July/August 2024

evolve medical education

A continuing medical education activity provided by Evolve Medical Education LLC.
This activity is supported by an independent educational grant from Genentech, a member of the Roche Group.

REAL-WORLD CHALLENGES MANAGING RETINAL DISEASES:

NEW SOLUTIONS WITH FEWER INJECTIONS


CARL D. REGILLO, MD,
PROGRAM CHAIR


MURTAZA ADAM,
MD, FASRS


AVNI P. FINN,
MD, MBA


JORDAN GRAFF,
MD, FACS


KATHERINE E. TALCOTT,
MD, FASRS


AKSHAY S. THOMAS, MD,
MS, FASRS

Distributed with
RT
Retina Today

Release Date: July 2024
Expiration Date: August 2025

REAL-WORLD CHALLENGES MANAGING RETINAL DISEASES:

NEW SOLUTIONS WITH FEWER INJECTIONS

Faculty

Carl D. Regillo, MD
Program Chair
Chief, Retina Service
Wills Eye Hospital
Professor of Ophthalmology
Thomas Jefferson University
Mid-Atlantic Retina
Philadelphia, PA

Murtaza Adam, MD, FASRS
Adjunct Associate Clinical Professor
Rocky Vista University
Chair of Clinical Research
Colorado Retina Associates
Denver, CO

Avni P. Finn, MD, MBA
Assistant Professor
Vanderbilt Eye Institute
Nashville, TN

Jordan Graff, MD, FACS
Barnet, Dulaney, and Perkins Eye Centers
Phoenix, AZ

Katherine E. Talcott, MD, FASRS
Assistant Professor of Ophthalmology
Cleveland Clinic Lerner College of Medicine
Cole Eye Institute, Cleveland Clinic
Cleveland, OH

Akshay S. Thomas, MD, MS, FASRS
Vitreoretinal Surgery and Uveitis
Director of the Uveitis Service
Tennessee Retina
Nashville, TN

Content Source

This continuing medical education (CME) activity captures content from a series of video case discussions.

Activity Description

This supplement summarizes a discussion on managing patients with serious retinal diseases with durable therapies that minimize treatment burden.

Target Audience

This certified CME activity is designed for ophthalmologists involved in the management of patients with nAMD, DME, and RVO.

Learning Objectives

Upon completion of this activity, the participant should be able to:

- **Assess** real-world evidence around the efficacy of traditional anti-VEGF agents for the management of serious retinal diseases (ie, diabetic macular edema [DME], neovascular age-related macular edema [nAMD], retinal vein occlusion [RVO])
- **Evaluate** the latest clinical evidence, including real-world efficacy and safety data, around more durable treatments options for serious retinal diseases (ie, DME, nAMD, RVO)
- **Integrate** management strategies that minimize treatment burden in patients with serious retinal diseases (ie, DME, nAMD, RVO)

Grantor Statement

This activity is supported by an independent educational grant from Genentech, a member of the Roche Group.

Accreditation Statement

Evolve Medical Education LLC (Evolve) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Credit Designation Statement

Evolve designates this enduring material for a maximum of 1 *AMA PRA Category 1 Credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

To Obtain Credit

To obtain credit for this activity, you must read the activity in its entirety and complete

the Pretest/Posttest/Activity Evaluation/Satisfaction Measures Form, which consists of a series of multiple-choice questions. To answer these questions online and receive real-time results, go to https://evolvemeded.com/course/2347-supp. Upon completing the activity and self-assessment test, your certificate will be available. Alternatively, please complete the Posttest/Activity Evaluation/Satisfaction Form and mail or fax to Evolve Medical Education LLC, 353 West Lancaster Avenue, Second Floor, Wayne, PA 19087; Fax: (215) 933-3950.

Disclosure Policy

It is the policy of Evolve that faculty and other individuals who are in the position to control the content of this activity disclose any real or apparent financial relationships relating to the topics of this educational activity. Evolve has full policies in place that will identify and mitigate all financial relationships prior to this educational activity.

