or nursing only if the potential benefit justifies the potential risk to the fetus or nursing infant.

To report SUSPECTED ADVERSE REACTIONS, contact Bausch + Lomb at 1-800-321-4576 or FDA at 1-800-FDA-1088 or visit www.fda.gov/medwatch.

Please see brief summary of full Prescribing Information on adjacent page.

References: 1. XIPERE® [prescribing information]. Alpharetta, GA: Clearside Biomedical, Inc.; 2021. **2.** Yeh S, Khurana RN, Shah M, et al. Efficacy and safety of suprachoroidal CLS-TA for macular edema secondary to noninfectious uveitis: phase 3 randomized trial. *Ophthalmology*. 2020;127(7):948-955. **3.** Khurana RN, Merrill P, Yeh S, et al. Extension study of the safety and efficacy of CLS-TA for treatment of macular oedema associated with non-infectious uveitis (MAGNOLIA). *Br J Ophthalmol*. 2021;0:0-6. **4.** Chiang B, Jung JH, Prausnitz MR. The suprachoroidal space as a route of administration to the posterior segment of the eye. *Adv Drug Deliv Rev*. 2018;126:58-66. **5.** Rai Udo J, Young SA, Thrimawithana TR, et al. The suprachoroidal pathway: a new drug delivery route to the back of the eye. *Drug Discov Today*. 2015;20(4):491-495. **6.** Henry CR, Shah M, Barakat MR, et al. Suprachoroidal CLS-TA for non-infectious uveitis: an open-label, safety trial (AZALEA) [published online ahead of print]. *Br J Ophthalmol*. 2021;0:1-5.

BAUSCH + LOMB

BRIEF SUMMARY OF PRESCRIBING INFORMATION
This Brief Summary does not include all the information needed to use XIPERE™ safely and effectively. See full Prescribing Information for XIPERE™.

XIPERE™ (triamcinolone acetonide injectable suspension), for suprachoroidal use

Initial U.S. Approval: 1957

INDICATIONS AND USAGE

XIPERE™ (triamcinolone acetonide injectable suspension) 40 mg/mL is indicated for the treatment of macular edema associated with uveitis.

CONTRAINDICATIONS

4.1 Ocular or Periocular Infections XIPERE™ is contraindicated in patients with active or suspected ocular or periocular infections including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and fungal diseases.

4.2 Hypersensitivity XIPERE™ is contraindicated in patients with known hypersensitivity to triamcinolone acetonide or any other components of this product.

WARNINGS AND PRECAUTIONS

5.1 Potential Corticosteroid-Related Effects Use of corticosteroids may produce cataracts, increased intraocular pressure, and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids should be used cautiously in patients with a history of ocular herpes simplex. Corticosteroids should not be used in patients with active ocular herpes simplex.

5.2 Alterations in Endocrine Function Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and hyperglycemia can occur following administration of a corticosteroid. Monitor patients for these conditions with chronic use. Corticosteroids can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Drug induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in dosage.

ADVERSE REACTIONS

6.1 Clinical Trials 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 the clinical trials of another drug and may not reflect the rates observed in practice. XIPERE™ was studied in a multicenter, randomized, sham-controlled, double-masked study in patients with macular edema associated with uveitis. Table 1 summarizes data available from the clinical trial for XIPERE™ treated patients and control patients. The most common ocular (study eye) adverse reactions occurring in ≥ 2% of patients and nonocular adverse reactions occurring in ≥ 5% of patients are shown in Table 1.

Adverse Reaction	XIPERE™ (N = 96) n (%)	Control (N = 64) n (%)
Ocular		
Increased intraocular pressure, non-acute [a,b]	13 (14%)	9 (14%)
Eye pain, non-acute [b]	11 (12%)	0
Cataract [c]	7 (7%)	4 (6%)
Increased intraocular pressure, acute [a, d]	6 (6%)	0
Vitreous detachment	5 (5%)	1 (2%)
Injection site pain	4 (4%)	2 (3%)
Conjunctival haemorrhage	4 (4%)	2 (3%)
Visual acuity reduced	4 (4%)	1 (2%)
Dry eye	3 (3%)	1 (2%)
Eye pain, acute [d]	3 (3%)	0
Photophobia	3 (3%)	0
Vitreous floaters	3 (3%)	0
Uveitis	2 (2%)	7 (11%)
Conjunctival hyperaemia	2 (2%)	2 (3%)
Punctate keratitis	2 (2%)	1 (2%)
Conjunctival oedema	2 (2%)	0
Meibomianitis	2 (2%)	0
Anterior capsule contraction	2 (2%)	0
Chalazion	2 (2%)	0
Eye irritation	2 (2%)	0
Eye pruritus	2 (2%)	0
Eyelid ptosis	2 (2%)	0
Photopsia	2 (2%)	0
Vision blurred	2 (2%)	0
Non-ocular		
Headache	5 (5%)	2 (3%)

[a] Includes intraocular pressure increased and ocular hypertension [b] Defined as not occurring on the day of the injection procedure, or occurring on the day of the injection procedure and not resolving the same day [c] Includes cataract, cataract cortical, and cataract subcapsular [d] Defined as occurring on the day of the injection procedure and resolving the same day

USE IN SPECIAL POPULATIONS

8.1 Pregnancy Risk Summary There are no adequate and well-controlled studies with XIPERE™ in pregnant women to inform drug-associated risks. In animal reproductive studies from the published literature, topical ocular administration of corticosteroids has been shown to produce teratogenicity at clinically relevant doses. There is negligible systemic XIPERE™ exposure following suprachoroidal injection [see Clinical Pharmacology (12.3)]. Corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Animal Data Animal reproduction studies using XIPERE™ have not been conducted. In animal reproductive studies from the published literature, topical ocular administration of corticosteroids to pregnant mice and rabbits during organogenesis has been shown to produce cleft palate, embryofetal death, herniated abdominal viscera, hypoplastic kidneys and craniofacial malformations.

8.2 Lactation Risk Summary It is not known whether ocular administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for XIPERE™ and any potential adverse effects on the breastfed infant from XIPERE™. There are no data on the effects of XIPERE™ on milk production.

8.4 Pediatric Use Safety and effectiveness of XIPERE™ in pediatric patients have not been established.

8.5 Geriatric Use No overall differences in safety or effectiveness have been observed between elderly and younger patients following XIPERE™ administration.

NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis No information is available on the carcinogenic potential of triamcinolone acetonide.

Mutagenesis No information is available on the mutagenic potential of triamcinolone acetonide.

Fertility No information is available on the effect of triamcinolone acetonide on fertility.

Manufactured for: Clearside Biomedical, Inc.
900 North Point Parkway, Suite 200
Alpharetta, GA 30005 www.clearsidebio.com/patents

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DEI: THE LONG GAME

BY GUEST EDITORS VIVIENNE S. HAU, MD, PHD, AND BASIL K. WILLIAMS JR, MD


Anyone who tuned into the Super Bowl this year—whether for the game, the commercials, or Rhianna's first public performance in 7 years—hopefully noticed the effort put forth to boost diversity and inclusion during the event. Some were obvious choices; some were lucky coincidences for the National Football League (NFL). This was the first Super Bowl in which both quarterbacks were Black, the flight crew for the military flyover consisted of all women, performers used both American and North American Indian sign language to share the music with deaf listeners, and Rhianna blew up social media as the first artist to headline the event while pregnant.[1]

Put together, it looked like the NFL had done its best to check all the boxes, and the event was touted as "delivering wins for inclusion" by *Forbes* magazine (apparently the commercials fell short, though).[1]

Like many, we were watching with family and friends, and the reactions to these "firsts" were a mix of the all-too-familiar. Many applauded the overt attempts at inclusion, while a select few grumbled that it was "over the top." The all-woman flight crew drew the adults' attention, but the confused reactions from the young girls in the room made it painfully clear that *not* having an all-woman flight crew was just as unfathomable. The halftime show was rife with controversy: complaints that it was boring, praise for Rhianna's vocals, and knowing nods from moms when Rhianna unapologetically took a seat mid-performance and then wrapped herself in what might as well have been a comforter—you go girl.

But now that the hubbub has died down, we must ask ourselves, why are we still having so many "firsts" in the first place? It's 2023, and this year was the 57th Super Bowl—why is it the first one with two Black quarterbacks, considering nearly 60% of NFL players are Black?[2] Why did it take commemorating 50 years of women flying in the US Navy to find five women to do the flyover?[3] Why was there such a frenzy over a performer daring to be pregnant at the same time?

The answer is because diversity, equity, and inclusion (DEI) is still very much a work in progress. We have much to do, and for now, it must be a conscious decision. That's why *Retina Today*, in addition to actively working to include diverse authors throughout the year, dedicates an entire issue to the topic. Within these pages, authors explore the gender gap in retina authorship, diversity in clinical trials, patient/physician concordance, retinal surgery in the developing world, mentoring underrepresented groups in retina, and one patient's inspiring journey with retinitis pigmentosa.

One group that was conspicuously missing (in our humble opinion) from the Super Bowl inclusion fanfare was the LGBTQ+ community. Maybe the NFL isn't ready to tackle this one. But we are. We convened what very well may be the first roundtable of superb retina specialists who are open about their status as part of the LGBTQ+ community. The article is an ode to the strength it takes to be your authentic self in a field once dominated by a very select group of practitioners. The panelists share poignant moments along their personal journeys in the hopes that it helps others better understand the struggles of those who are underrepresented in medicine—and where, exactly, they can work toward a more inclusive atmosphere for patients, staff, and colleagues.

Making DEI a priority takes effort and forethought. Right now, that intention may feel uncomfortable and forced for those who have yet to understand the need and embrace the benefits. But we must talk about it anyway so that, one day, it won't be an obvious decision; instead, it will just be an integral part of who we are. ■

1. Thompson S. SuperBowl LVII delivered wins for inclusion. Almost none came from the ads. *Forbes*. February 13, 2023. Accessed February 14, 2023. www.forbes.com/sites/soniathompson/2023/02/13/superbowl-lvii-delivered-wins-for-inclusion-almost-none-came-from-the-ads
2. Gough C. Share of African Americans in the National Football League in 2021, by role. Statista. July 20, 2022. Accessed February 14, 2023. www.statista.com/statistics/1154691/nfl-racial-diversity
3. US Navy Super Bowl LVII flyover team. Navy Outreach. Accessed February 14, 2023. www.navy.mil/Portals/1/features/superbowl/Navy-SuperBowl-Flyover-Bios-6Feb23.pdf

ON THE COVER

- Abdul-Hadi Kaakour, MD, MS, assists Aleksandra Rachitskaya, MD, in the OR.
- Vivienne S. Hau, MD, PhD, poses with her staff in the OR.
- Luc Dupuy Pierre, MD, performs his first vitrectomy in Cap-Haïtien, Haiti.
- Richard Hunter finishes a marathon with his guide, Scott Jurek.
- Roberto Diaz-Rohena, MD, enjoys a day in the office with his past fellows, Blanca Flores, MD, who is currently training in England, and Cooper Clark, MD, now a retina specialist in San Antonio.

RT NEWS

MARCH 2023

VOL. 18, NO. 2 | RETINATODAY.COM

HISTORIC FDA APPROVAL FOR GEOGRAPHIC ATROPHY TREATMENT

For the first time, patients with geographic atrophy (GA) secondary to AMD now have access to a therapy with the FDA approval of pegcetacoplan intravitreal injection (Syfovre, Apellis Pharmaceuticals).[1] Pegcetacoplan is approved for patients with GA with or without subfoveal involvement and can be dosed every 25 to 60 days—providing flexibility for physicians and patients.

The approval is based on positive 24-month data from the phase 3 OAKS and DERBY studies, which enrolled a broad population of patients. In the studies, pegcetacoplan reduced the rate of GA lesion growth by up to 22% compared with sham and demonstrated increasing treatment effects, with the greatest benefit (up to 36% reduction in lesion growth) occurring between months 18 and 24.[2]

To hear our medical editors' hot takes on the approval, scan the QR code or visit New Retina Radio on Eyetube at eyetube.net/podcasts.

"With Syfovre, we finally have a safe and effective GA treatment for this devastating disease, with increasing effects over time," said Eleonora Lad, MD, PhD, the lead investigator of OAKS and director of ophthalmology clinical research at the Duke University Medical Center in Durham, North Carolina.[1]

The safety profile of pegcetacoplan is well-demonstrated, and the most common adverse reactions (≥ 5%) reported were ocular discomfort, new onset wet AMD (rate of 11.9% and 6.7% in the monthly and every-other-month groups), vitreous floaters, and conjunctival hemorrhage.[1,2]

Apellis expects pegcetacoplan to be available nationwide by March. Additionally, the European Medicines Agency is reviewing the marketing authorization application, with a decision expected in early 2024, and a marketing application has been submitted to Health Canada.[1]

1. FDA approves Apellis' Syfovre (pegcetacoplan), first and only treatment for geographic atrophy [press release]. Eyewire+. February 17, 2023. Accessed February 21, 2023. eyewire.news/news/fda-approves-apellis-syfovre-pegcetacoplan-first-and-only-treatment-for-geographic-atrophy

2. Apellis announces 24-month results showing increased effects over time with pegcetacoplan in phase 3 DERBY and OAKS studies in geographic atrophy (GA) [press release]. Apellis. August 24, 2022. Accessed February 21, 2023. investors.apellis.com/news-releases/news-release-details/apellis-announces-24-month-results-showing-increased-effects

STUDY PROPOSES UPDATED MACULAR HOLE CLASSIFICATION

The CLOSE study group has proposed a new surgical classification for large full-thickness macular holes (FTMHs) based on a systematic review of new treatments.[1] Due to the numerous innovative techniques that have been developed to address FTMHs, the group saw a need for an updated classification to assist in the decision-making process for surgery.

The study included an analysis of 31 articles and a total of 1,135 eyes, which were divided into five groups based on the surgical technique used: internal limiting membrane (ILM) peeling, ILM flaps, macular hydrodissection, human amniotic membrane graft, and autologous retinal transplantation. For each method, the researchers used a chi-square test to determine a connection between the minimal linear diameter (measured in micrometers) and how well the hole closed. They also compared the postoperative BCVA gains between the groups. While baseline BCVA and hole size were heterogenous between the treatment groups, closure rates differed based on hole size.

The new classification suggests that ILM peeling can lead to successful closure for FTMHs that are 535 µm or smaller, with a closure rate of nearly 97%. However, FTMHs that measured between 535 µm and 799 µm fared better with an ILM flap technique, with a closure rate of 99%. For the few macular holes included in the study that measured 800 µm or greater, human amniotic membrane graft, macular hydrodissection, and autologous retinal transplantation led to closure rates of 100%, 83.3%, and 90.5%, respectively.

The group noted that further studies are necessary to determine which technique is best for the largest holes, given the small sample size in the study.

1. Rezende FA, Ferreira BG, Rampakakis E, et al. Surgical classification for large macular hole: based on different surgical techniques results: the CLOSE study group. *Int J Retina Vitreous*. 2023;9(1):4.

0.18 mg
YUTIQ®
(fluocinolone acetonide intravitreal implant) 0.18 mg

Discover continuous calm in uveitis[1]

YUTIQ is designed to deliver a sustained release of fluocinolone for up to 36 months for patients with chronic non-infectious uveitis affecting the posterior segment of the eye[1]

- Proven to reduce uveitis recurrence at 6 and 12 months[1,*]
  At 6 months–18% for YUTIQ and 79% for sham for Study 1 and 22% for YUTIQ and 54% for sham for Study 2 (P<.01). At 12 months–28% for YUTIQ and 86% for sham for Study 1 and 33% for YUTIQ and 60% for sham for Study 2.
- Extended median time to first recurrence of uveitis[1,2]
  At 12 months–NE[†] for YUTIQ/92 days for sham in Study 1; NE for YUTIQ/187 days for sham in Study 2.
- Mean intraocular pressure (IOP) increase was comparable to sham[1,2]
  Study was not sized to detect statistically significant differences in mean IOP.

*Study design: The efficacy of YUTIQ was assessed in 2 randomized, multicenter, sham-controlled, double-masked, Phase 3 studies in adult patients (N=282) with non-infectious uveitis affecting the posterior segment of the eye. The primary endpoint in both studies was the proportion of patients who experienced recurrence of uveitis in the study eye within 6 months of follow-up; recurrence was also assessed at 12 months. Recurrence was defined as either deterioration in visual acuity, vitreous haze attributable to non-infectious uveitis, or the need for rescue medications.

[†]NE=non-evaluable due to the low number of recurrences in the YUTIQ group.

For more information, visit
YUTIQ.com

INDICATIONS AND USAGE

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Ocular or Periocular Infections: YUTIQ is contraindicated in patients with active or suspected ocular or periocular infections including most viral disease of the cornea and conjunctiva including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections and fungal diseases.

Hypersensitivity: YUTIQ is contraindicated in patients with known hypersensitivity to any components of this product.

WARNINGS AND PRECAUTIONS

Intravitreal Injection-related Effects: Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. Hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection.

Steroid-related Effects: Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

Risk of Implant Migration: Patients in whom the posterior capsule of the lens is absent or has a tear are at risk of implant migration into the anterior chamber.

ADVERSE REACTIONS

In controlled studies, the most common adverse reactions reported were cataract development and increases in intraocular pressure.

Please see brief summary of full Prescribing Information on adjacent page.

References: 1. YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg full US Prescribing Information. EyePoint Pharmaceuticals, Inc. February 2022. **2.** Data on file.

EYEPOINT® PHARMACEUTICALS

480 Pleasant Street, Suite B300, Watertown, MA 02472
02/2023
US-YUT-2300016

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg, for intravitreal injection
Initial U.S. Approval: 1963

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

1. INDICATIONS AND USAGE. YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

4. CONTRAINDICATIONS. 4.1. Ocular or Periocular Infections. YUTIQ is contraindicated in patients with active or suspected ocular or periocular infections including most viral disease of the cornea and conjunctiva including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections and fungal diseases. **4.2. Hypersensitivity.** YUTIQ is contraindicated in patients with known hypersensitivity to any components of this product.

5. WARNINGS AND PRECAUTIONS. 5.1. Intravitreal Injection-related Effects. Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. Hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection *[see Patient Counseling Information (17) in the full prescribing information]*. **5.2. Steroid-related Effects.** Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection. **5.3. Risk of Implant Migration.** Patients in whom the posterior capsule of the lens is absent or has a tear are at risk of implant migration into the anterior chamber.

6. ADVERSE REACTIONS. 6.1. Clinical Studies 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 the clinical trials of another drug and may not reflect the rates observed in practice. Adverse reactions associated with ophthalmic steroids including YUTIQ include cataract formation and subsequent cataract surgery, elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera. Studies 1 and 2 were multicenter, randomized, sham injection-controlled, masked trials in which patients with non-infectious uveitis affecting the posterior segment of the eye were treated once with either YUTIQ or sham injection, and then received standard care for the duration of the study. Study 3 was a multicenter, randomized, masked trial in which patients with non-infectious uveitis affecting the posterior segment of the eye were all treated once with YUTIQ, administered by one of two different applicators, and then received standard care for the duration of the study. Table 1 summarizes data available from studies 1, 2 and 3 through 12 months for study eyes treated with YUTIQ (n=226) or sham injection (n=94). The most common ocular (study eye) and non-ocular adverse reactions are shown in Table 1 and Table 2.

Table 1: Ocular Adverse Reactions Reported in ≥ 1% of Subject Eyes and Non-Ocular Adverse Reactions Reported in ≥ 2% of Patients

Ocular		
ADVERSE REACTIONS	**YUTIQ (N=226 Eyes) n (%)**	**Sham Injection (N=94 Eyes) n (%)**
Cataract[1]	63/113 (56%)	13/56 (23%)
Visual Acuity Reduced	33 (15%)	11 (12%)
Macular Edema	25 (11%)	33 (35%)
Uveitis	22 (10%)	33 (35%)
Conjunctival Hemorrhage	17 (8%)	5 (5%)
Eye Pain	17 (8%)	12 (13%)
Hypotony Of Eye	16 (7%)	1 (1%)
Anterior Chamber Inflammation	12 (5%)	6 (6%)
Dry Eye	10 (4%)	3 (3%)
Vitreous Opacities	9 (4%)	8 (9%)
Conjunctivitis	9 (4%)	5 (5%)
Posterior Capsule Opacification	8 (4%)	3 (3%)
Ocular Hyperemia	8 (4%)	7 (7%)
Vitreous Haze	7 (3%)	4 (4%)
Foreign Body Sensation In Eyes	7 (3%)	2 (2%)
Vitritis	6 (3%)	8 (9%)
Vitreous Floaters	6 (3%)	5 (5%)
Eye Pruritus	6 (3%)	5 (5%)
Conjunctival Hyperemia	5 (2%)	2 (2%)
Ocular Discomfort	5 (2%)	1 (1%)
Macular Fibrosis	5 (2%)	2 (2%)
Glaucoma	4 (2%)	1 (1%)
Photopsia	4 (2%)	2 (2%)

(continued)

Table 1: Ocular Adverse Reactions Reported in ≥ 1% of Subject Eyes and Non-Ocular Adverse Reactions Reported in ≥ 2% of Patients

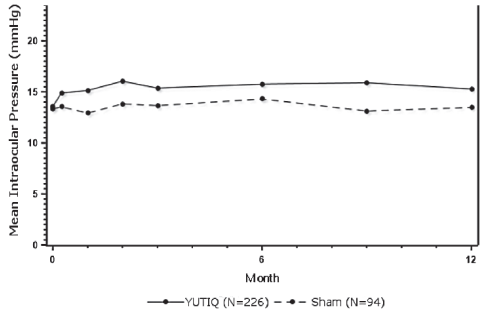
Ocular		
ADVERSE REACTIONS	**YUTIQ (N=226 Eyes) n (%)**	**Sham Injection (N=94 Eyes) n (%)**
Vitreous Hemorrhage	4 (2%)	0
Iridocyclitis	3 (1%)	7 (7%)
Eye Inflammation	3 (1%)	2 (2%)
Choroiditis	3 (1%)	1 (1%)
Eye Irritation	3 (1%)	1 (1%)
Visual Field Defect	3 (1%)	0
Lacrimation Increased	3 (1%)	0
Non-ocular		
ADVERSE REACTIONS	**YUTIQ (N=214 Patients) n (%)**	**Sham Injection (N=94 Patients) n (%)**
Nasopharyngitis	10 (5%)	5 (5%)
Hypertension	6 (3%)	1 (1%)
Arthralgia	5 (2%)	1 (1%)

1. Includes cataract, cataract subcapsular and lenticular opacities in study eyes that were phakic at baseline. 113 of the 226 YUTIQ study eyes were phakic at baseline; 56 of 94 sham-controlled study eyes were phakic at baseline.

Table 2: Summary of Elevated IOP Related Adverse Reactions

ADVERSE REACTIONS	YUTIQ (N=226 Eyes) n (%)	Sham (N=94 Eyes) n (%)
IOP elevation ≥ 10 mmHg from Baseline	50 (22%)	11 (12%)
IOP elevation > 30 mmHg	28 (12%)	3 (3%)
Any IOP-lowering medication	98 (43%)	39 (41%)
Any surgical intervention for elevated IOP	5 (2%)	2 (2%)

Figure 1: Mean IOP During the Studies



8. USE IN SPECIFIC POPULATIONS. 8.1 Pregnancy. Risk Summary. Adequate and well-controlled studies with YUTIQ have not been conducted in pregnant women to inform drug associated risk. Animal reproduction studies have not been conducted with YUTIQ. It is not known whether YUTIQ can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. YUTIQ should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus. All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the United States general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. **8.2 Lactation.** Risk Summary. Systemically administered corticosteroids are present in human milk and can suppress growth, interfere with endogenous corticosteroid production. Clinical or nonclinical lactation studies have not been conducted with YUTIQ. It is not known whether intravitreal treatment with YUTIQ could result in sufficient systemic absorption to produce detectable quantities of fluocinolone acetonide in human milk, or affect breastfed infants or milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for YUTIQ and any potential adverse effects on the breastfed child from YUTIQ. **8.4 Pediatric Use.** Safety and effectiveness of YUTIQ in pediatric patients have not been established. **8.5 Geriatric Use.** No overall differences in safety or effectiveness have been observed between elderly and younger patients.

Manufactured by:
EyePoint Pharmaceuticals US, Inc., 480 Pleasant Street, Watertown, MA 02472 USA

Pharma Updates From Eyewire+

- Regeneron Pharmaceuticals' biologics licensing agreement for 8 mg aflibercept for the treatment of wet AMD, diabetic macular edema, and diabetic retinopathy is now under priority review by the FDA with a target action date of June 27, 2023.
- The FDA cleared HuidaGene Therapeutics' investigational new drug application for the multinational clinical trial of HG004, an ophthalmic injection being developed for the treatment of retinal dystrophies associated with *RPE65* mutations.
- Clearside Biomedical announced positive 6-month data for its OASIS clinical trial of axitinib injectable suspension (CLS-AX), administered suprachoroidally, for the treatment of wet AMD. The results show a 77% to 85% reduction in treatment burden in cohorts three and four (who received doses of 0.5 mg and 1.0 mg, respectively), with 67% of participants able to go at least 6 months without additional therapy.
- The FDA granted fast track designation to EA-2353 (Endogena Therapeutics) for the treatment of retinitis pigmentosa. The small-molecule therapy selectively activates endogenous retinal stem and progenitor cells, which differentiate into photoreceptors, to potentially restore visual function.
- Three-month safety and efficacy data from a single-surgeon case series (n = 24) evaluating the smaller-incision new-generation implantable miniature telescope (Samsara Vision) in patients with bilateral central vision impairment due to advanced AMD were published in the *Journal of Clinical Medicine*. At 3 months, the study eye showed significantly better CDVA and near VA compared with the fellow eye ($P < .0001$ for each); the average change from baseline in CDVA of the study eye was +14.9 ± 7.1 letters ($P < .0001$).
- The Centers for Medicare & Medicaid Services issued a permanent, product-specific J-code (J2403) for 3% chloroprocaine hydrochloride ophthalmic gel (Iheezo, Harrow), a single-use, preservative-free ophthalmic gel used for ocular surface anesthesia. The code will become effective April 1, 2023.
- The European Commission has granted Class IIb medical device certification to Eyenuk to market its EyeArt artificial intelligence eye screening system in the European Union for the new uses of detecting AMD and glaucomatous optic nerve damage—adding to the previous approval to detect diabetic retinopathy.
- Aflibercept (Eylea, Regeneron) injection received FDA approval for the treatment of retinopathy of prematurity. In two phase 3 clinical trials, approximately 80% of infants treated with aflibercept experienced an absence of active retinopathy of prematurity and had no unfavorable structural outcomes by week 52. No new safety signals were observed in either trial.

Check out ***Eyewire+*** for more of the latest news in retina.

PHASE 2 DATA REPORTED FOR ORAL DIABETIC RETINOPATHY THERAPY

Ocuphire Pharma announced topline results from its ZETA-1 phase 2 trial of oral APX3330 for the treatment of diabetic retinopathy (DR).[1] While the trial did not meet the primary endpoint of ≥ 2-step improvement in DR severity score at week 24 in the study eye, it demonstrated a statistically significant reduction of disease progression at 24 weeks.

The trial met a key secondary endpoint showing a binocular 3-step or more worsening of DR severity score. This outcome demonstrates the therapy's ability to slow the worsening of DR and is a potential phase 3 registration endpoint, according to a company release.[1]

The drug demonstrated a favorable safety and tolerability profile, with no serious adverse events reported. Additional trial data analysis is in progress and detailed results are forthcoming, according to the company.

1. Ocuphire announces topline results from ZETA-1 phase 2 trial of oral APX3330 in diabetic retinopathy. EyeWire+. Published January 26, 2023. Accessed February 10, 2023. eyewire.news/news/ocuphire-announces-topline-results-from-zeta-1-phase-2-trial-of-oral-apx3330-in-diabetic-retinopathy

SURVEY REVEALS HOW RETINA SPECIALISTS FEEL ABOUT BIOSIMILARS

The results of a 16-question survey showed that concerns around safety, efficacy, and immunogenicity of biosimilar anti-VEGF agents persist among retina specialists in the United States and Europe.[1]

The Bio-USER survey, designed to assess awareness of anti-VEGF biosimilars among retina specialists, was distributed online via email, WhatsApp, and LinkedIn, and had 112 total respondents. According to the findings, 56.3% were familiar with anti-VEGF biosimilars, although 18.75% felt they needed more information and 25% wanted more real-world data. Respondents also expressed concerns related to safety (50%), efficacy (58.9%), and immunogenicity (50%).

The analysis also compared attitudes of retina specialists in the United States with those of specialists in Europe. The results showed that US retina specialists were less inclined to switch from using off-label bevacizumab (Avastin, Genentech/Roche) to a ranibizumab biosimilar or, potentially, an on-label bevacizumab than European retina specialists ($P = .0001$). Clinicians in the United States also shared that they were more concerned about biosimilar safety ($P = .0371$) and efficacy ($P = .0078$) compared with clinicians in Europe. These findings suggest that more education on biosimilars is warranted. ■

1. Sharma A, Holz FG, Freund KB, et al. Biosimilars for retinal diseases: United States-Europe awareness survey (Bio-USER – survey) [preprint published online February 1, 2023]. *Expert Opin Biol Ther*.

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By Levent Akduman, MD, FASRS; Serhat Ermis, MD; and Ozgur Artunay, MD

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.

References: 1. Boyer DS et al. *Retina*. 2017;37:819-835. 2. Lindblad AS et al, and AREDS Research Group. *Arch Ophthalmol*. 2009;127(9):1168-1174. 3. Holz FG et al. *Ophthalmology*. 2014;121(5):1079-1091. 4. Sunness JS et al. *Ophthalmology*. 2007;114(2):271-277. 5. Kimel M et al. Invest *Ophthalmol Vis Sci*. 2016;57(14):6298-6304. 6. Sadda SR et al. *Retina*. 2016;36(10):1806-1822. 7. Singh RP et al. *Am J Ophthalmic Clin Trials*. 2019;(1):1-6. doi:10.25259/ajoct-9-2018. 8. Sivaprasad S et al. *Ophthalmol Ther*. 2019;8(1):115-124. 9. Patel PJ et al. *Clin Ophthalmol*. 2020;14:15-28. 10. Chakravarthy U et al. *Ophthalmology*. 2018;125:842-849.

Apellis

CONDUCTING IMPACTFUL RESEARCH AS A RETINA FELLOW

A look at how clinical, translational, and basic research fits into a clinical fellowship.

BY ASAD F. DURRANI, MD; SAAGAR PANDIT, MD, MPH; ANAND GOPAL, MD; AND LINNET RODRIGUEZ, MD

As we move beyond the midpoint of the academic year, first-year fellows have adjusted to the clinical demands of fellowship and are beginning to conduct research, while second-year fellows are finishing projects and deciding how their research will fit into their ongoing careers.

In this article, prominent retina specialists discuss how research fits into a busy retina fellowship.

—Asad F. Durrani, MD

DR. DURRANI: WHY DID YOU CHOOSE TO MAKE RESEARCH A COMPONENT OF YOUR CAREER?

Mark W. Johnson, MD: During my residency and fellowship, I enjoyed the thrill of discovering new clinically relevant knowledge and the rewarding feeling of sharing that knowledge with colleagues through presentations and publication.

I also loved attending scientific meetings and participating in the scientific and social exchange there. Those early experiences convinced me that clinical and translational research should be an important part of my career.

David N. Zacks, MD, PhD: Ever since I was an undergraduate, I have been interested in sensory biology and exploring the frontiers of science. That is what compelled me to do the MD/PhD program. I never saw myself as doing only research because I wanted to have a mechanism through which to apply my learnings—a thought that solidified in residency and fellowship. Seeing patients for whom there were limited treatment options motivated me to understand disease processes more deeply and seek the development of new therapies.

Jason Hsu, MD: For me, it stemmed from a desire to have a larger impact on our field. There's also something exciting about expanding our understanding of a disease or treatment and discovering better ways to care for our patients. Sometimes, the best part about research is the results of the analysis, especially when it changes our understanding of a disease or treatment algorithm.

Finally, I think it may help extend my career and perhaps help avoid burnout because it gives me a greater sense of purpose beyond the day-to-day clinical duties.

Jose S. Pulido, MD, MS, MBA, MPH: I was so impressed by my residency mentors that I couldn't think of doing anything else. It's fun to be at the cutting edge and know that you are not only helping the patient next to you but also a patient 5,000 miles away. It has kept me young, and every day I learn something new.

DR. DURRANI: WHY SHOULD FELLOWS BE INVOLVED IN RESEARCH?

Ajay E. Kuriyan, MD, MS: Research opportunities as a fellow can provide a foundation for learning how to formulate research questions, conduct literature reviews, choose study designs, collaborate within and outside of your institution, write in a scientific manner, effectively convey data, present posters and presentations, submit manuscripts and respond to reviewer comments, and, if applicable, think of the next steps for a research project.

Dr. Johnson: I strongly recommend that fellows get involved in research during their fellowship for several

reasons. First, fellows are in an excellent position to ask and help answer meaningful clinical questions—and thereby benefit patients.

Second, engaging in the research process allows fellows to determine their interest level in pursuing research throughout their careers.

Third, most fellows find that presenting the results of their research is a highly rewarding, interesting, and entertaining experience (and a good way to connect).

Fourth, involvement in research adds a layer of enrichment to patient care activities, changing the way we view our patients' conditions and helping us avoid burnout in our professional lives.

DR. DURRANI: WHAT ARE THE BEST TYPES OF RESEARCH TO CONDUCT DURING A FELLOWSHIP?

Dr. Zacks: The best type of research to do is on a topic that interests you. Still, time constraints will put some limitations on the work that can be done. For example, bench research is often only doable if you are part of a larger team (eg, the fellow does the surgical manipulation and tissue harvesting with the technician running the western blots or other bench assays).

Carl D. Regillo, MD: The best type is original, independent studies (retrospective or prospective) designed to address an unanswered clinical question. Ideally, the fellow should be the lead in all aspects of a study—from design to data acquisition and analysis and then to presenting and/or publishing the work. There is also value in being an investigator in multicenter trials to understand good clinical practices in large-scale clinical research and gain experience in this type of research. This will make it easier to continue such investigative work in practice.

Sunir J. Garg, MD: I encourage our fellows to explore original research ideas. These can be ideas that the fellow comes up with or, often, ideas that the attending has been thinking about but needs help to bring to fruition. Fellows should also complete a project themselves during fellowship. This is important not only for the intellectual pursuit, but also to ensure that the fellow remains the lead author on the project they spent so much time working on.

DR. DURRANI: HOW SHOULD FELLOWS GO ABOUT DEVELOPING A PARTICULAR RESEARCH INTEREST?

Dr. Zacks: I recommend fellows develop their research focus based on their interests. There is no shortage of topics to study—just look around your clinic and you will see lots of unsolved problems.

Dr. Kuriyan: If you're a fellow who doesn't already have a specific research interest, I recommend using your fellowship to learn research skills and gain as much exposure to research topics as possible to figure out what you want to focus on.

Dr. Pulido: At different points in my life, I concentrated on different areas but I am always open to going beyond my area of concentration. Keep learning, be open to new, but biologically valid, ideas, and move the boundaries.

Dr. Johnson: I have enjoyed writing about a wide variety of topics during my career. That said, if a

MEET THE EXPERTS

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fellow finds their interest drawn to a particular area of investigation, there can be advantages to concentrating their energies and expertise in one direction.

Dr. Regillo: My advice is to start with a general category of interest (eg, medical vs surgical, diagnostic vs therapeutic, big data, etc.) and then ask questions that need to be answered to come up with potential studies to pursue.

Dr. Garg: Retina is such an amazing field; there are a million and one questions to pursue. From an academic perspective, it is helpful to have some specific focus. It helps when people think that you are the expert in a disease. During fellowship itself, however, there isn't much time or need to concentrate your efforts on one particular research area.

Dr. Hsu: While it's great to have a predetermined niche, it's not essential. As a clinical researcher, the great thing is that there are always questions and ideas that are coming up on a regular basis both from my clinical and surgical experiences. Sometimes, a single idea generates a sequence of inquiries that becomes of interest and leads to multiple publications.

DR. DURRANI: HOW CAN FELLOWS TAKE ADVANTAGE OF CLINICAL TRIALS?

Dr. Zacks: As a fellow, it is hard to get involved in clinical trials directly beyond just being a subinvestigator. The big clinical trials all take years to develop. That said, fellows can approach their mentors and get involved in data analysis. A fellow can also consider starting a smaller investigator-initiated trial to answer a focused question. This can provide good experiences in the design and implementation of these trials.

Dr. Regillo: At the fellowship level, fellows need to rely on the attendings and clinical research staff to get involved as a coinvestigator. It is a valuable experience to be able to go to an investigator meeting of a new clinical trial and then be involved in both patient recruitment and clinical care.

Dr. Hsu: If you are interested in either of these routes, the first step is to establish yourself as a site principal investigator once in practice and recruit well for the studies in which you are involved. It's also important to get noticed by actively participating in investigator meetings.

Also, if there is a specific drug you are interested in using in a novel way, you can work with a mentor to propose an investigator-initiated trial to a pharmaceutical company. This way, you have the opportunity to design a study on a smaller scale and essentially apply for funding from the company.

DR. DURRANI: ANY LAST PEARLS FOR RETINA FELLOWS REGARDING RESEARCH?

Dr. Garg: Even if you don't think you want to pursue research as part of your day-to-day career, having some research exposure will help you critically evaluate the literature and improve your skills as a thoughtful journal reviewer.