The following faculty/staff members have the following financial relationships with ineligible companies:

Murtaza Adam, MD, FASRS, has had a financial relationship or affiliation with the following ineligible companies in the form of *Consultant:* Genentech and Regeneron. *Speaker's Bureau:* Apellis Pharmaceuticals, Genentech, Iveric Bio, and Regeneron.

Avni P. Finn, MD, MBA, has had a financial relationship or affiliation with the following ineligible companies in the form of *Consultant:* Allergan, Apellis Pharmaceuticals, EyePoint Pharmaceuticals, Genentech, and Iveric Bio.

Jordan Graff, MD, FACS, has had a financial relationship or affiliation with the following ineligible companies in the form of *Consultant:* Alimera Sciences, Genentech/Roche, Hi-Health, Iveric Bio, Regeneron, and Regenxbio. *Research/Grant Support:* Genentech/Roche and Regenxbio.

Carl D. Regillo, MD, has had a financial relationship or affiliation with the following ineligible companies in the form of *Consultant:* 4DMT, Adverum Biotechnologies, Alcon, Allergan, Annexon Biosciences, Apellis Pharmaceuticals, Aviceda Therapeutics, Bausch + Lomb, Carl Ziess Meditec, Clearside Biomedical, Cognition, EyePoint Pharmaceuticals, Genentech, Iveric Bio, Janssen, Kodiak Sciences, Lineage Cell Therapeutics, Merck, NGM Biopharmaceuticals, Novartis, Novelty Nobility, Ocugen, Ocular Therapeutix, OcuTerra, Ocuphire Pharma, Opthea, Ray Pharma, Regeneron, Regenxbio, Stealth BioTherapeutics, Théa Pharma. *Grant/Research Support:* 4DMT, Adverum Biotechnologies, Allergan, Annexon Biosciences, Apellis Pharmaceuticals, Astellas, EyePoint Pharmaceuticals, Genentech, Gyroscope Therapeutics, Iveric Bio, Janssen, Kodiak Sciences, Lineage Cell Therapeutics, NGM Biopharmaceuticals, Notal Vision, Novartis, Ocugen, OcuTerra, Opthea, Regeneron, and Regenxbio. *Shareholder:* Aviceda Therapeutics.

Katherine E. Talcott, MD, FASRS, has had a financial relationship or affiliation with the following ineligible companies in the form of *Consultant:* Alimera Sciences, Apellis Pharmaceuticals, Bausch + Lomb, Carl Zeiss Meditec, EyePoint Pharmaceuticals, Genentech, Iveric Bio, Outlook Therapeutics, Regeneron, and Regenxbio. *Grant/Research Support:* Carl Zeiss Meditec, Regeneron, and Regenxbio. *Speaker's Bureau:* Carl Zeiss Meditec, Genentech, and Iveric Bio.

Akshay S. Thomas, MD, MS, FASRS, has had a financial relationship or affiliation with the following ineligible companies in the form of *Consultant:* Alimera Sciences, Allergan, Avesis, Bausch + Lomb, EyePoint Pharmaceuticals, and Novartis. *Grant/Research Support:* Knight's Templar Eye Foundation. *Speaker's Bureau:* Genentech.

Editorial Support Disclosures

The Evolve and staff, planners, reviewer, and writers have no financial relationships with ineligible companies.

Off-Label Statement

This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The opinions expressed in the educational activity are those of the faculty. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

Disclaimer

The views and opinions expressed in this educational activity are those of the faculty and do not necessarily represent the views of Evolve, *Retina Today* or Genentech.

This activity is designed for educational purposes. Participants have a responsibility to utilize this information to enhance their professional development to improve patient outcomes. Conclusions drawn by the participants should be derived from careful consideration of all available scientific information. The participant should use his/her clinical judgment, knowledge, experience, and diagnostic decision-making before applying any information, whether provided here or by others, for any professional use.