I'm always amazed at how much work goes into even a simple project and what you learn from the peer review process. There is a great satisfaction in taking something from an idea to a finished project.

Finally, many papers will get rejected on their first submission. Do not let the paper you spent so much time on die because you did not keep submitting it to a journal. Almost all research projects find a home; you just have to figure out where that home is going to be.

Dr. Zacks: Regardless of your practice environment, it is possible to be active in research and contribute to the profession. By staying curious, asking questions, and seeking answers, you will have a much higher level of satisfaction with your career. I wish all the fellows good luck, and I look forward to hearing their presentations at future meetings! ■

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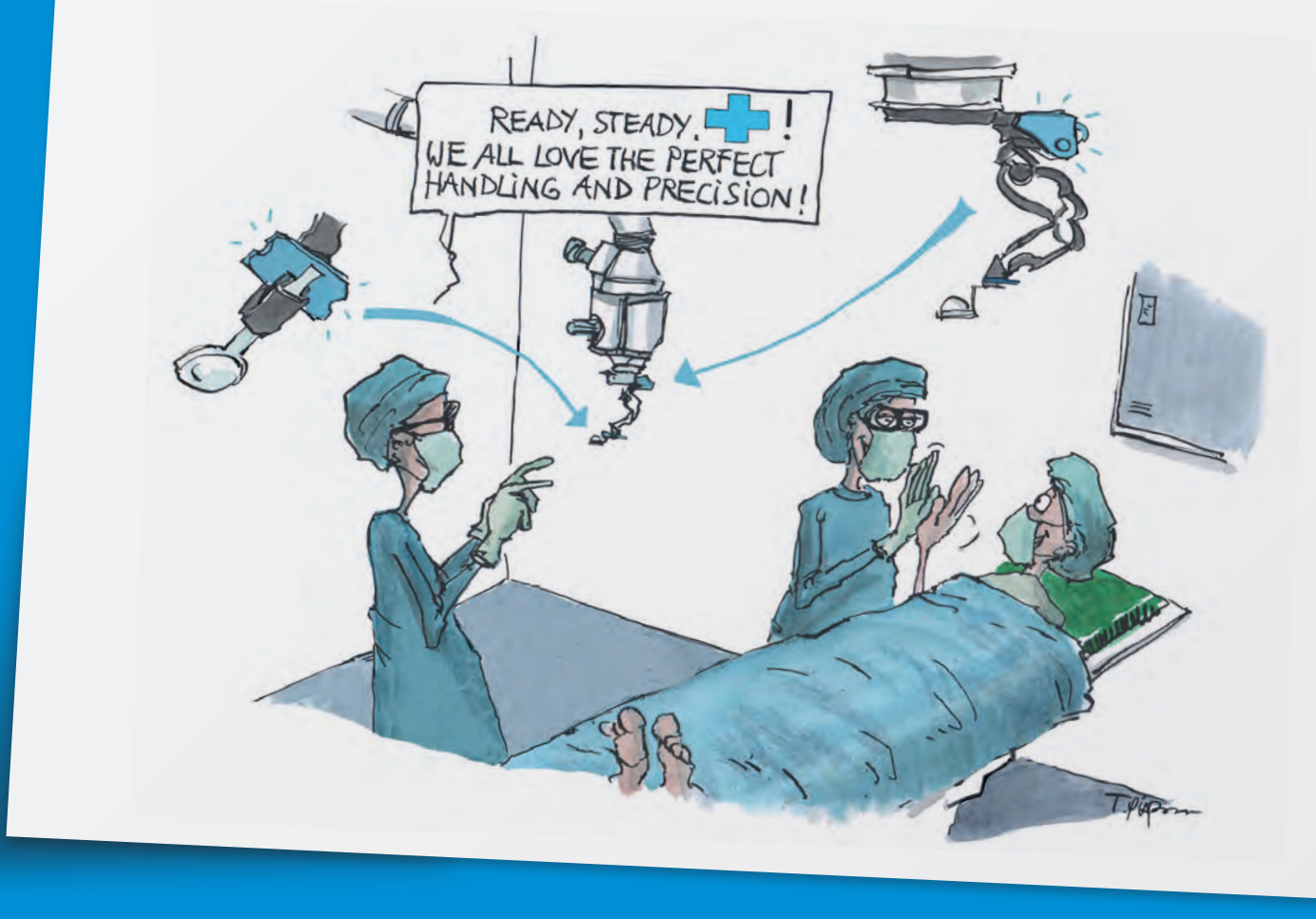

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WHERE IT ALL BEGAN

Talia R. Kaden, MD, grew up in Pittsburgh, Pennsylvania as the third of four children. She played sports throughout her childhood and loved math and robotics. She also loved sewing; her Hungarian grandmother was a seamstress and taught her to sew when she was 8 years old. When Dr. Kaden was 14, her parents bought her a sewing machine, which she still uses today. During her time at the local public high school, she made her own prom dress. She has always liked working with her hands.

HER PATH TO RETINA

Even before medical school, Dr. Kaden knew that she wanted to do something surgical. She seriously considered neurosurgery and orthopedic surgery before deciding that the combination of surgery and outpatient medicine offered by ophthalmology was the most compelling path forward.

While a Howard Hughes Medical Institute Research Scholar at the National Eye Institute, she studied mitochondrial function in ground squirrels and found that they selectively protect their retinas while in hibernation. This remarkable learning moment underscored the importance of sight and highlighted just how complicated and crucial a tiny part of an already small organ could be. By the time she began her residency, she was committed to retina, and though she considered other fields, they were never able to draw her attention in quite the same way.

SUPPORT ALONG THE WAY

Her first mentor was her high school science teacher and track coach, Gina Pacitti Barone. She pushed Dr. Kaden to think beyond her textbooks, graded on a curve, and provided the first example of an unapologetic woman in science. Dr. Kaden and Coach Barone are still in touch.

More recently, her fellowship mentors have become colleagues, partners, and friends, but they still serve as important sounding boards for difficult clinical and surgical cases. Dr. Kaden is indebted to them for their support and encouragement and for every time they have recommended her as a speaker or conference organizer. Her colleagues are a wonderful example of how to be a mentor, and she keeps them in mind as she trains her own fellows.

Dr. Kaden's Advice: The choices you make about with whom and where you practice are important for both your day-to-day experience and your long-term success.

AN EXPERIENCE TO REMEMBER

Dr. Kaden had the pleasure of serving as the curriculum chair for the 2022 OSN Retina meeting in New York City in November 2022. It was a special opportunity to meet an amazing faculty and help craft the educational direction and structure of a national meeting.

ADVICE FOR THOSE WHO FOLLOW

Dr. Kaden said that fellows should be honest with themselves about the parts of their training that have brought them joy and seek out environments that maximize those moments while helping them achieve their broader career goals. For her, those include taking care of complex cases, seeing a diverse patient population, and engaging with the retina community as an educator and a participant in local and national meetings. And be sure you like your colleagues, she added. She feels lucky to work with remarkable physicians who make her days even more enjoyable. ■

Talia R. Kaden, MD, is an assistant professor of ophthalmology at Northwell Health, New York's largest health care provider. She sees patients in both Manhattan and Queens and takes care of a diverse patient population; more languages are spoken in Queens than in any other place in the world. She teaches medical students, residents, and fellows in the clinic and the OR. She is also the director of the retina fellowship at Manhattan Eye, Ear, and Throat Hospital. She is an advisory board member for Genentech/Roche and Allergan/AbbVie. She can be reached at **tkaden1@northwell.edu**.

VITRECTOMY FOR UVEITIS

Taking the patient to the OR may be helpful when dealing with diagnostic dilemmas or complications.

BY SRUTHI AREPALLI, MD

Uveitis encompasses a heterogeneous mix of diseases. The main culprits include noninfectious and infectious etiologies; rarely, masqueraders, such as neoplastic conditions, are responsible.[1,2] The differentiation between these is important to determine the appropriate treatment and long-term management for patients.

In straightforward scenarios, the clinical examination coupled with laboratory testing yields a diagnosis and tenable treatment plan. However, with challenging cases (particularly those with infectious and neoplastic etiologies), a more invasive approach with vitrectomy remains a vital tool in the analytical armamentarium. With diagnostic vitrectomy, clinicians can examine ocular fluid and tissues with bacterial or fungal cultures, gram stain, polymerase chain reaction (PCR), and/or metagenomic deep sequencing. In addition, lymphoma testing includes an evaluation for the *MYD88* mutation, *IgH* gene rearrangement, and the examination of ocular tissue with a pathologist.[3,4]

PERIOPERATIVE PLANNING AND TECHNIQUE

The perioperative management surrounding vitrectomy can impact diagnostic yield, visual outcomes, and potential complication rates. As a general rule, vitrectomy should be avoided in inflamed eyes; but in certain cases, such as suspected infection, it may be necessary. In these scenarios, clinicians must have a careful discussion with the patient regarding the potential complications, including iatrogenic breaks and proliferative vitreoretinopathy. Surgeons must also consider the potential for a masquerading disease in which vitrectomy would be contraindicated. For example, retinoblastoma with a pseudohypopyon can mimic uveitis, and entering the eye can seed cancer cells.

In cases of suspected ocular lymphoma, steroids should be tapered at least 2 weeks before surgery to increase cellular yield, and care should be coordinated with oncology for a brain MRI and possible lumbar puncture for disease staging.[5] When an infection is suspected, ceasing steroids and the administration of intravitreal and/or systemic therapy can improve outcomes.[4] If there is concern for a concurrent infection or inflamation with an intraocular foreign body, ocular and orbital imaging with OCT or gentle ultrasound can be helpful. After obtaining the samples, orchestrating the processing of samples between laboratories and an ocular pathologist is necessary to avoid delays and sample degeneration.

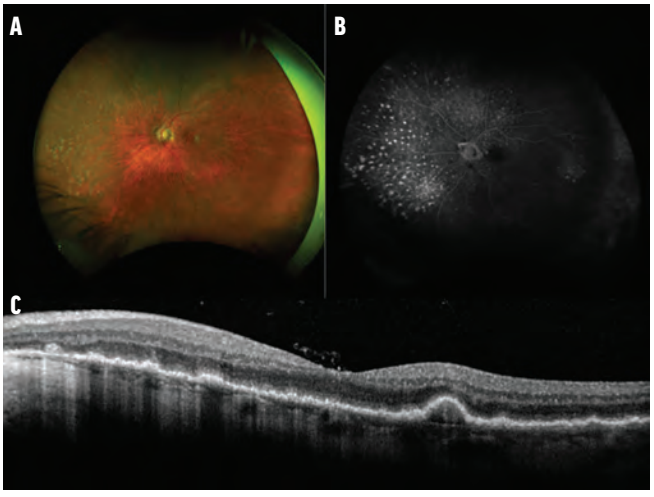

Figure 1. A 67-year-old woman presented with blurred vision in her left eye. Fundus examination showed vitritis and subretinal lesions in the macula and nasally (A). Fluorescein angiography showed staining of the lesions (B). OCT revealed a pigment epithelial detachment and subretinal deposits (C). Vitreous biopsy confirmed the diagnosis of vitreoretinal lymphoma.

During a vitrectomy, the priority is to collect samples safely, identify pathology requiring immediate treatment, and if applicable, administer anti-infectious agents. A standard three-port vitrectomy with a wide-angle viewing system is preferable to obtain sufficient vitreous and maintain visualization. Any existing anterior chamber hypopyon or hyphema should be cleared and can also be sent for analysis. Additionally, a lensectomy may be necessary in phakic patients due to inflammatory debris, vitreous opacities, or to enable a peripheral vitrectomy. In difficult cases, the view can be poor and prevent evaluation of the peripheral retina; avoid extensive peripheral vitreous manipulation in these situations to minimize iatrogenic breaks. Additional techniques and considerations for specific conditions are discussed below.

DIAGNOSING LYMPHOMA

Lymphoma often presents with posterior involvement, and it can mimic panuveitis or posterior uveitis.[4,6] Keep a high level of clinical suspicion in cases that initially respond to steroids but later flare and for patients older

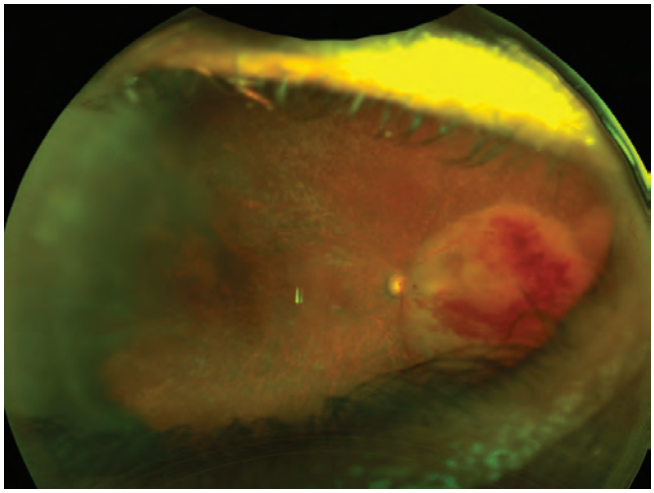

Image courtesy of Steven Yeh, MD, and Ghazala O'Keefe, MD

Figure 2. A 73-year-old woman with a history of diffuse large B-cell lymphoma was referred for worsening vision. Given her presentation of hemorrhage and retinal whitening, an infectious etiology was considered; however, the lesion continued to grow despite repeated injections of antiviral therapy. A retinal biopsy confirmed diffuse large B-cell lymphoma and the intraocular manifestations were managed with intravitreal methotrexate.

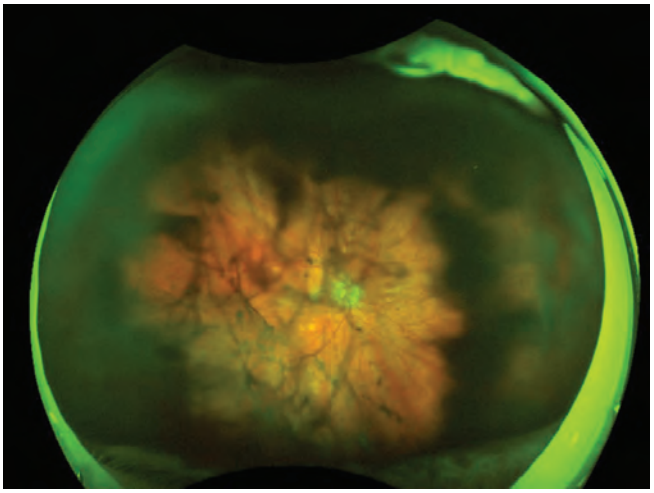

Image courtesy of Arthi Venkat, MD, MS

Figure 3. An 80-year-old man with metastatic melanoma on immunotherapy with Opdivo (nivolumab, Bristol-Myers Squibb) presented with decreasing vision. The fundus examination revealed dense vitritis that was initially assumed to be inflammation secondary to immunotherapy; however, the vitritis worsened with steroid therapy. Diagnostic vitrectomy with cytology revealed metastatic cells.

than 50 years who present with vitritis, especially those with neurological or personality changes (Figure 1).

Ideally, an undiluted specimen that provides a higher cellular yield is best for cytological analysis.[7] When gathering an undiluted sample, the surgeon can leave the infusion off or turn it to air to maintain pressure without diluting the sample. Decreasing the cut rate also increases cellular yield, and although there are no strict criteria, studies show decreased cellularity at speeds above 600 cuts per minute.[8] Despite optimizing surgical parameters, the yield of cytological analysis can be low, and ancillary tests—such as flow cytometry or *MYD88* testing—can help with the diagnosis.[3]

In rare cases, a fine needle aspiration biopsy (FNAB) or tissue sample of subretinal deposits, the retina, and/or the choroid can also help identify lymphoma (Figure 2).[9] An FNAB can be performed through either a transvitreal or transscleral approach with a 25-gauge needle attached to the tubing and a syringe, but the surgeon may have difficulty accessing or visualizing lesions that are anterior. When a subretinal biopsy makes the most sense, use diathermy to create a retinotomy overlying or adjacent to the infiltrate and aspirate the subretinal material with a soft tip.

If obtaining a retinal biopsy, perform a vitrectomy first and be sure to remove all vitreous overlying the biopsy site. If there is cellular material, this vitreous can be sent for pathology examination as well. After the vitrectomy, use endolaser or diathermy to delineate the area of interest (usually about 2 mm by 2 mm). This area can be cut with intraocular scissors and forceps and removed through an enlarged sclerotomy. An increase in infusion pressure during these steps helps control hemorrhage. A gas or oil tamponade is often used afterward, along with reinforcement of the area with endolaser.[6]

Rarely, a chorioretinal biopsy is required. In these cases, endolaser is also preemptively applied to the biopsy site. To access the tissue, create a 90% to 95% full-thickness scleral flap overlying the area of interest, with one side left as a hinge. Next, apply diathermy to the choroid and retina underneath the scleral flap to make two incisions parallel to the limbus, spaced 1 mm to 2 mm apart. The surgeon grasps this section with forceps and then makes two more incisions, this time perpendicular to the limbus, to yield a slab of chorioretinal tissue. After obtaining the tissue, suture the scleral flap closed and instill an intraocular tamponade.[9]

BIOPSIES BEYOND LYMPHOMA

Outside of lymphoma, other oncological conditions can present with vitreous, retinal, or choroidal involvement and require biopsy for their diagnosis. Rarely, ocular metastases can mimic retinitis, and this presentation can delay a patient's diagnosis and portends a poor prognosis and life expectancy.[10] Melanoma infrequently metastasizes to the vitreous and mimics uveitis unresponsive to steroids. Diagnostic vitrectomy and/or tissue biopsy coupled with cytological analysis can help elucidate the diagnosis in these cases (Figure 3).

When infection is suspected, the first steps are to obtain a sample through a vitreous or aqueous tap and administer appropriate therapy. However, vitrectomy may be necessary for patients where clinical samples do not yield an answer, the clinical course is unexpected, or in cases where better visualization is required to make a diagnosis and/or treat the underlying pathology. For example,

nocardia endogenous endophthalmitis has been reported to mimic lymphoma, among other possibilities, and can require a subretinal biopsy to confirm the diagnosis and determine treatment.[11] Intraoperative samples are sent for gram stain and culture, as well as PCR for viral etiologies and toxoplasmosis. Additionally, more extensive testing can reveal a diagnosis often missed on routine cultures or PCR. These include panbacterial PCR and metagenomic deep sequencing, also known as metagenomics next-generation sequencing (mNGS).[12,13]

Panbacterial PCR may be particularly useful because of its ability to detect organisms even after the administation of intravitreal therapy. In one study, panbacterial PCR detected an infectious etiology more often than vitreous cultures in patients who had been previously treated with intravitreal antibiotics.[14] mNGS also presents an exciting possibility to isolate causative pathogens. The utility of mNGS lies in its ability to analyze both DNA and RNA, thus allowing for all genomic material to be sequenced, even from very small clinical samples. This development has allowed for the identification of rare or even previously unidentified pathogens, as well as those that are culture resistant. This can further help to delineate which instances of uveitis may be inflammatory versus infectious and guide treatment.[3,15]

CONSEQUENCES OF INTRAOCULAR INFLAMMATION

Vitrectomy is also a helpful adjunct when managing the sequela of intraocular inflammation. Complications of inflammation include vitreous debris, retinal detachment, epiretinal membrane, and macular holes. A vitrectomy can remove visually significant vitreous debris, alleviate traction, and identify pathology often blocked by vitritis. When approaching retinal detachments, it is important to counsel patients on the higher rate of redetachment compared with traditional retinal detachment surgery. A few reports have evaluated retinal reattachment rates after infectious retinitis, with primary reattachment rates of about 60%.[16] Additionally, patients may more often require silicone oil, which can have antimicrobial properties and provide an effective tamponade (Figure 4).