Digital Edition

To view the online version of the material, log in to your Evolve account and go to **https://evolvemeded.com/course/2347-supp** or scan the QR code with your smartphone's camera.

To view the webinars associated with this supplement, log in to your Evolve account and go to: **https://www.evolvemeded.com/course-collection/2347_retinaldiseases_newsolutions.**

evolve medical education

PRETEST QUESTIONS

Please complete prior to accessing the material and submit with Posttest/Activity Evaluation/Satisfaction Measures for credit.

1. Please rate your confidence in your ability to manage patients with serious retinal diseases (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).

a. 1
b. 2
c. 3
d. 4
e. 5

2. A 48-year-old patient presents to your office for evaluation. He has a history of diabetic macular edema in his right eye that was initially treated with bevacizumab with only mild resolution of cystic intraretinal fluid. He was switched to aflibercept 2 mg with some improvement, but he still has some resistant cystic intraretinal fluid after 4 monthly injections. All of the following are reasonable management options for this patient EXCEPT?

a. Observation without injections
b. Consider intravitreal steroid therapy
c. Consider faricimab
d. Consider high-dose aflibercept (8 mg)

3. A 42-year-old patient with a history of macular edema secondary to branch retinal vein occlusion has been maintained on monthly bevacizumab with adequate drying of the retina. Unfortunately, this patient reaccumulates fluid whenever bevacizumab is extended beyond 4 weeks. He is becoming increasingly frustrated with his treatment burden. All of the following are reasonable management options for this patient EXCEPT:

a. Switch to aflibercept 2 mg
b. Switch to high-dose aflibercept
c. Switch to faricimab
d. Continue bevacizumab

4. A 77-year-old woman with new onset neovascular age-related macular degeneration presents to your office for consultation. She notes 3 weeks of distortion in her left eye. Her OCT shows central subretinal fluid and elevation at the level of the retinal pigment epithelium. Her fluid resolves after 3 monthly injections of intravitreal aflibercept 2 mg, but her subretinal fluid returns after an 8-week injection holiday. Which of the following is a reasonable treatment option?

a. Switch to a more durable anti-VEGF
b. Consider focal laser
c. Switch to bevacizumab
d. Extend treatment with aflibercept 2 mg to 10 weeks

5. A 74-year-old woman with age-related macular degeneration presents to your office with a large, tall pigment epithelial detachment with overlying intraretinal fluid and adjacent subretinal fluid. You decide to initiate intravitreal anti-VEGF therapy. What is an important risk of treatment to discuss with this patient prior to initiation of treatment?

a. Cataract formation
b. Neovascular glaucoma development
c. Retinal pigment epithelium rip development
d. Iris atrophy

6. According to real-world data, which of the following statements about the ability to drive and diabetic macular edema are TRUE?

a. The probability of maintaining driving vision over 4 years is 72%
b. The probability of maintaining driving vision is higher amongst patients who receive a higher number of anti-VEGF injections per year
c. Both A and B
d. None of the above

7. A 72-year-old man presents to your clinic for evaluation with new vision loss in his right eye. Examination of his right eye shows a pigment epithelial detachment with overlying intraretinal fluid and adjacent subretinal fluid. He has previously been treated with four injections of bevacizumab every 4 weeks, with no significant improvement in fluid. Which of the following is a reasonable next step in management?

a. Switch to faricimab
b. Continue bevacizumab
c. Consider dexamethasone intravitreal implant 0.7 mg
d. Switch to pegcetacoplan

8. A patient with a history of diabetic macular edema presents to your office for evaluation. He has macular edema that is inadequately controlled with bevacizumab injections. Fluorescein angiography shows diffuse leakage in the macula. Which of the following is the next best treatment option?

a. Switch the patient to faricimab and schedule a follow-up for 12 weeks after the first injection
b. Switch the patient to faricimab and perform three loading doses 4 weeks apart prior to extending
c. Perform focal laser photocoagulation
d. Start the patient on topical NSAIDs and steroids

Real-World Challenges Managing Retinal Diseases:
New Solutions With Fewer Injections