Patients can also develop epiretinal membranes or macular holes in the setting of intraocular inflammation. Like retinal detachments, the success rates of macular hole closure are lower than those with uveitis; one study showed a success rate of approximately 80%.[17]

In any patient with uveitis undergoing vitrectomy, perioperative control of inflammation is essential. This may require topical, local, oral, and/or intravenous steroids before, during, and after the surgery. In cases of mild and remote uveitis, heavy topical steroids with an extended taper may suffice. In cases of more extensive inflammation, oral or local steroids are required with an appropriate postoperative taper schedule. In patients with active inflammation who require emergent surgery, intravenous steroids can help quell inflammation in addition to pre- and postoperative medications. Additionally, in infectious cases requiring surgery, it is wise to pretreat or simultaneously administer anti-infectious agents. Careful examination is also required in the postoperative period to evaluate for the recurrence of inflammation and its potential complications, which can be visually devastating. ■

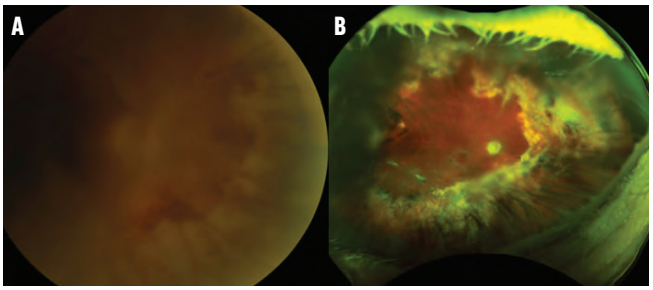

Image courtesy of Steven Yeh, MD

Figure 4. A 52-year-old man presented with retinal whitening and vitreous haze (A). Acute retinal necrosis was suspected and PCR testing was positive for herpes simplex virus. The patient initially received intravitreal antivirals and responded, but later developed a combined tractional and rhegmatogenous retinal detachment that required vitrectomy and silicone oil (B).

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PASSIVE SHAVING: A NOVEL APPROACH FOR A MOBILE RETINA


Maintain better control when treating giant retinal tears, retinal dialysis, and bulbous retinal detachments.

BY ANDRES AQUEVEQUE, MD, PHD, AND KARIM HAMMAMJI, MD

Countless improvements to vitrectomy have been implemented since its inception in the 70s with the aim of optimizing this procedure. Still, removing the vitreous body from the intraocular cavity continues to present challenges. One of the most significant is extracting the greatest amount of vitreous per unit of time, while maintaining a controlled IOP and preserving the retina from new breaks due to vitreoretinal traction.

TRIED AND TRUE

During vitrectomy for retinal detachment, surgeons must shave the peripheral vitreous as closely as possible without creating new tears in a highly mobile retina that is detached from the retinal pigment epithelium (RPE). Increasing the cut rate to the maximum level while decreasing the vacuum (thus reducing the suction force to levels that are easier to control) is one of the most widely used techniques to avoid excessive retinal movement and prevent iatrogenic damage, especially in bullous detachments or giant retinal tears.

Another effective method is to use heavy liquids, such as perfluorocarbon liquid, as a "third hand" to support the retina during the vitrectomy and prevent it from being cut and/or aspirated by the vitrector.

Each of these techniques, with the addition of scleral indentation and the use of vitreous staining agents, such as triamcinolone, allows for safe and efficient balance when maneuvering the peripheral vitreous, especially in a mobile or even extremely friable retina.

ADVANCES IN CUTTING TECHNOLOGY

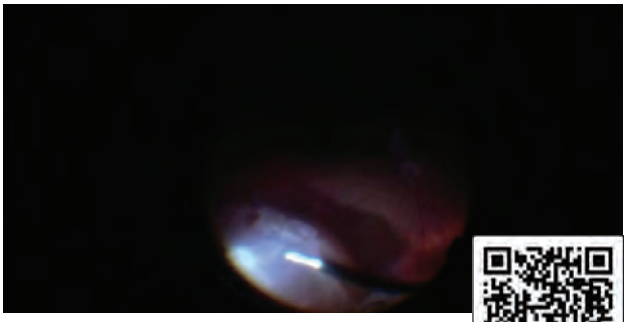
With updates in the different vitrectomy systems available on the market, it is possible to increase the cutting frequency to between 15,000 and 20,000 cuts per minute (cpm), in both single-blade and bi-blade modes. This increase in cutting capacity enhances the vitrector dynamics, preventing excessive traction and retinal breakage during both core vitrectomy and shaving. With this technology, the tip of the vitrector remains open almost the entire time, achieving a duty cycle (DC; the percentage of open port time for each complete cut cycle) close to 100% and thus reaching the so-called "ideal vitrectomy" cutter profile.

A NOVEL APPROACH TO SHAVING

Usually, in core vitrectomy mode, the vacuum and cut rate can be set to maximum because there is an extremely low risk of iatrogenic damage when working on a peripheral retina that is well attached to the RPE. On the other hand, in active shaving mode, surgeons should use high cut values (ie, between 7,000 and 10,000 cpm) and low vacuum values (ie, between 150 mm Hg and 250 mm Hg) to achieve a controlled vitrectomy without excessive traction of the peripheral retina from the RPE.

In the case of passive shaving, the much higher cut rate ensures a DC close to 100%, which allows vitreous to enter the vitrector passively due to the infusion pressure. In this passive shaving mode, active vacuum is not needed or is kept to a minimum. Thus, the vitreous is not actively aspirated by the vitrector, which helps to minimize the vitreous and retinal traction (Video 1).

WATCH IT NOW



Video 1. Passive Shaving Technique in Retinal Detachment Repair

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Figure. A vacuum setting between 0 mm Hg and 30 mm Hg in a linear mode is recommended, depending on the amount of vitreous that needs to be suctioned.

SETUP PEARLS FOR PASSIVE SHAVING

Vacuum: A vacuum setting between 0 mm Hg and 30 mm Hg in a linear mode is recommended. The setting can be maneuvered between these aspiration values depending on the amount of vitreous to be suctioned (Figure). Generally, the entire peripheral shave can be carried out with cutting and suction at 0 mm Hg.

Cut rate: The recommended values for passive shaving are between 15,000 cpm and 20,000 cpm, which can be achieved with the latest vitrectomy machines available on the market. The cut rate should be set to the maximum and in a fixed manner. Passive shaving cannot be achieved with cut rates of 7,000 cpm to 10,000 cpm, as the DC drops to approximately 50%, making the vitreoretinal interface much more turbulent and vulnerable to iatrogenic breakage.

IOP (infusion line): Based on the same principles of passive aspiration for drainage of subretinal fluid or perfluorocarbon liquid, the IOP should be set to the minimum level necessary to allow passive drainage through the tip of the vitrector, which should be open nearly 100% of the time. This value is achieved with infusion pressure between 25 mm Hg and 40 mm Hg. We recommend starting passive shaving at 25 mm Hg and gradually increase IOP as needed. In the setting of dense vitreous, high-pressure levels (eg, 40 mm Hg) may be required, in contrast to more liquefied vitreous, which requires lower pressures.

BENEFITS AND LIMITATIONS

The main benefit of passive shaving is the possibility of working on detached, mobile retinal tissue in a much safer and more controlled way than is possible with active shaving (Video 2). In the case of retinal detachments associated with giant retinal tears and/or retinal dialysis, the manipulation of the flap is more predictable, allowing a generous and efficient removal of the vitreous adhered to the edge of the tear. The same applies with bullous retinal detachments, where a mobile retina can make surgery a challenge.

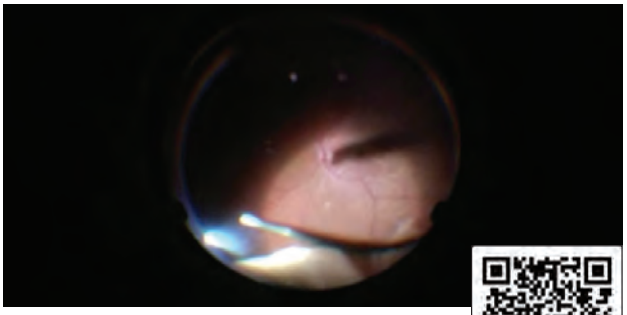
Other benefits are related to specific situations. For example, when shaving a highly adherent posteriorly attached vitreous base, passive shaving can prevent tearing of the retina. The same applies when dealing with extensive lattices along the peripheral retina and lesions associated with strong adherence between the vitreous and its edges.

One limitation of this technique is the fact that during a passive vacuum, the amount of vitreous that is aspirated by the tip is significantly reduced, so the shaving process will take longer than active shaving. For this reason, although a passive mode of vitrectomy can be set as the default for shaving, this technique is recommended when dealing with highly mobile retinas and for the treatment of giant retinal flaps. It is therefore recommended to configure the machine for active and passive shaving modes, such that the attached retina can be approached by the first mode and the detached retina by the second mode, making the surgery more secure and effective.

FINAL PEARLS

Passive shaving is a safe and effective option for dealing with a peripheral detached retina as well as a highly adherent vitreoretinal interface, where less traction applied during the procedure leads to a mostly physiological release of the vitreous from the retina, avoiding iatrogenic damage of the tissue and other intraoperative complications. ■

WATCH IT NOW



Video 2. Passive Shaving Allows for Improved Stability During Vitrectomy

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RISING STARS IN RETINA

Get to know outstanding retina fellows from the class of 2023.

Tedi Begaj, MD

***Retina Today:* When did you first know that you wanted to become a retina specialist?**

I was fortunate to study engineering and optics at the University of Rochester, which introduced me to ophthalmology early. Thus, I went to medical school already knowing that I wanted to pursue ophthalmology. Between my 3rd and 4th year of medical school at the University of Massachussets (UMass), I spent a year working with Connie Cepko, PhD, the Bullard Professor of Genetics and Neuroscience at Harvard Medical School, and one of the most brilliant people I have met. Her lab focused on viral gene therapy for retinitis pigmentosa, which was my first exposure to the field of retina. The amazing basic science research coupled with a motivating and supportive mentor showed me that retina was right for me.

***RT:* Who do you look to as mentors in the field?**

Like many people in our field, I feel lucky to have had many mentors throughout various periods of life. At UMass, Shlomit Schaal, MD, PhD, MHCM, was a great advocate—she has made monumental progress within the department at UMass. Dr. Cepko, Yash Chinchore, PhD, and David Wu, MD, PhD, were pivotal during my time in the lab.

In residency at Mass Eye and Ear, John Miller, MD, and Dean Eliott, MD, fueled my passion for retina. They are outstanding supportive faculty, and I feel privileged to have learned from them. Dr. Miller and I both love the NBA and (of course) the Boston Celtics, so we talk most nights when the Celtics are playing!

***RT:* What has been one of the most memorable experiences of your fellowship?**

The faculty at Associated Retinal Consultants/Beaumont is like an immigrant family that, despite small differences between individuals, ultimately cares for its own community by ensuring that all members do well. At graduation in 2021, everyone, including Michael T. Trese, MD, gave speeches that applauded and roasted the graduating fellows and each other—and they certainly didn't hold back! It felt like a family at Thanksgiving, and it was certainly an unforgettable moment for me and my co-fellows.

***RT:* What are you hoping to accomplish once you are in practice?**

My goal is to be a compassionate physician and a competent surgeon. I come from a family of educators, and I also hope to be a motivating peer and mentor involved in educating fellows. I want to give back the same excitement that I felt during my training.

FIRST CAREER MILESTONE

Dr. Begaj is pursuing a uveitis fellowship at Northwestern University before returning to Associated Retinal Consultants/Beaumont Hospital to practice retina and uveitis.

***RT:* What advice can you offer to residents who are considering retina?**

The field of retina is a gem because it is so diverse, and any physician can pursue any part of science or medicine within the field. Depending on your interests, you can pursue basic science, translational research, heavy clinic, or a busy surgical focus. This field has everything from amazing neuroanatomy to complex pathophysiology to both easy and extremely difficult clinical and surgical cases. There are many different avenues to explore, and I recommend that residents delve into the field of retina and figure out which part they love best. ■

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DIVERSITY IN CLINICAL TRIALS: A WORK IN PROGRESS

Researchers must overcome obstacles to improve representation in retina clinical trial populations.

By Abdul-Hadi Kaakour, MD; Hong-Uyen Hua, MD; and Aleksandra Rachitskaya, MD



Randomized clinical trials represent a high standard of evidence-based medicine and are cornerstones of clinical practice. Yet, the lack of diversity among study participants remains a well-documented challenge throughout many medical specialties. Despite successive statutes, regulatory requirements, policies, and guidance documents, as well as surveys demonstrating overwhelming agreement of the benefits of a well-represented trial, many remain insufficiently diverse in their recruitment.[1-6] The paucity of clinical trial diversity perpetuates rooted disparities in health care, which constrains our ability to properly care for all our patients.

WHY DIVERSITY IN CLINICAL TRIALS IS IMPORTANT

Between 2010 and 2020, the US Census revealed that the US population grew more racially and ethnically diverse;[7] without capturing these demographic changes in scientific research, more individuals will be left with subpar medical care.[7] Diverse populations have diverse needs, and studies show significant racial and ethnic differences in the natural history, progression, and treatment of disease—including in ophthalmology.[8-10] Yet, without adequate representation in medical research, clinicians cannot ascertain how safe or effective a therapy will be for certain populations.

A lack of diversity in clinical trials not only negatively affects those who are poorly represented but leads to financial repercussions. A study published by the National Academies of Sciences, Engineering and Medicine, with subsequent analysis by the University of Southern California Schaeffer Center, showed that billions of dollars will be lost in the next 2 to 3 decades solely from increasing disability, decreased life expectancy, and reduced working years by individuals from poorly represented populations.[11]

To address this challenge at the federal level, Congress introduced the Health Equity and Accountability Act (HEAA) of 2022 to improve the health of minorities in the United States.[1] Building on the DIVERSE Trials Act introduced in August 2021,[2] the HEAA seeks to formalize FDA guidance by mandating that clinical trial sponsors recruit adequately from historically underrepresented groups. This would be accomplished through financial incentives and would require an action plan outlining how a study organizer plans to recruit and retain participants from underrepresented groups.[1] Though not likely to resolve this challenge outright, it represents an important step in the right direction.

HOW ARE WE DOING IN RETINA?

The issue of diversity in clinical trials does not spare the field of retina, and important gaps in the representation

AT A GLANCE

- Of 23 diabetic macular edema and macular edema from retinal vein occlusion phase 3 trials, 96% had different racial/ethnic compositions than the 2020 US Census.
- Many patients may not be aware of the existence of trials due to poor health literacy, cultural considerations, language barriers, or poor outreach.
- Research suggests that the onus of change is on researchers, who must work to establish and foster community-based relationships with each underrepresented group.

of racial and ethnic minorities exist.[12-14] The first challenge is reporting; one study found that, of articles published in the retina literature in 2019, only 43% reported patients' race or ethnicity.[15] If it was reported, it was done so heterogeneously—78 distinct categories of race and ethnicity were identified.[15] In 2016, the FDA published a guidance document that provided explicit recommendations on how to collect and report this information in a standardized format, encouraging study organizers to offer options that mirror what is offered in the US Census.[3]

When retina clinical trials did report full participant demographics, it became clear that there was still much work to be done. Our study found that, of 23 diabetic macular edema and macular edema from retinal vein occlusion phase 3 clinical trials, 96% had significantly different racial and ethnic compositions than what would be expected in the 2020 US Census.[14] In 15 of the 23 clinical trials, the demographic group that was most underrepresented was the Hispanic/Latino population. This was followed by participants who identified as Asian (underrepresented in 10 of 23 trials) and by those who identified as Black (underrepresented in nine of 23 trials).[14]

For Hispanic/Latino participants, this underrepresentation was worse than what was experienced by other groups; nine of the 15 trials had underrepresented this group by greater than 10% from what is expected per the US Census.[16] Given that this is the fastest growing racial/ethnic group in the United States, which additionally experiences a higher burden of diabetes and hypertension (along with individuals who identify as Black), these findings are worrying and highlight the importance of engaging with these communities.[17]

OBSTACLES TO DIVERSE RECRUITMENT

There are many intrinsic and extrinsic factors that affect participation and diverse recruitment. Many patients may not be aware of the existence of trials—or that they are potential candidates—due to poor health literacy, cultural considerations (eg, certain groups may defer to a physician to make the suggestion), language barriers, or poor outreach and patient education on the investigator's behalf. Structural access issues can prevent interested patients from reaching a specialist or a clinical trial site, and a lack of insurance or legal status may prevent or hinder access as well.[18]

The issues of historical research abuse and fear and/or experience of discrimination in the health care setting are complex factors that cannot be ignored. Clinicians should not conflate a lack of implicit trust with a lack of willingness to engage. In fact, patients may feel that the lack of engagement from traditional health care institutions is a manifestation of a lack of concern for their health outcomes.[4]

Financial considerations, be they realized costs or opportunity costs, often play a significant role in a patient's willingness to participate in a clinical trial. Some patients cannot take time off work to attend each trial appointment, which is often longer than the average office visit. Transportation can be a challenge, and many patients depend on family or friends for transportation, which may preclude trial completion.

WHILE NO SINGLE SOLUTION IS GOING TO RESOLVE THE CURRENT SITUATION OVERNIGHT, EVEN SMALL STEPS CAN HAVE A SIGNIFICANT EFFECT.

Even if an individual can navigate the obstacles noted above and reach the screening stage, they may find that they do not qualify due to restrictive eligibility criteria. This often occurs for patients with advanced disease or comorbidities, which tend to affect both older patients and racial/ethnic groups that experience worse disease.

POTENTIAL REMEDIES

While these obstacles may seem insurmountable, clinical trialists and scientists are not without tools and guidance. The literature supports interventions that can improve representation among multiple demographics, and the onus of change is on researchers, who must work to establish and foster community-based relationships.[4] Importantly, the conversations must be bidirectional, and researchers may need to meet individuals where they already receive care such as community health centers (including faith-based and federally qualified health centers, retail pharmacies, or other institutions with long-term community trust [ie, historically Black colleges or universities]).[19] Financial incentives at the national level may help to develop these non-traditional health care spaces into research sites.

Another important initiative is the improvement of diversity among medical and research personnel. This includes changes that can be made locally (eg, increased recruitment at training programs) coupled with actions at the national level (eg, the AAO Minority Ophthalmology Mentoring Program).[20]

One future model found that if clinical trial diversity improved to reduce health disparities by just 1%, the health care system could save at least $100 billion in spending for diabetes and heart disease care alone—not to mention the improved health outcomes for these populations.[11]

(Continued on page 33)

EXPLORING THE GENDER GAP THROUGH AUTHORSHIP IN RETINA

Significant progress in gender equity has been made in retina; here's how we can continue the momentum.

By Ankur Nahar, BS, and Julia A. Haller, MD

Although it has been nearly 175 years since Elizabeth Blackwell became the first woman to receive an MD in the United States, women continue to face challenges. Lack of recognition by patients and peers, a persistent pay gap, professional isolation in surgical specialties, and a paucity of mentors and role models are just a few barriers women face that impede their career advancement.[1] These obstacles then make attaining positions of leadership more difficult. In academic medicine, women currently account for just 18% of departmental chairs and deans. Furthermore, while 41% of full-time faculty are women, only 25% are full professors.[2]

In academic ophthalmology, similar disparities exist. A study by Tuli et al showed that the number of faculty who are women in ophthalmology has risen from 24% in 2003 to 35% in 2017. However, this was primarily due to an increase in assistant professors, and the gap between male and female professors persists.[3] Similarly, women made up just 2.1% of departmental chairs in ophthalmology in 2003, which increased to 8.4% in 2017.[4]

With fewer women in these key positions of authority, their representation in domains that are dependent on rank—such as research—is significantly lower. For example, Camacci et al found that the editors-in-chief of 23 of the 24 (95.8%) journals in ophthalmology and the presidents of 13 of the 15 (86.7%) professional societies in ophthalmology were men as of 2020.[5]

THE IMPORTANCE OF AUTHORSHIP

For women to attain positions of influence in academic medicine, their research productivity as trainees and early career physicians is critical. Specifically, authorship in key first and last author positions is an important component of advancement in academia. Therefore, gender composition in authorship can be examined as a proxy for gender disparities within the field.

Based on this hypothesis, we looked at trends in first and last authorship of women within clinical retina literature over the last 25 years.[6] Notably, we found a statistically significant rise in women as first and last authors, which contrasts with prior authorship studies in glaucoma and cornea.[7-9] This finding is particularly encouraging, as retina has traditionally been a male-dominated field; as of 2018, only 19.8% of retina physicians were women, according to the American Board of Ophthalmology.[10]

All signs point to retina moving in the right direction. The proportion of women retina fellows is now 30%, in part due to the evolution of retina as a specialty and societal shifts toward acceptance and inclusion.[11] More underrepresented groups have been drawn to the field due to greater time flexibility through medical retina and the acceptance of family-friendly policies. In addition, gender norms are changing, and more women feel comfortable breaking out of stereotypes and into traditionally male-dominated fields of medicine.

Not only is the representation of women in retina improving, but when women get opportunities in the field, they excel. Our study showed that the number of last

AT A GLANCE

- Authorship in key first and last author positions is an important component of advancement in academia.
- The authors found a statistically significant rise in women as first and last authors, which contrasts with prior authorship studies in glaucoma and cornea.
- When women were last authors, the first author was more likely to be a woman, supporting the hypothesis that mentorship is leveling the playing field.

OUR FINDINGS INDICATE THAT RETINA IS LEADING OPHTHALMOLOGY IN CLOSING THE GENDER GAP. NEVERTHELESS, IMPLICIT AND EXPLICIT BARRIERS REMAIN FOR WOMEN, ESPECIALLY IN HISTORICALLY MALE-DOMINATED SPECIALTIES.

authors who were women in the United States was significantly higher than the number of retina specialists who were women registered with the American Society of Retina Specialists (ASRS), indicating that women are disproportionately productive relative to their representation in the field.[6] This may also be due to a tendency for women to choose academic positions more often than men, as has been documented in other surgical fields.[12]

Our findings indicate that retina is leading ophthalmology in closing the gender gap. Nevertheless, implicit and explicit barriers remain for women, especially in historically male-dominated specialties. Furthermore, a disparity continues to persist among leadership in academic ophthalmology, despite the disproportionate productivity of women in retina. We still have work to do.

MENTORSHIP IS KEY

An important finding from our analysis is that mentorship is leveling the playing field. We found that when women were last authors, the first author was more likely to be a woman.[6] This suggests that women trainees may feel more comfortable asking for guidance from a mentor who is a woman, or may be more likely to receive it. Mentorship, therefore, plays a critical role in increasing authorship by women in retina and improving female representation and academic advancement.

The role of mentors extends beyond gender to apply to other underrepresented groups in medicine. Thus, programs such as those facilitated by Women in Ophthalmology, Women in Retina, the AAO's Minority Ophthalmology Mentoring program, the ASRS, Retina Society, and others, are important. These groups function as support systems for women to help them traverse the difficult landscape of medicine and may also improve their sense of belonging.

NEXT STEPS

By raising awareness about disparities, providing opportunities to connect underrepresented groups within the field, and elevating these individuals within leadership positions, we can help break down the barriers of entry and continue to promote diversity within retina. Furthermore, greater diversity increases the variety in approaches and perspectives, which can be a source for innovation and aid in solving challenges within the field.

We can be proud that, regarding leadership in research publications, retina is a field where women are already excelling. Most importantly, by achieving greater equity among the ranks of retina specialists, we foster an atmosphere that is welcoming and inclusive, conducive to personal and professional growth, and more likely to deliver the highest quality patient care. ■

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LGBTQ+ PEARLS FOR COLLEAGUES

Experts share ways to foster inclusivity in the workplace and work toward inclusive policies.

A conversation with Jessica Weinstein, MD; Roberto Diaz-Rohena, MD; Steven Sanislo, MD; and Brandon Johnson, MD. Moderated by Vivienne S. Hau, MD, PhD, and Basil K. Williams Jr, MD

Gathering a group of LGBTQ+ physicians who are open about it within our field is groundbreaking; it hasn't been done before, and the need to do so has only recently come to the forefront. Thus, we have invited this wonderful group of retina specialists to talk about how we can be more inclusive in the clinic and touch on ways that our institutions can change policies to be more inclusive.

– Vivienne S. Hau, MD, PhD (she/her/hers)

BASIL K. WILLIAMS JR, MD (HE/HIM/HIS): IS IT IMPORTANT TO SHARE YOUR STATUS AS PART OF THE LGBTQ+ COMMUNITY?

Roberto Diaz-Rohena, MD (he/him/his): Sexual identity and gender identity are fundamental to who we are as three-dimensional people, and it defines who we truly are. I entered retina 30 years ago as probably the only Afro-Caribbean Latino man at the time, but it was a label I was comfortable with because it's who I was as a young man.

But the field of retina in the '90s consisted mostly of straight, older, married, white men, and it led me to believe erroneously that the best thing I could do as a gay man was to hide, which is what many of us did.

I thought that Dr. Diaz could be amazing at lecturing, teaching, doing research, and running a practice, and that would be enough in my professional role; Roberto would go to bars, meet men, maybe boyfriends, eventually meet the man that I legally married and that I could keep those two worlds apart. But it doesn't work.

In retina, we see patients over and over and they begin to feel comfortable asking, "Are you married? Do you have a wife? What does she do? Do you have children?"

There comes a time when you decide that you can't keep avoiding these questions because you are not ashamed of who you are. In the last 10 years, I decided to come out at work and answer the patients' questions because I know that my sexual identity is integral to who I am. Now the staff, administration, and colleagues all know I'm gay, and it is an amazing and powerful feeling because now I can talk about my husband openly. I can take him to meetings, talk about my life, and finally be my most authentic self (Figure 1).

AT A GLANCE

- According to the Association of American Medical Colleges, 3.6% of approximately 16,000 respondents to the 2022 matriculating medical students questionnaire identified as LGBTQ+.
- Organizations should have LGBTQ+ inclusive policies, signage, and representation, and they should recruit people who are diverse.
- The best way to change people's minds is through their hearts—and that comes through sharing ourselves and being authentic and vulnerable.

Figure 1. Dr. Diaz-Rohena enjoys a birthday in the office with staff and colleagues and spending time with his husband (inset).

Figure 2. Dr. Hau and her team aren't afraid to be themselves in the office, which makes for a fun (and often festive) work environment.

DR. HAU: WHAT HURDLES HAVE YOU OVERCOME AS PART OF AN UNDERREPRESENTED GROUP IN RETINA?

Jessica Weinstein, MD (she/her/hers): This is a hard one because, first, I am a woman in retina. Retina used to be a male-dominated field, and you must contend with the usual problems like patients thinking you're the nurse or the tech. But in terms of my LGBTQ+ identity, when I was a resident and I made a comment to one of my attendings about not feeling included, they said, "Well, you always say, 'your girlfriend,' and you always say it as if it's a badge of honor. Why does that have to be such a big part of your identity?"

I had to ask them how that was any different from those who are constantly saying, "my fiancé." You constantly hear that in the heterosexual community, and it's the norm. One of the hurdles is simply explaining to people how you are left out and you aren't included in things unless you put yourself out there. You want to be frustrated and you wonder why people don't understand you.

To help others understand where you're coming from, you need to have a lot of patience—and be prepared to come from a place of understanding, even when someone says something that may be hurtful or ignorant. We must be patient, take a step back, and find a way to explain ourselves without always getting defensive.

DR. WILLIAMS: HOW DO YOU NAVIGATE MOMENTS WHEN YOU PERCEIVE A BIAS WITH A COLLEAGUE OR PATIENT?

Brandon Johnson, MD (he/him/his): Very gingerly. Being a man of color and gay, I've experienced a variety of biases and microaggressions. When I have a difficult patient, I fall back on the fact that we often see patients at their worst. I don't know what's going on in their heads, so I try my best to not let the doctor-patient relationship get disrupted.

If they are being rude to my staff or are being discriminatory, I have no problem directly communicating about it with the patient. But I always do my best to deliver the best care possible, no matter what.

It's also easy to fall into the habit of just ignoring the topic altogether, especially as a gay man. The medical community was so conservative when I was training, and I didn't talk much about my personal life. I kept to myself for the most part. That does so much damage not only to the person who is keeping those secrets but also to the greater community that doesn't realize the pressures that they're putting on underrepresented groups.

That's why it is important to have representation and talk about these issues so that the next generation doesn't have to be afraid to be authentic.

Dr. Hau: The best way we can change people's biases is by being ourselves (Figure 2). As more people get to know us, like our patients and colleagues, it changes their opinions. It's hard to discriminate against someone you know and respect.

DR. HAU: WHAT ARE SOME OFFICE POLICIES THAT ARE IMPORTANT FOR INCLUSIVITY?

Steven Sanislo, MD (he/him/his): I am lucky because Stanford has always been a highly inclusive place. I spent a lot of my life suppressing even to myself that I was gay, but once I accepted myself and became open with friends and family, I was completely accepted at Stanford.

Before I even came out to myself, I had been working with a lot of these people and they knew me as a person, and you don't tend to discriminate against people you know. It's the others that you discriminate against.

The difficulty for me has been around patients because they are constantly wanting to know about your private life. At the very beginning of my practice, before I was out, many of my older patients would try to set me up with their daughters, and I would have to avoid that. It was uncomfortable.

After I was married and I came out, when patients asked about my wife and her profession, I would correct them and say, "I have a husband and he does this, and we have these kids." Every patient accepted me for that and then they want to ask me about my kids, which is much easier to talk about.

Rising Numbers

The Association of American Medical Colleges' matriculating medical student questionnaire recently started collecting information on sexual orientation. In 2022, 3.6% of approximately 16,000 respondents identified as LGBTQ+, so close to 600 medical students in this year's first-year class.[1] The numbers are growing, and the reality is that many of us just weren't comfortable disclosing this information when we were training.

– Vivienne S. Hau, MD, PhD

1. Matriculating Student Questionnaire (MSQ). Association of American Medical Colleges. Accessed January 25, 2023. www.aamc.org/data-reports/students-residents/report/matriculating-student-questionnaire-msq

I've had several patients say, "You were a lot crabbier 10 years ago. You seem happier and joke more now." If you can't be out and honest with your patients and colleagues, you're not going to be as happy, and patients will not relate to you on the same level.

Dr. Diaz-Rohena: Working at the Veterans Affairs (VA), I don't fit a lot of the patients' boxes. I've had patients say, "I know you're gay, but that's okay with me. You do good work." It's hard to know how to respond to that, but I think they are just trying to say that what matters is that we do a good job as physicians. Much of it has to do with the personal attention and the compassion that we give as physicians.

Dr. Williams: We're talking a lot about experiences, being comfortable in your own skin, and the challenges of keeping some things hidden. But that's something patients can feel to some degree, and your co-residents, co-fellows, and faculty don't get to know you fully if you're not expressing the full complete version of yourself.

That's why it is so important to have a diverse and inclusive environment so people can be themselves, and we all benefit from that diversity.

DR. WILLIAMS: HOW CAN WE FOSTER AN ENVIRONMENT OF INCLUSION IN RETINA?

Dr. Weinstein: Organizations should have inclusive policies, signage, and representation. They should look at their recruitment statistics and, if there are deficits or a lack of representation, recruit those types of people because representation is important.

I used to work in Kentucky and North Carolina in medium-to-small cities, and now I'm in another medium-to-small city, and the diversity and inclusion policies are different than in places like Stanford. But there are national groups that can make sure that they are applying inclusive policies to all their offices, regardless of location.

Creating a space for people is important. Organizations such as the AAO and the American Society of Retina Specialists (ASRS) have diversity, equity, and inclusion (DEI) committees and task forces, LGBTQ+ committees, and mentoring programs to make sure that diversity and inclusion improves. If you don't create an intentional task force, culture, or path for it to happen, it won't.

Dr. Hau: Much has changed since the very first *Retina Today* DEI article with LGBTQ+ representation in 2021. Now, there are LGBTQ+ people in leadership, organizations like the AAO LGBTQ+ community, and the ASRS ad-hoc DEI committee that includes LGBTQ+ representation. We've come so far in a few short years.

DR. HAU:HOW CAN WE HELP COLLEAGUES APPROACH EACH PATIENT ENCOUNTER WITH INCLUSION IN MIND?

Dr. Diaz-Rohena: We all love to learn, and we've been learning our whole careers, so we must be willing to evolve in our awareness of LGBTQ+ issues. For example, I'm learning a lot about gender identity and pronouns. As we learn, we show more empathy and are less judgmental because we're open to understanding. When we're less judgmental and more compassionate, we are more comfortable, our body language makes more sense, and we can work with patients. We may not understand them completely, but we can share some of the uniqueness of being human and being different.

We must accept that we don't know all the answers, and we may not understand the ignorance, but we are willing to learn from it. The key is to show empathy.

DR. WILLIAMS: WHAT EDUCATIONAL RESOURCES ARE AVAILABLE FOR PRACTITIONERS WHO WANT TO LEARN MORE ABOUT LGBTQ+ PATIENTS AND THEIR NEEDS?

Dr. Sanislo: I once reached out to one of my trans patient's primary care doctor, and I learned a lot from speaking with that doctor. When this patient first came to me, I treated them the same way I treat everyone else. I didn't realize that I could have used some words that were different that might have been better for that particular patient. After talking with their physician, I learned to approach people who may be slightly different than myself in other ways.

You don't treat everyone the same; you treat everyone the way that you think they would like to be treated. I'm sure that there are organizations too, but reaching out to other physicians, especially those who are involved in the community, can help. Become aware of physicians who are active within the LGBTQ+ community; they are very willing to talk with other doctors and help you on that journey.

Dr. Hau: We have many colleagues within medicine who may have certain expertise within this area and can connect. There are also some great websites and organizations, such as GLAAD (glaad.org) and the human rights campaign (hrc.org). Also, check out *Retina Today*'s DEI articles from the last two years. In the 2022 issue, I wrote an article that includes a section on resources to help when working with trans folks within the office.

LGBTQ+ Terminology Cheat Sheet

Language is inherently complex and continuously evolving, and terminology associated with the lesbian, gay, bisexual, transgender, and queer+ (LGBTQ+) community is no exception.*
Here are some common terms you may encounter when caring for this patient population.[1]

GENDER

- **Cisgender (adj.):** Describes a person whose gender identity aligns with the sex they were assigned at birth.
- **Gender dysphoria:** Marked and persistent incongruence between a person's experienced gender and assigned sex at birth.
- **Intersex (adj.):** Describes a person with one or more innate sex characteristics (such as genitals, internal reproductive organs, or chromosomes) that fall outside of traditional conceptions of male or female bodies.
- **Nonbinary (adj.):** Describes a person who experiences their gender identity and/or gender expression as outside the binary genders of man and woman.
- **Transgender (adj.):** Describes a person whose gender identity differs from the sex they were assigned at birth.
- **Transition or gender affirming care:** The process a person undertakes to bring their body and/or gender expression into alignment with their gender identity; may involve social, medical, or legal transitions. *Note: A person is not required to transition socially, legally, or medically to be considered transgender. Transitioning is a unique experience for each individual and may involve all, none, or some of these processes.*
  - **Social:** may include going by a different name, using different pronouns (eg, she, he, or they), and dressing or otherwise presenting themselves differently.
  - **Medical:** may include procedures such as hormone replacement therapy and/or one or more gender confirmation surgeries.
  - **Legal:** may include changing one's name or sex on legal documents such as a passport, driver's license, or bank account.

SEXUALITY

- **Allosexual (adj.):** Describes a person who experiences sexual attraction to others (ie, who is not asexual).
- **Asexual (adj.):** Describes a person who does not experience sexual attraction.
- **Bisexual (adj.):** Describes a person who has the potential to be physically, romantically, and/or emotionally attracted to people of more than one gender (not necessarily at the same time, in the same way, or to the same degree).
- **Gay (adj.):** Describes a person whose enduring physical, romantic, and/or emotional attractions are to people of the same sex.
- **Lesbian (adj. or n.):** A woman whose enduring physical, romantic, and/or emotional attraction is to other women; some lesbian women may also describe themselves as gay.
- **Pansexual (adj.):** Describes a person who has the capacity to form enduring physical, romantic, and/or emotional attractions to any person regardless of gender identity.
- **Sexual orientation:** A person's enduring physical, romantic, and/or emotional attraction to another person (distinct from gender identity).
- **Queer (adj.):** Describes a person whose sexual orientation is not exclusively heterosexual (a term used by some but not all members of the LGBTQ+ community).