Degenerative retinal conditions such as age-related macular degeneration (AMD), diabetic retinopathy (DR), and diabetic macular edema (DME) are a common causes of visual impairment in older patients and people living with diabetes.[1] Treatment with first-generation anti-VEGF inhibitors (eg, aflibercept 2 mg, bevacizumab, and ranibizumab) have been the gold standard for decades,[2,3] with their safety and efficacy established in numerous clinical trials.[4-9] However, patients frequently struggle with the injection burden, with some patients requiring monthly treatment to maintain disease control.[10] Other patients experience suboptimal response or lose vision over time.[11] The advent of second-generation agents (eg, faricimab, brolucizumab, and high-dose aflibercept [8 mg]) offer potential solutions to these challenges.[12-16] The following case studies illustrate how these second-generation agents can be used in the real world to reduce the treatment burden in patients with retinal diseases and help them regain vision.

—Carl D. Regillo, MD

CASE 1: A PATIENT WITH AMD AND PED WHO WAS SWITCHED FROM AFLIBERCEPT TO FARICIMAB

Jordan Graff, MD, FACS: Our first case is a 74-year-old woman with a diagnosis of AMD for two years. It has likely been there longer, but it was diagnosed when she lost vision in the right eye. Her baseline OCT (Figure 1 Column A) shows this large geographic atrophy (GA) and a VA of 20/150 OD. In her only remaining good eye, she presents with a large, tall pigment epithelial detachment (PED), a little intraretinal fluid, and a cuff of subretinal fluid at the edge of the PED (Figure 1 Column B). She had cataract surgery about a year ago. She was initially treated with aflibercept 2 mg as part of a small pharmacokinetic trial. Dr. Talcott, what are your thoughts on this PED, the angiographic presentation, and how to handle this kind of a case?

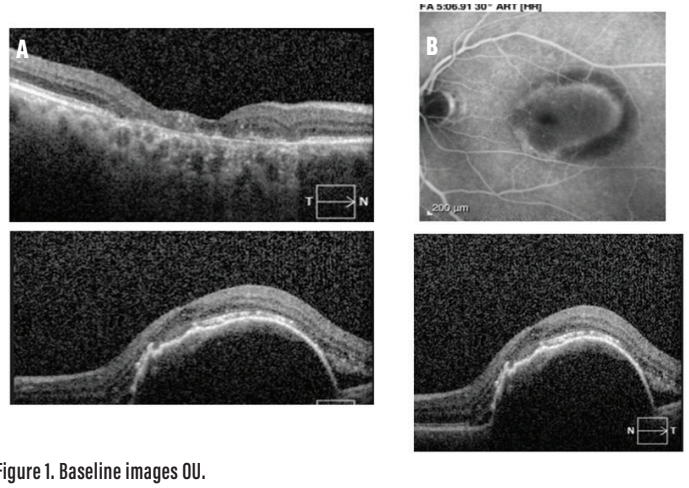

Figure 1. Baseline images OU.

Katherine E. Talcott, MD, FASRS: These are some of our most challenging patients. This is her only remaining eye, so the risk is high. It's possible she had a PED in the right eye and, at some point, that collapsed and led to atrophy. I always find it challenging to see these patients because in the OCT you have this large PED and some fluid. It's hard to know if that's draping or not. Then you obtain the fluorescein angiography (FA) and it appears as though there's a fibrovascular PED. I'm concerned there's a neovascular process happening. It's important to treat these patients, but I worry about a retinal pigment epithelial (RPE) tear. The other point to consider is that even with monthly anti-VEGF treatment, the PED doesn't always change much; there's still persistent fluid. It can be frustrating for both patients and providers.