Language to Avoid

- Referring to a person as "biologically/genetically" a man, woman, boy, or girl.
- "Lifestyle" or "sexual preference" to refer to a person's sexual orientation.
- Calling a person "homosexual" who identifies as lesbian, gay, bisexual, pansexual, or queer.

GENERAL

- **Ally (n.):** Describes a straight and/or cisgender person who supports and advocates for LGBTQ+ people.
- **Closeted (adj.):** Describes a person who is not open about their sexual orientation.
- **Coming out:** A lifelong process of self-acceptance that may or may not involve telling others about one's sexuality.
- **Out (adj.):** Describes a person who self-identifies as gay, lesbian, bisexual, queer and/or transgender in their personal, public, and/or professional lives.
- **Outing:** The act of publicly revealing a person's sexual orientation or gender identity without that person's consent; considered inappropriate and potentially dangerous by many members of the LGBTQ+ community.
- **Questioning (adj.):** Describes a person who is in the process of exploring their sexual orientation and/or gender identity.

*This list, dated to March 2023, is not exhaustive, and the appropriate language is subject to change. In addition, there is no one "right" away to identify with any of the above terms. You can always ask your patients how they describe themselves (eg, what pronouns they use).

1. GLAAD Media Reference Guide. Accessed February 8, 2023. www.glaad.org/reference/terms

For additional resources on appropriate language to use for describing LGBTQ+ individuals or issues, check out:

GLAAD

The Human Rights Campaign

DR. HAU: HOW CAN WE HELP LGBTQ+ PATIENTS FEEL MORE COMFORTABLE COMING TO OUR OFFICES?

Dr. Johnson: Being in a private practice, the onus is on the physician owner, so I set the tone. To set a tone of inclusivity and compassion, I enter the room with the mindset of curiosity and compassion, not fear and ignorance. If I am unsure of a patient's pronouns, because of my own curiosity, I have a knee-jerk reaction to ask directly, "My pronouns are he/him/his; what are your pronouns?" The reactions to that approach have been very positive. I also make sure that I have options on my intake form for people who have different gender identities to make them feel welcome. The infrastructure that we have set up is traditionally binary, but that's not the reality of how we practice and how we live.

Dr. Sanislo: The fact that our infrastructure is binary is a big problem. If the patient's chart says male or female when that's their chosen gender identity, I know to address that person as a woman or a man. If it said nonbinary or they, I would know to use their preferred pronoun. I think that would be great. In our EHR, there is a way to add their preferred gender identity rather than their sex assigned at birth, but it's not something that pops up that you could see easily.

That would be very helpful because I don't want to make someone feel uncomfortable by asking. For example, asking about their preferred pronouns might make them feel like they're not very successful at portraying the gender that they believe they are, which could be uncomfortable for them.

Dr. Johnson: If I am in a situation where I feel like it is relevant or if I might be misgendering a patient in some way, I'll ask. It feels uncomfortable for me, and it may feel uncomfortable for them, but that's a risk that I'm willing to take because it may foster a more connected experience.

Dr. Hau: As a trans woman and knowing some who are nonbinary, it's the mere fact that we are sensitive to the issue of gender that shows compassion and sensitivity. If a person is struggling with their gender identity or misrepresentation, they often don't get asked. Therefore, making a policy that applies to everyone at intake to ask for their pronouns can make a big difference. It is part of our Kaiser Permanente EHR, and hopefully, most systems are moving toward that.

Another approach is simply sharing your own pronouns first—"Hi, my name is Dr. Vivienne Hau, and my pronouns are she, her, and hers"—which may prompt the person to be comfortable sharing their pronouns as well.

Dr. Diaz-Rohena: I don't use ma'am or sir anymore in my clinics because I've gotten in trouble. So now I say, "Good afternoon, what brings you in? How can we help you?" to make it very gender neutral. At the VA, they added unisex bathrooms, which is very helpful. If your intake form has the legal and the preferred names, it gives you a head start before you meet the patient. When I walk in the room, it makes me more comfortable knowing that their legal name may be Joe, but their preferred name is Susan. Intake forms that use only male and female are so difficult because there's fluidity that we must be aware of.

Dr. Weinstein: Many of us have put our foot in our mouth when we walk into a room and say something to the patient about their wife or husband and it's actually their mother, father, or sister. Many of us have changed that approach and stopped making assumptions. When we are educating others about these LGBTQ+ changes, comparing it to something like this that they have already changed is easy enough and it makes it more familiar.

DR. WILLIAMS: WHAT PEARLS CAN YOU SHARE WITH LGBTQ+ TRAINEES?

Dr. Johnson: If I could talk to my 20-year-old self, I would say, "be your authentic self." That might come with a lot of pain and hurt and trauma, but you either pay for it upfront or you pay for it later because I can tell you, as a 40-year-old who repressed my sense of self for years, it affected everything in my life from interpersonal relationships to my self-esteem and how I view myself. No one can be the best doctor if they split themselves—they're not a whole person. Try to live as a whole person and it will allow you to be your best self and the best physician you can be.

Dr. Weinstein: Coming out of the closet or being your authentic self is still really hard. My advice is to try, but at the same time, you can present yourself the best that you can. Maybe you aren't out to your grandmother but you're comfortable with your medical school friends or colleagues. That's okay. It doesn't have to be perfect. We all come from different places, and I wish everyone would be comfortable and out, but it's okay not to have it all figured out yet.

Dr. Sanislo: It's very hard to change systems and the community you live in, but it's easier to change by becoming a leader. When other people are drawn to you as an LGBTQ+ person they respect as a good physician and teacher, that will drive change. Change is driven by individual pioneers.

I encourage all of us who are in leadership positions to be our authentic selves to drive change in our communities and in our nation.

Dr. Diaz-Rohena: Hiding is a very important concept for us in the LGBTQ+ community. Often, we hide as long as we can. But when I was hiding, looking back 30 years, I lost the ability to have great relationships with some of my colleagues. We lose the ability to have good mentors, be it gay or straight, because we retreat and try to live a quiet life. The important aspects of mentorship and friendship are lost along the way. Getting to know all of you, I feel that I have

Want to hear the conversation as a Podcast? Scan the QR code or visit New Retina Radio on Eyetube at eyetube.net/podcasts.

the friends and mentors that I wish I had had 30 years ago.

Dr. Hau: I can't tell you how much it would have meant to me as a trainee to have a group of LGBTQ+ physicians talking about their lives like this. I'm glad that we can do this now for our own trainees so that they have mentors and role models to show them that they have the potential to excel and become future leaders.

The best way to change people's minds is through their hearts. And that comes through sharing ourselves, being authentic, and being a little bit vulnerable. If we were all more vulnerable with colleagues and patients, our relationships would be stronger and more fulfilling. I've found that to be the case for myself.

Hopefully, we have taught our field a little about our community and showed our colleagues how to be stronger allies to each other and patients who are LGBTQ+. ■

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(Continued from page 25)

FIRST STEPS

It is incumbent on all providers to identify and decrease barriers to inclusion for individuals in all underrepresented groups to enhance health outcomes. To neglect this mandate would be to perpetuate negative effects on health equity, medical ethics, and scientific rigor. In an increasingly diversifying world, we cannot leave any patient behind. ■

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TIME TO GO MULTICULTURAL

A diverse office is necessary to care for patients in the melting pot of America: New York City.

By Julia P. Shulman, MD; Constance Mei, MD; and Jonathan A. Feistmann, MD



"Buenas Días!" The first patient of the day is through the door. She is an 87-year-old woman from the Dominican Republic who requires frequent visits due to severe proliferative diabetic retinopathy with diabetic macular edema. Although she does not speak English, she can navigate the office by herself. When asked about her experience at NYC Retina, she states, "It is not just that they speak Spanish. It is the way I am treated from the front desk to the doctors. It is the warmth I feel when I am here. It is the jokes the doctors tell to make me at ease. Though I don't enjoy getting injections or lasers, I love coming to the office. I feel like a human being."

The *Harvard Review* defines *multiculturalism* within individuals as the degree to which they know, identify with, and internalize more than one culture.[1] Individuals who are multicultural often have more creative minds, perform better at problem-solving tasks, and are more successful leaders in many areas of life, including medicine.[1,2]

THE PATIENTS

Our practice, NYC Retina, is a retina-only practice with offices in Manhattan and Queens. As such, we serve one of the most culturally diverse areas in the world. All our physicians and staff are multicultural and multilingual to meet the unique demands of practicing in such a proverbial melting pot. Our team speaks a total of 10 languages, but this is only a small sampling of the 160 languages spoken in Queens County.[3]

When patients are nonnative English speakers and require translation services, we still make it a point to learn how to say hello and goodbye in their language. Patients appreciate this extra effort and often respond with a chuckle or a smile.

In addition to speaking a patient's language, we work to recognize and celebrate the multicultural fabric of our patient population. For example, in 1 day, we looked up the best recipe for khachapuri, the meaning of Guru Nanak Jayanti, and how a certain gesture communicates respect to the elderly in Filipino culture.

From the physician's perspective, we see tremendous cultural differences in how patients communicate and prefer to receive information. For example, patients from certain backgrounds hesitate to ask questions of the physician, whom they perceive as a figure of authority. It is important to bridge that divide, and patients appreciate the effort to explain their diagnosis and the treatment options.

THE PROVIDERS

As a multicultural individual myself, I (J.S.) find enormous satisfaction in understanding where my patients are coming from and learning about their backgrounds and customs.

AT A GLANCE

- *Multiculturalism* can be defined as the degree to which an individual knows, identifies with, and internalizes more than one culture.
- Individuals who are multicultural often have more creative minds, perform better at problem-solving tasks, and are more successful leaders.
- When patients are nonnative English speakers and require translation services, consider learning how to say hello and goodbye in their language.
- Having a practice where patients feel seen and heard leads to an improved patient experience and increased adherence to treatment and follow-up.

Figure 1. Dr. Shulman's staff love connecting with patients of any age.

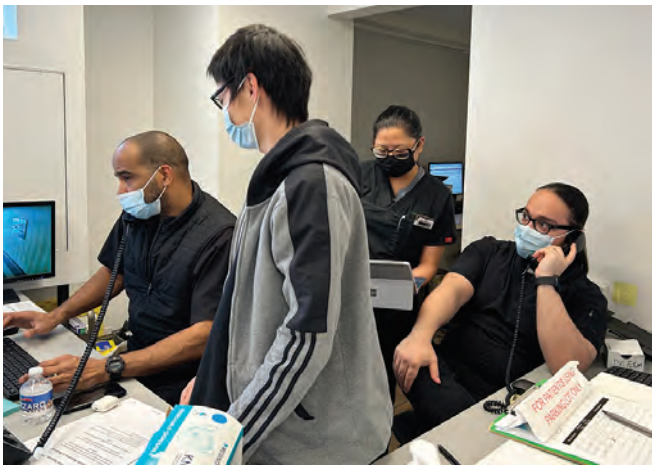

Figure 2. To help communicate with patients, front desk staff answer calls and make appointments in several languages.

I find that doing this consistently builds strong patient-doctor relationships and empowers the patient to be more engaged in their care.

I (J.F.) enjoy talking to my patients about the holidays they celebrate, their traditions, and their families. Recently, I saw a patient from Sierra Leone who spoke Krio, an English-based creole language. I was surprised that I could understand him!

As a fellow in this practice, I (C.M.) was immediately struck by the multiculturalism and inclusivity within the practice. Our patients appreciate that we respect them as individuals and try to understand where they are coming from when they voice their concerns or fears. In addition, the diversity of pathology has been tremendous; besides the usual bread-and-butter retinal diseases, we see a wide range of rare cases of posterior uveitis and inherited retinal disease that only occur in certain populations.

THE VALUE OF PHYSICIAN/PATIENT CONCORDANCE

By T.Y. Alvin Liu, MD

Have you ever had a patient drive 3 hours to see you? And not because you are the only retina specialist within 3 hours—but because you speak their language? I have, and it was a humbling reminder of the value of cultural sensitivity and diversity within our field.

I am originally from Hong Kong, and although I have been in the United States since high school, my family still lives in Hong Kong. I go between the two worlds often, and I speak both Cantonese and Mandarin. Like many who speak another language, I am not overly confident when explaining precise medical terms to my patients and still use a translator at times. Nonetheless, I have noticed that my patients appreciate my effort to connect with them in their preferred language. For example, I often introduce myself in Cantonese or Mandarin, say a few things and chit-chat, and then switch to using English and a translator to ensure I convey the medical information properly. From the patient's point of view, having doctors who show cultural sensitivity is very important.

Often, the conditions that we treat—such as wet AMD or retinal vascular diseases—require repeated injections, and many patients, even native English speakers don't, understand that it is a chronic condition that requires ongoing treatment. Thorough education is crucial for every patient, but it can be particularly important for patients whose first language isn't English. That's when retina specialists should use an official translator to help explain everything in a culturally sensitive way and to convey that it is not a one-time treatment. Physicians should also do their best to have family members present when explaining this to build trust with the patient and their support network.

That patient who drove so far to see me was lucky with her diagnosis of stable dry AMD, making it a quick appointment that did not require frequent visits (yet). Still, it was an important reminder that speaking the same language, and connecting culturally, can significantly affect a patient's care.

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WHEN PATIENTS ARE NONNATIVE ENGLISH SPEAKERS AND REQUIRE TRANSLATION SERVICES, WE MAKE IT A POINT TO LEARN HOW TO SAY HELLO AND GOODBYE IN THEIR LANGUAGE. PATIENTS APPRECIATE THIS EXTRA EFFORT.

THE STAFF

We believe that our practice's multiculturalism has contributed to increased staff satisfaction and improved staff retention rates.

"It is satisfying to come to work every day," our scribe, Nancy, said. "The patients we see are so grateful to be able to communicate with us freely. They bring pictures of their families and home-cooked food. I feel that I am part of something amazing and that we are making a difference in people's lives."

"When speaking with a patient from Ecuador, Dr. Shulman knew that the word cataract (catarata) is used to refer to a pterygium and was able to clarify some of the confusion the patient had about the risk of cataract formation after her retina surgery," Althea, our office manager, explained. "The doctors can tailor how they educate patients to the patient's cultural background. This is a unique aspect of our practice."

According to Joel, one of our technicians, "our retina patients often see multiple eye providers such as glaucoma specialists or comprehensive ophthalmologists. Many patients tell me that they wait for their retina appointment for the doctors to explain to them what is going on with all their other conditions in a way they can understand."

GO MULTICULTURAL

There is increasing pressure on all medical practices to increase productivity, and often the unfortunate side effect of this process is the dehumanization of the physician-patient encounter. We experience this ourselves when we are in the patient role and feel that every effort should be made to create a practice in which patients feel heard, seen, and recognized. This leads to improved patient experience and increased adherence to the prescribed treatment and follow-up. Fostering a multicultural practice is our way of taking a step in that direction. ■

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Want to highlight your own multicultural practice? Send your story to **rhepp@bmctoday.com.**

PATIENT TESTIMONIALS FROM NYC RETINA:

"When I met Dr. Feistmann, he was able to guide my mother through the eye examination in Bengali. I couldn't believe it! She left the office with a big smile on her face and brags about him to all her friends."

"Dr. Shulman examined and treated my mother, who is a Russian speaker. My mom has a multitude of ocular issues, and I am a physician myself, but I could not have explained more clearly the diagnosis, prognosis, and plan of treatment. On one particular visit, Dr. Shulman was able to pick up on my mom's nervousness before a procedure. She took her hand, looked her in the eye, and asked her what was bothering her. Dr. Shulman seems to have a sixth sense when communicating with my mother."

"Dr. Mei was able to reassure me in Cantonese during my surgery. Since I was awake, it was nice to hear a friendly voice and understand what was going on. She also made sure to go over the instructions on how to position my head and use my drops after surgery."

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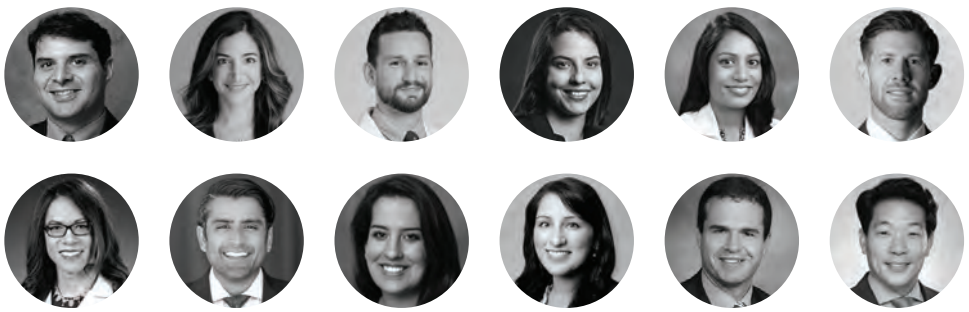

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RUNNING WITH RP: A GUIDE TO FOSTERING HOPE

One man's mission is to keep running, despite blindness due to retinitis pigmentosa—and help others do the same.

By Rebecca Hepp, Editor-in-Chief

"In the face of adversity, you need to focus on what you can do, not on what you can't do and the barriers that present themselves," Richard Hunter, a renowned endurance athlete, told *Retina Today* in an interview. While his Ironman, 100-mile endurance run, and 27 marathons (and counting) speak for themselves, his advice comes from experience with adversity far beyond the rigors of a marathon course. After all, he completed all these events after experiencing rapid vision loss due to retinitis pigmentosa (RP).

HOW IT ALL BEGAN

Mr. Hunter vividly remembers receiving the diagnosis as a 22-year-old second lieutenant in the US Marine Corp. Doctors noted an abnormality during a routine eye examination, and within days he was told he had RP, was going to go blind, and was being discharged from the Marines.

"It felt like I was receiving a death sentence," he recalled. "I didn't have any family history of RP at that time and didn't know anyone who was blind. Everything I had done up to that moment was to pursue my dream of being an officer in the military."

With his dreams dashed and a discharge slip within a year, Mr. Hunter had to reassemble his life.

"I was numb and couldn't even start thinking long-term—and I didn't even have any noticeable functional vision impairment at the time."

Mr. Hunter enjoyed good vision without the need for accommodations for 14 years, but the fear of losing his vision loomed, with the yearly follow-ups with his retina specialist to remind him of it.

Once his vision began deteriorating, he knew he had to do something. He was a school psychologist and a part-time lecturer for the graduate department at Sacramento State, yet he found himself on disability retirement and taking mobility classes, learning to read braille, and working with assistive technology. But what bugged him most was the drive to do something other than shuffle around the house.

"I needed to be a positive role model to my daughters and show them that you could still be relevant and set ambitious goals in the face of adversity," he explained. "Many people with vision loss become depressed and isolated, and I didn't want my daughters to see me laying around being sad. There's no way you make it through life without adversity, whether it's personal health issues, family things, or death. I thought, 'well, if my daughters are going to face adversity in their life, what kind of example can I set for them?'"

He thought through all his strengths and talents, and one thing he could do, sighted or not, was run. But just running wasn't enough for this former Marine. He wanted to set an ambitious goal and wondered if he could qualify for the Boston Marathon.

He ran his first Boston Marathon in 2008 after qualifying for his age group (not as a visually impaired runner). And the rest, as they say, is history.

AT A GLANCE

- United in Stride is a program, run by the Massachusetts Association for the Blind and Visually Impaired, that registers guides so that visually impaired athletes can connect with them.
- Guides who are also eye doctors are invaluable for visually impaired athletes; where else could a patient spend hours with someone who has intimate knowledge of the vision journey they are on?
- An astute retina practice should be prepared to make timely referrals for low vision services when the patient needs it, not only at the time of diagnosis.

THE NEXT MOUNTAIN TO CLIMB

When Mr. Hunter began his running career, he didn't know of a single visually impaired athlete, and the learning curve was steep, he recalled. He vowed to shorten that learning curve for others, and he has since pioneered several initiatives to make good on that personal goal.

First, Mr. Hunter helped to establish the Marathon National Championships for the visually impaired, which is held in conjunction with the California International Marathon (Figure). He started from scratch with just two athletes running in the inaugural race in 2007—since then, it has swelled to include nearly 50 visually impaired runner prior to COVID-19 pandemic.[1]

In addition to tracking down and personally inviting visually impaired runners from all over the world, Mr. Hunter also developed the extensive guide network that was necessary to guide the visually impaired runners once they got to the race course.

Like most runners who are visually impared or blind, Mr. Hunter runs with a guide, which inevitably garners some attention on the course.

"I was doing all these different races, and there would be other people running the course who would see us out there and ask how they could get involved in guiding," he said. "Of course, my answer used to be something like, 'how good is your memory? Here's my email address. When you get home, send me an email.'"

He realized that, unless you happened to know one of a handful of visually impaired runners, the information just wasn't out there. There was a huge need, and Mr. Hunter decided that he would find a way to help others network and connect with guides. He approached the nonprofit Massachusetts Association for the Blind and Visually Impaired with his idea, and together they founded United in Stride, a program that registers guides so that visually impaired athletes can connect with them. Now, runners don't have to memorize an email address while chugging through mile 18 of their marathon—they can search online by zip code.

The outpouring of support for the guide program has been wonderful, according to Mr. Hunter. "I'm hearing stories and seeing things in the news about United in Stride and how important it was because they met a new friend, and they met running guides that helped them prepare and run in a race."

While it's heart-warming to see other endurance runners attain their goals, that's not all United in Stride is meant for, according to Mr. Hunter. He is working on expanding its scope so that all visually impaired people, wherever they are in their vision and fitness journeys, can connect with volunteers looking to help them get out and participate.

"There are visually impaired people who want to power walk and jog in every community across the United States if they only had it modeled for them and had resources to do it. United in Stride has been a great resource for people who've been runners, but it was always intended to be a resource for power walkers, joggers, and runners—people who may never run a race but just need to find power walking or jogging partners."

Image courtesy of Richard Hunter

Figure. In 2019, Richard Hunter completed the California International Marathon with his guide, Scott Jurek.

THE RETINA CONNECTION

Guiding the blind is where the story intersects with the field of retina, beyond Mr. Hunter's excellent retina specialist (Joel A. Pearlman, MD, at Retina Consultants Medical Group in Sacramento, California, in case you were wondering). That's how he met Vivienne S. Hau, MD, PhD, a clinical assistant professor and surgical vitreoretinal specialist at Kaiser Permanente in Riverside, California—known as *scalpel* among her running buddies.

Dr. Hau runs her own marathons but also guides the blind in theirs. She and Mr. Hunter have been running together for years, and they teamed up in 2019 to support the first all-blind team of runners for the 199-mile Hood to Coast Relay. Mr. Hunter was the co-captain of the team (10 blind/visually impaired runners and 10 guides), while Dr. Hau was the logistics lead. The team finished in 186th place of more than

What Advice Can You Offer Retina Specialists Who Are Treating Patients With Inherited Retinal Diseases And Visual Impairment?

Richard Hunter: While many cling to the hope for a cure or treatment for themselves or a loved one, hope for the future needs to be more than the possibility of a cure. Once someone experiences the life-changing effects of vision impairment, hope also must be about believing that they can live a fulfilling life regardless of their vision impairment.

Retina specialists delivering the news of a diagnosis need to fully appreciate that their patient is receiving news that can be quite traumatic, especially if there is the prospect of irreversible and permanent vision loss. Those of us on the receiving end of that conversation are far from having a positive outlook in the near term.

Because doctors have limited time with their patients, I personally believe that the team needs to include someone on staff, like a nurse navigator, who has more time to educate, intervene, and follow up with patients. It would make a big difference if a retina specialist would be able to say, "You have just received some very difficult news and it's a lot to take in; I'm going to have our navigator talk with you and your family before you go home and follow up with you in a few days. You will have many questions and we want to help."

I am fortunate to have a wonderful trusting relationship with my retina specialist, Joel A. Pearlman, MD, PhD. He takes an interest in who I am as a person and has a wonderful bedside manner. He takes the time to share relevant X-linked and *RPGR* RP research and has gone out of his way several times to direct me to important resources. I have faith that Dr. Pearlman will know what is best for me, and I trust any advice he offers because of this positive relationship.

Retina specialists will not have a cure for everyone, so the human connection becomes critical. They are the first responders to those receiving that life-changing diagnosis. The hope they offer is more than the hope of a treatment that may be 5 or 10 years away. Hope starts with compassionate treatment and a human-to-human connection to timely resources. For many of us, the greatest hope for the future is meeting others who are thriving and who have similar interests. If the retina practice is the only touchpoint for patients, it becomes increasingly important that someone on the staff has a relationship with the patient to facilitate timely introductions to individuals and programs. Hope does not come in the form of a flyer or a link on a website. It must come through a trusting relationship.

1,000 teams, averaging less than an 8 min/mile pace.

"I have so much respect and admiration for Dr. Hau," Mr. Hunter said. "She has made a point of developing friendships with visually impaired athletes and has learned our stories, which she can share directly with her patients. By volunteering to guide runners like me, she shows by her actions that she cares. I'm confident that this fosters a higher level of trust with her patients whose vision she cannot restore."

Guides who are also eye doctors are a rare find but are the most valuable, in Mr. Hunter's opinion. Where else could a patient spend hours with someone who has intimate knowledge of the vision journey they are on? Beyond the day-to-day information gathering such a pairing can enable, having doctors involved in the cause shows patients that they care. And at the end of the day, caring is what matters most.

"I hope that there are more people out there like Dr. Hau and Dr. Pearlman who take an interest in my story," Mr. Hunter said. "When we know that retinal specialists care about us, whether they can fix our eyes or not, and they take personal interest in making sure that we're being directed at the right time to the right people, it's helpful."

Mr. Hunter added that, for many with inherited retinal diseases, the vision journey is life-long. He had no need for low vision services for 14 years before his vision deteriorated, and any referral at the initial diagnosis was a waste. He needed those later in his journey, and an astute retina practice should be prepared to make those timely referrals when needed, he suggested.

"I'm going to continue to see my retinal specialist every year that I walk this earth, but I'm not always going to be in a rehabilitation program," he explained. "We'll all have seasons of challenges and victories during this constant adjustment to life, with maybe decreasing vision or blindness."

"People who are traumatized by a diagnosis are going to have questions and fears," Mr. Hunter continued. "Often, they're not going to know a single other person with vision loss. The retina specialists know all of them, and they are in a unique position to be a first responder. If they direct their patients to the right resources at the right time, it could literally be the difference between life and death." ■

Want to know more about United in Stride? Follow the QR code or visit www.unitedinstride.com.

1. USABA Marathon National Championships 2022 - Sponsored by Allworth Financial. Accessed January 19, 2023. usabamnc.corvin.org/2022

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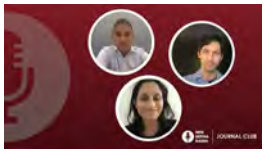

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RETINA SURGERY IN THE DEVELOPING WORLD

Operating in Haiti and Rwanda presents unique challenges. Here's how we can overcome them.

By Daniel C. Alter, MD, PhD

Resources are sorely needed to create and maintain retina programs in the developing world, but it can be done. I would know because I have helped to develop three retina surgery sites in Haiti and Rwanda and have a fourth in the works in Burundi, Africa.

HOW IT STARTED

My first experience with global ophthalmology came as a mid-career retina specialist. In 2014, I traveled to Port-au-Prince, Haiti, and had a successful week of teaching vitrectomy surgery to Reginald Taverne, MD. Dr. Taverne is a comprehensive ophthalmologist who completed a residency in Haiti and then a second one in Israel. During that second residency, he was exposed to medical retina and learned scleral buckling for retinal detachment repair, although he was already well-known in Port-au-Prince for providing those services. He had a driving desire to perform vitrectomy and had acquired a vitrectomy machine (Accurus, Alcon) but needed instrumentation, a widefield viewing system, and other equipment. After much planning, my son and I visited Dr. Taverne with everything we needed to complete 12 complex vitrectomies in his small office-based OR in Port-au-Prince (Figure 1); it was a life-altering event for all of us.

Since then, I have made 25 trips to Haiti and recruited other visiting retina surgeons to make similar trips. In 2018, Dr. Taverne was awarded a vitreoretinal fellowship certificate signed by six members of the American Society of Retina Specialists at the annual Haitian Society of Ophthalmology meeting in Port-au-Prince. Dr. Taverne has now become the vitreoretinal mentor and is currently training Shakespeare Saintil, MD (Figure 2). Dr. Saintil is a recent graduate of the residency program in Haiti and completed a FOCUS/USAID ROP fellowship as part of an USAID CBP grant that supports the development of pediatric eye care services in Haiti.

GROWTH

During my trips to Haiti, I helped to start a second program in Cap-Haïtien with Luc Dupuy Pierre, MD, a talented comprehensive ophthalmologist who had visited Port-au-Prince. This second project required more extensive planning and logistics because the existing clinic did not have a vitrectomy machine. In the end, I had to design and build a crate to ship one with the other required equipment.

Over the next few years, several visiting retina specialists have trained with Dr. Dupuy, and he continues to perform vitrectomy regularly. Unfortunately, the vitrectomy machine is no longer supported, and manufacturer support is limited in countries that have a US State Department level 4 warning (do not travel)—all of which has hampered success in Cap-Haïtien. Private donations are all that support this program.

We continue to expand our support of ophthalmology in

AT A GLANCE

- The major challenge to starting retina programs in developing countries is access to resources.
- FOCUS is a nonprofit organization that aims to develop and improve eye care systems in the developing world.
- Retina programs in Haiti and Rwanda now provide retina care to a vast population in need, including patients with complex retinal detachments of all varieties, often with bilateral blindness.
- These programs are always in need of ongoing surgical training, equipment, and financial aid.

Figure 1. Dr. Alter (left) and Dr. Taverne (middle) performed vitrectomy in his office-based OR in Port au Prince, Haiti.

Haiti despite the political turmoil and unrest, but travel has become challenging. We made three trips in 2021 after being vaccinated against COVID-19, but now the worsening security situation in Haiti has prevented further visits.

BRANCHING OUT

In May 2022, I made my first trip to Rwanda to help develop a retina program at the Rwanda International Institute of Ophthalmology (RIIO). Although travel is more difficult, the governmental and institutional capacities are much stronger in Rwanda than in Haiti, and safety is not an issue. During my second visit to RIIO in October 2022, we completed the first vitrectomies at the Kibagabaga Hospital that houses the residency program. John Cropsey, MD, a missionary doctor who trained at Wills Eye Hospital in Philadelphia and spent the last 10 years in Burundi, recently relocated to help full-time at RIIO.

PROGRAM SPECIFICS

Proper planning and preparation are key to the success of any new program in the developing world, and nothing should be taken for granted. For example, reliable sources of electricity and compressed air are a given in developed countries but are often not available or reliable in other parts of the world. Unless the electricity is very reliable, a generator and/or battery backup with an inverter is necessary.

Many other obstacles exist, including the cost per case. In addition, the used vitrectomy platforms are no longer supported, and newer machines are expensive. Hopefully, we will have a better supply of used machines in the next few years as the next generation of technology comes along.

Figure 2. Dr. Alter (left) and Dr. Saintil (right) performed widefield fundus photography at St. Damien Hospital in Port au Prince, Haiti.

The case mix in Haiti is mostly complex retinal detachments of all varieties, often with bilateral blindness. There are many ethical and practical considerations when deciding whom to operate on while actively training local retina surgeons. This typically leads to a very steep learning curve. Because the number of patients needing retina surgery far exceeds the program's capacity, we usually make case selections based on monocular status and youth.

HELPING HANDS

These programs were made possible by FOCUS, a 501c3 that was founded by three ophthalmologists in 1961 and aims to develop and improve eye care systems in the developing world. The organization's main mission is to train, mentor, and equip eye care professionals and residency programs in the developing world to reduce the burden of blindness. In addition, FOCUS has developed subspecialty fellowships in Haiti for recent graduates and now has fellows in training for pediatrics, retina, glaucoma, and cornea.

FOCUS has built a strong team of ophthalmologists with experience in global ophthalmology. Working with several nongovernmental organizations such as SEE International, corporate sponsors like the Alcon Foundation, and academic global ophthalmology programs like Wills Eye Hospital, Moran Eye Center, and the University of Illinois Chicago, FOCUS has concentrated on strengthening the ophthalmology residency program at Hôpital de l'Universite d'Etat d'Haiti (HUEH), the state hospital in Port-au-Prince, and the new residency at the nearby Grace Hospital. Projects have included the following: installing water cisterns, storage solutions, examination lanes and equipment, high-speed internet, surgical beds, and surgical video capabilities with large screens; building a full wet lab with two microscopes and four operating microscopes; equipping the OR with green laser, Nd:YAG laser, indirect laser, B-scan, A-scan, and

(Continued on page 46)

THIORIDAZINE RETINAL TOXICITY

Beware of this rare differential when faced with what seems to be an atypical case of AMD.

BY DAVID GRASIC, MD; JORGE A. FORTUN, MD; AND LUIS J. HADDOCK, MD

Thioridazine is an older-generation psychotropic medication used to treat schizophrenia and psychosis.[1] Although efficient in treating mood disorders, the medication has a long list of side effects, including prolonged cardiac QTc interval, neuroleptic malignant syndrome, tardive dyskinesia, blood dyscrasias, hypotension, and retinal toxicity.[1] Newer-generation psychotropic medications—with more favorable safety profiles—have largely replaced its use, and thioridazine retinal toxicity is exceedingly rare nowadays.

The risk of developing thioridazine retinal toxicity increases when ingesting a daily dose exceeding 800 mg/day, and toxicity usually manifests as blurred vision, nyctalopia, and dyschromatopsia 3 to 8 weeks after initiating therapy.[2]

Regardless of the shift away from thioridazine as a treatment option for schizophrenia and psychosis, clinicians should remain vigilant when reviewing a patient's medical history because retinal toxicity can manifest years after stopping the medication.

Here, we present a rare case of assumed retinal toxicity due to thioridazine, which illustrates the classic clinical features to look out for.

THE CASE

A 69-year-old White man with a long-standing medical history of schizophrenia was referred for ocular evaluation due to a 25-year history of bilateral visual decline, nyctalopia, and blurred vision. His medical history was also remarkable for bipolar disorder, grand mal seizures, depression, and early Alzheimer disease. His current list of medications included memantine, lamotrigine, benztropine, mirtazapine, valproic acid, and paliperidone palmitate. The patient had been taking thioridazine 1 g/day for schizophrenia for 20 years prior to switching to paliperidone palmitate 10 years ago. The patient's family history was negative for any inherited retinal dystrophies.

The ocular examination revealed BCVA of hand motion OD and 20/60 OS. Slit-lamp examination revealed lenticular changes in each eye. Dilated examination and retinal imaging revealed marked chorioretinal atrophy in the macula extending into the midperiphery, vascular attenuation, pigment plaques, retinal pigment epithelium (RPE) mottling, and optic nerve pallor (Figure 1).

Fundus autofluorescence imaging showed marked hypoautofluorescence in the macula and midperiphery with a surrounding ring of hypoautofluorescent

Figure 1. The fundus photographs of our patient's right (A) and left (B) eyes showed marked macular atrophy, extensive chorioretinal atrophy, vessel attenuation, peripapillary changes, and pigmentary changes.

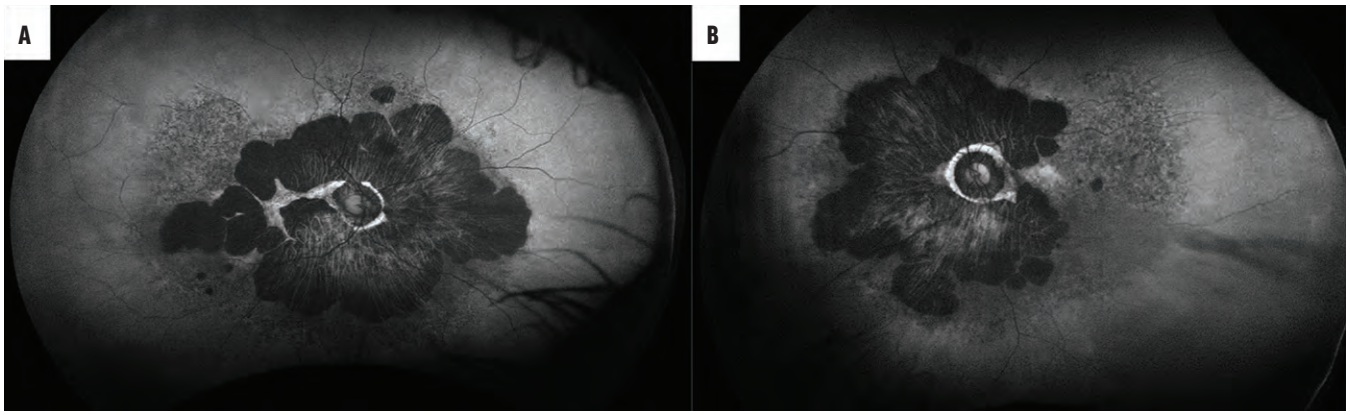

Figure 2. Fundus autofluorescence images of the right (A) and left (B) eyes showed marked hypoautofluorescence in the macula and midperiphery with a surrounding ring of hypoautofluorescent granularity.

granularity (Figure 2). OCT imaging showed diffuse loss of the outer retina and RPE in the right eye and loss of the outer retina and RPE with sparing of the central ellipsoid zone in the left eye (Figure 3).

Laboratory testing ruled out infectious and noninfectious diseases. The findings were suggestive of drug toxicity secondary to thioridazine. Due to the end stage of the retinal toxicity and the patient not being on the medication, the patient was followed by observation with no intervention.