Dr. Graff: We immediately started her on aflibercept 2 mg, four injections. She had a good response. Figure 2 shows her imaging after four injections. You can see the collapsing PED, there's no RPE tear, and the central subfield thickness (CST) between those mounds of the PED is now 425 µm. But fluid remains in the sub-RPE space and a tiny cuff of subretinal fluid appears between the mounds. There's intraretinal fluid nasally, and some hyperreflective fluid temporally. We could continue to treat with aflibercept 2 mg, but I opted to switch the patient to faricimab. We administered three injections of faricimab and started to extend out to 8 weeks and then 10 weeks. Her VA was 20/70 at the last aflibercept 2 mg injection. After treatment with faricimab, you can see the collapse of the PED further and reduction of the edema, but now there's a small naturally progressive cataract (Figure 3).

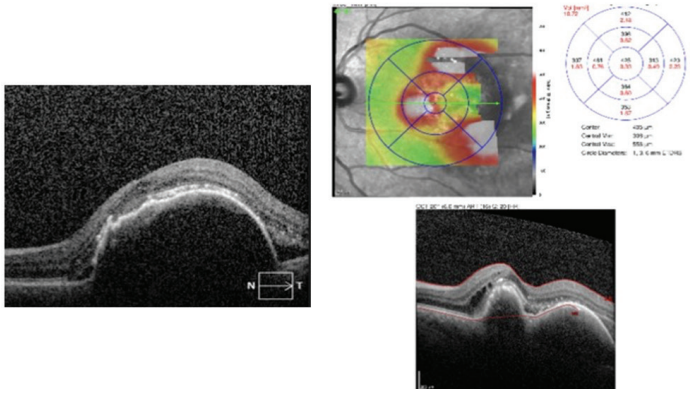

Figure 2. Imaging after four injections of aflibercept 2 mg.

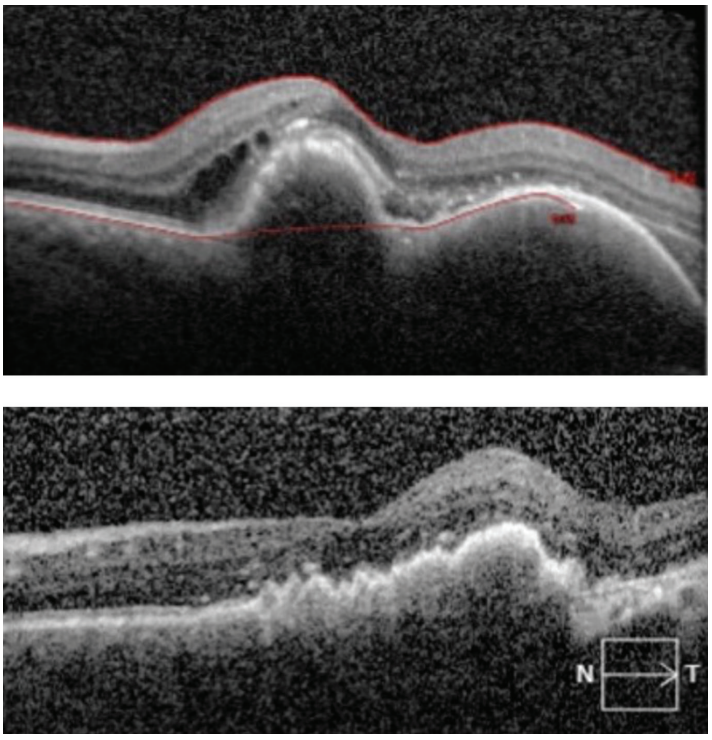

Figure 3. Imaging after faricimab injections.

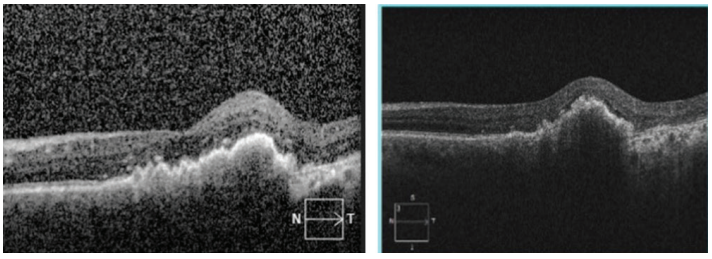

Figure 4. OCT after faricimab injections, 10-week follow-up.