DISCUSSION

Thioridazine retinal toxicity is an extremely rare diagnosis since the advent of newer-generation psychotropic medications for the treatment of schizophrenia. Thioridazine accumulates within melanin granules of the RPE, affecting enzyme kinetics.[3] The accumulation of thioridazine leads to damage to the RPE, outer retina, and choriocapillaris.[3] Clinically, early-stage patients develop granular pigmentary changes in the macula and sometimes in the midperiphery; as the toxicity increases, it progresses into extensive areas of patchy and nummular atrophy.[4]

Thioridazine retinal toxicity can present with characteristics similar to atypical AMD, making it important to perform multimodal imaging and an extensive review of the patient's history to establish a diagnosis. Based on our patient's clinical picture, our list of differentials included atypical AMD, infectious and noninfectious causes, inherited retinal dystrophies, and drug toxicity.

Due to our patient's symptoms spanning more than 20 years and the extent of atrophy on examination, in addition to no visible drusen, we ruled out atypical AMD. The clinical picture and negative laboratory testing—which included syphilis, tuberculosis, and sarcoidosis—helped to rule out infectious and noninfectious causes. The patient had no family history of inherited retinal dystrophies. In addition, the patient ingested a daily dose of the medication that exceeded the recommended dose for a period of 20 years, with the visual symptoms beginning a few years after starting the medication. Because of this, we decided to forego genetic testing due to the high suspicion for drug toxicity.

That left us with drug toxicities, and toxicity from chlorpromazine, thioridazine, and pentosan polysulfate can cause similar retinal findings. Pentosan polysulfate has a similar mechanism of action to thioridazine in which its metabolite is directly toxic to the RPE, causing impaired retinal pigment processing of the ellipsoid zone.[5]

After reviewing the patient's medications, we pinpointed his 20-year history of taking thioridazine as the cause, and he had a classic presentation of thioridazine retinal toxicity: loss of the outer retina, RPE, and choriocapillaris as seen on OCT.

Our patient developed presumed thioridazine retinal toxicity due to the long-term ingestion of greater than 800 mg/day of thioridazine. Dosages of thioridazine below 800 mg/day are generally considered safe, even in those who are on the medication long term.[6] One study found that the severity of retinal toxicity correlates to the maximum daily dose more so than with the cumulative dose.[7]

Unfortunately, once the toxicity has progressed to the end stage, no treatment can reverse the damage. Thus, we followed our patient by observation.

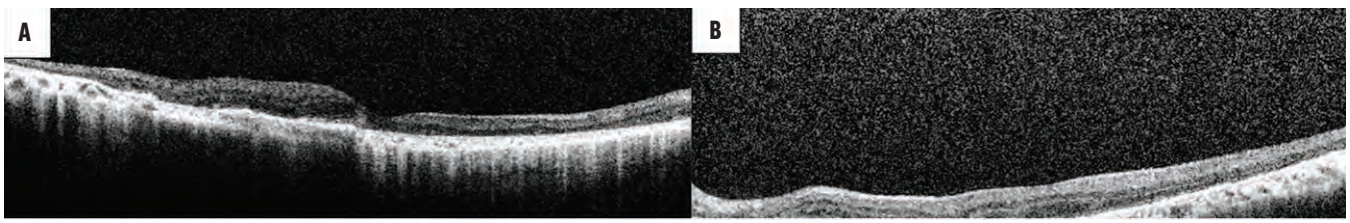

Figure 3. OCT showed diffuse loss of the outer retina in the right eye (A) and loss of the outer retina with sparing of the central ellipsoid zone in the left eye (B).

For patients still taking thioridazine, it is important to immediately stop the medication at the first sign of retinal changes to preserve retinal functionality. One study showed that although atrophy may progress after a patient stops the medication, visual acuity may improve or remaine stable.[8] It is also important to note that even if a patient who is on this medication does not have signs of retinal toxicity, consulting the patient's primary care provider about switching to a newer generation psychotropic with fewer side effects may be beneficial for the patient.

CLINICAL PEARLS

When there is a concern for atypical AMD, it is important to perform further multimodal imaging and take a more detailed medical history to establish the correct diagnosis. Our patient's medical history, clinical examination, and retinal imaging findings were sufficient evidence for us to establish a presumed diagnosis of thioridazine retinal toxicity. Although it is a rare diagnosis with the advent of newer medications, patients who have an underlying psychiatric history and atypical retinal findings on examination might have been taking or are currently taking a psychotropic medication that is the culprit. ■

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indirect ophthalmoscopes; training clinical coordinators; and providing lenses to all residents. In addition, electricity at HUEH is only available about 25% of the time, and the generator must be turned on manually and is often out of diesel fuel. Because electricity often goes out during cases, we installed solar panels with marine battery backup. We hope to install a similar or larger unit for the clinic.

Successful resident training at HUEH has been challenging with the lack of full-time attendings and part-time attendings who are poorly compensated and cannot provide appropriate coverage. In addition, the 3-year residency is often interrupted by strikes, lockouts, protests, and other disruptive events. To address this, FOCUS now offers post-graduate subspecialty training with a commitment to stay at HUEH after graduation to train residents. This has provided a critical mass of knowledge at HUEH and provides more continuity and support for residents. FOCUS also provides stipends and five fellowships in various subspecialties who have a responsibility to attend and train junior residents.

WHAT'S NEXT

HUEH's ophthalmology department is now the best department in the hospital by far, but there is still much to do. We are currently renovating part of the clinic that was damaged by the 2021 earthquake to house the subspecialty clinics that we hope to have fully operational in 2023.

Our next mission is establishing a retina center in Burundi with Jean Claude Niyonzima, MD, who is fully retina trained and needs help with equipment and supplies.

Compared with anterior segment surgery in the developing world, there is scant participation by retina specialists. I would like to encourage more retina specialists to get involved—you will likely find significant enjoyment in participating. Surgical projects in the developing world need more than our talents because the biggest obstacle is often the lack of resources. I always encourage visiting surgeons to donate their time, expertise, and financial support in a balanced way; if the country had ample resources, they wouldn't need our help in the first place. ■

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To learn more about FOCUS and how you can help, follow the QR code or visit 1focus.org.

BEWARE OF CONGENITAL PIGMENTED OCULAR FINDINGS

These could indicate overlooked oculodermal melanocytosis, or nevus of Ota, a risk factor for uveal melanoma.

BY DEVON SHATZMAN, BS; MRITTIKA SEN, MD; AND CAROL L. SHIELDS, MD

Oculodermal melanocytosis is a congenital pigmentary disorder characterized by unilateral or bilateral periocular and temporal fossa cutaneous pigmentation with additional ipsilateral scleral, uveal, orbital, and meningeal pigmentation, often manifesting with heterochromia. This melanocytic pigmentary abnormality, also known as *nevus of Ota*, can manifest with sectoral or diffuse involvement. Often, the pigmentation is limited to the sclera and uvea, hiding behind the upper and lower eyelids.

This pigmentation is an important predisposing feature for the development of uveal melanoma. Affected patients should be made aware of the implications and the benefits of routine dilated ophthalmic examination.[1] Herein, we describe the case of a middle-aged woman with choroidal melanoma in the setting of oculodermal melanocytosis.

CASE REPORT

A 56-year-old White woman of Ukrainian descent was referred to the Ocular Oncology Service at Wills Eye Hospital with blurred vision in her left eye for 2 weeks. She had no past ocular or medical history and claimed to have had several eye examinations over the past few years. Her BCVA was 20/20 OD and 20/30 OS, and her IOPs were 13 mm Hg OD and 14 mm Hg OS.

On examination, there was subtle hyperpigmentation of the periocular skin of the left eye, which the patient recalled was present since birth. Additionally, there was slight heterochromia with the iris (medium brown in the right eye and dark brown in the left eye) surrounded by extensive dark scleral melanocytosis in the left eye. The patient knew of these "freckles" but was never made aware of the potential risk for intraocular tumor. The right eye was unremarkable.

On fundus examination, the left eye had diffuse choroidal melanocytosis imparting a brown color to the choroid with loss of choroidal vascular detail. A 10 x 8 x 3.5 mm choroidal melanoma was noted in the macular region, with overlying hyperautofluorescence corresponding to lipofuscin orange pigment and a trough of dependent subretinal fluid on fundus autofluorescence and OCT.

Ocular ultrasonography confirmed an echolucent mass of 3.5 mm thickness with no extrascleral extension (Figure). Based on these features, a diagnosis of choroidal melanoma in an eye with oculodermal melanocytosis was made. Treatment with iodine-125 plaque radiotherapy and genetic testing for prognostication was performed.

DISCUSSION

Oculodermal melanocytosis most commonly involves the sclera (92%), followed by the iris (17%), which presents as iris heterochromia. The choroid (12%), eyelid (8%), and the temporal fossa (1%) are less frequently affected.[1] Other less common sites of pigmentation include the palate, meninges, and tympanic membrane.[1,2] This condition is often overlooked as a birthmark by patients and ophthalmologists alike. However, several studies have shown that oculodermal melanocytosis is a risk factor for the development of uveal melanoma, as was the case in our patient.[3,4]

Other pigmented birthmarks that have malignant potential but often escape attention without necessary follow-up include congenital nevocellular nevus, dysplastic melanocytic nevus, and cellular blue nevus, all of which can lead to cutaneous melanoma. Other potential malignancies include nevus sebaceous, which can lead to basal cell carcinoma, and phacomatosis pigmentokeratotica.[5,6]

Larsen et al reported the case of a 41-year-old man with an "undiagnosed" spot on his skin that was treated with laser and subsequently proved to be cutaneous melanoma with metastasis.[7] Gündüz et al reported two children with bluish

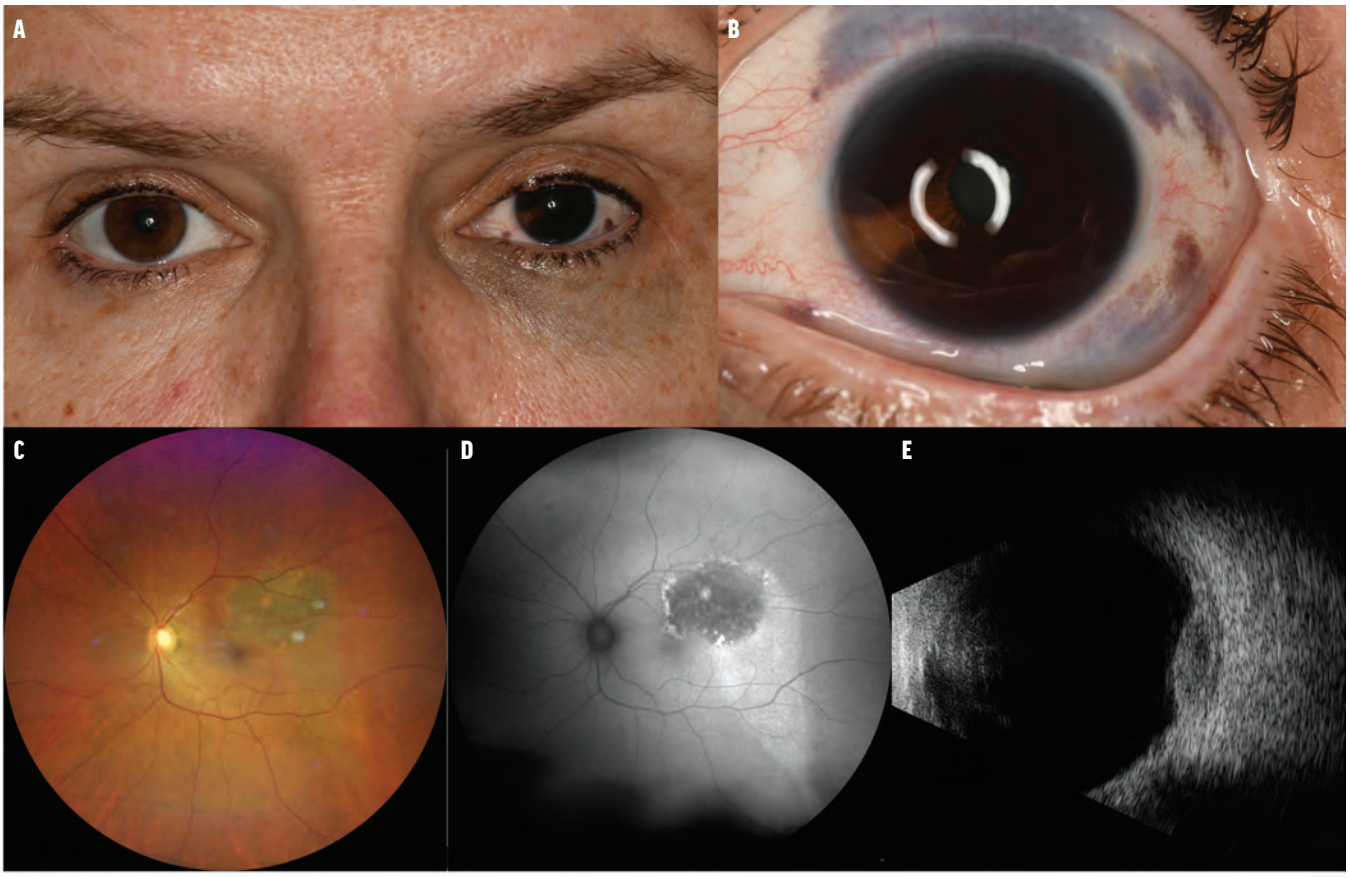

Figure. This 56-year-old woman presented with congenital oculodermal melanocytosis and a choroidal melanoma in the left eye. The external examination showed periocular cutaneous pigmentation of the left side and left iris heterochromia (A) and diffuse, slate-gray scleral melanocytosis (B). The fundus photograph (C) revealed the choroidal melanocytosis and a small choroidal melanoma, measuring 10 x 8 x 3.5 mm with overlying lipofuscin orange pigment, which is best depicted on fundus autoflourescence showing associated subretinal fluid (D). Ultrasonography showed a dome-shaped, echolucent choroidal melanoma (E).

cutaneous discoloration of the eyelids who were later diagnosed at the ages of 29 years and 32 years with periorbital cellular blue nevus with transformation to cutaneous and orbital melanoma with metastasis.[8]

Quantifying the Risk for Uveal Melanoma

In eyes demonstrating ocular melanocytosis, the risk of developing uveal melanoma is estimated at 1 in 400, in contrast to the general White population (1 in 13,000).[2] Conversely, Shields et al found that 3% of patients in a large cohort (n = 7,872) with uveal melanoma demonstrated underlying oculodermal melanocytosis, and many were unaware of the risk of congenital pigmentation.[1] In addition, patients with oculodermal melanocytosis are also at a higher risk of developing multifocal uveal melanoma and bilateral melanoma.[9]

In 2013, our team of researchers published two reports on the rate of systemic metastasis in patients with uveal melanoma and found it to be nearly double in those with oculodermal melanocytosis compared with eyes without this condition.[1,10] The first study revealed Kaplan-Meier estimates for systemic metastasis at significantly higher rates in patients with uveal melanoma associated with melanocytosis compared with those with uveal melanoma without melanocytosis (5 years and 15 years: 27% and 59% vs 15% and 33%, respectively; $P = .013$; hazard ratio = 1.99).[10]

The second study of 7,872 consecutive eyes with uveal melanoma revealed that the risk of metastasis varied depending on the tissues involved (iris = 2.8 times higher; choroid = 2.6 times higher; and sclera = 1.9 times higher).[1] The Kaplan-Meier estimates for metastasis in patients with oculodermal melanocytosis versus no melanocytosis in this study were 2% versus 1.8% at 1 year, 27% versus 15% at 5 years, and 48% versus 24% at 10 years ($P < .001$).[1]

A genetic basis for this observation was revealed in another study by Shields et al, which determined that eyes with oculodermal melanocytosis showed a higher rate of chromosome 8q gain. This was associated with a 20 times higher risk for metastasis.[11] In addition, *GNAQ* mutations have been found in 46% of uveal melanoma and *GNA11* mutations in 32% of patients with uveal melanoma.[12]

CATCH IT EARLY

Early detection is the key to appropriate management and better prognosis. Patients with diffuse or sectoral oculodermal melanocytosis should be evaluated every 6 months with a high index of suspicion for uveal melanoma. Being cognizant of the importance of both the obvious periocular cutaneous and slate-gray scleral pigmentation is essential. Multimodal imaging with autofluorescence, ultrasonography, and OCT is helpful in identifying related small uveal melanoma. ■

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JAY CHHABLANI, MD

What led you to a career as a vitreoretinal specialist?

Ophthalmology was fascinating to me as a young medical student. I was struck by the effect an eye disease could have on a patient's life. As an ophthalmology resident, I was mesmerized by retinal surgery, and I was fascinated by the spectrum of disease and the unique combination of medical and surgical expertise that is needed to be a retina specialist. Emerging therapies and imaging in medical retina are very interesting. Seeing their evolution over the last decade continues to amaze me. Retinal surgery also has changed so much since I started my fellowship in 2007, and I truly enjoy managing complex surgical cases.

You recently reached 500 peer-reviewed publications on PubMed. What motivated you as you strove to reach that milestone?

It's just a number, but the overall journey to reach 500 publications has been rewarding. The motivation to keep moving forward was the evolving imaging techniques, particularly those related to my special interest in the choroid. As we move forward, we have few answers but so many more questions, which is what keeps researchers like me motivated. I am truly thankful to my team, my mentors, and my patients. We still have miles to go.

What interests you most about imaging techniques?

I have a particular interest in choroidal imaging, which has been revolutionized by swept-source OCT. Our group focuses on choroidal biomarkers using volumetric swept-source OCT scans—a few of them are already in clinical practice. Recently, we have been using deep learning techniques to visualize, characterize, and quantify choroidal vessels in a three-dimensional analysis. We have also recently established a novel imaging system—laser Doppler holography—which allows us to visualize choroidal vessels without dye injection. Widefield imaging is becoming more common and with much higher resolution, which is also fascinating. The use of multimodal imaging with image registration in the prediction of disease progression and treatment outcomes is the future.

Figure. Dr. Chhablani and his wife Preeti Patil, MD, a pediatric opthalmologist, enjoying vacation in North Carolina with their two children, Atharv and Naman.

What has been one of the most memorable moments of your career?

I don't think I can pick one specific moment that is memorable in my career; however, when I look back, it surprises me how life kept taking turns and how everything fell into place. I started my career with minimal interest in research, and a decade later, I have an academic career with an active research profile. I truly feel blessed and grateful to my mentors and my family for always being there for me (Figure).

What is your favorite hobby outside of work?

I love spending time with my family. My wife and I have two young boys (8 and 4), and we love watching hockey games together. I enjoy playing chess and ping pong with my boys and having family movie nights! My wife and I enjoy cooking and traveling together. ■

TO GET TO KNOW OTHER RETINA SPECIALISTS, CHECK OUT RECENT *RETINA TODAY* 5Q COLUMNS:

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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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South San Francisco, CA 94080-4990
U.S. License No.: 1048

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VABYSMO™
faricimab-svoa injection 6 mg

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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