The patient goes in for the cataract evaluation and missed the planned 10-week follow-up with us. Incidentally, the cataract team obtained an OCT (Figure 4). Although there's no fluid at 10 weeks, there's some atrophy on that right side. What are your thoughts on this, Dr. Talcott?

Dr. Talcott: This is a great case example that reflects what often happens with these patients. I'm impressed by the ability to dry that PED out by switching to faricimab. Faricimab can also decrease PED height,[17] which I've appreciated in clinic. Many of us have started introducing faricimab in our practice by switching some of our recalcitrant patients, and I've found it to be beneficial. However, when patients have large PEDs, they are at risk for an RPE tear at some point during their treatment. I'm concerned that's what happened here; this patient had an RPE tear that occurred as part of the drying of their PED. Thankfully, it appears it occurred outside of the fovea. Whenever this happens, I tell patients that this occurred and remind them that this is part of the natural history of the disease while treating it. The alternative is to not treat, which places them at risk for fluid or a large hemorrhage that could result in complete vision loss.

Dr. Graff: The patient has the cataract removed, but she misses her appointment with us for treatment. She returns at 19 weeks. I never would've intentionally extended this patient that far. Her VA is 20/50 19 weeks after her last injection (Figure 5). Faricimab was very durable. On the far-right side, there is a small RPE tear. You can see the light coming through the absence of the RPE, but the fovea is fine. There are a few minimal hyperreflective foci and a few microcysts. Her vision is good, but the exam revealed a dot of hemorrhage. Dr. Talcott, how would you proceed? What does maintenance look like for this patient?

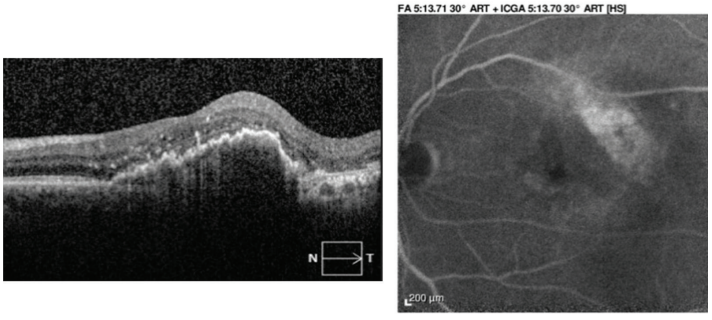

Figure 5. Nineteen weeks after last faricimab injection.

Dr. Talcott: It's great that the patient was able to do so well for so long, but 19 weeks is a little long for a follow-up. I stress to my patients that although their OCT looks better than expected after this amount of time, we shouldn't extend that far. I would tighten to 12 or 14 weeks, knowing it may end up being 16 weeks with scheduling. It would be ideal to be able to extend to 16 weeks and have the patient come in three times a year.

Dr. Graff: Like yourself, we were investigators in the TENAYA and LUCERNE trials.[13] We have good randomized clinically controlled data that we can approach 80% even with very strict retreatment criteria of patients extending out to 12 weeks or longer. About 50% of those patients could obtain that 16-week mark. We don't have data to support anything longer than that. Because life is unpredictable, I'm glad faricimab is a very durable agent, but I wouldn't intentionally extend further than 16 weeks. We tightened the interval to 12 weeks and administered two additional injections. Her VA hovers between 20/50 and 20/60 OS. She's being maintained on 12-week injections and is thrilled with the outcome in her only good eye. We're continuing to observe her at 12-week intervals.

CASE 2: A 43-YEAR-OLD WOMAN WITH TYPE 2 DIABETES, DME, AND DRIVING CONCERNS

Murtaza Adam, MD, FASRS: Our second case is a 43-year-old woman with type 2 diabetes. She presented with blurred vision in

the right eye, which was worse than her left eye. She's concerned about her ability to drive. Her HbA1c is 8.5. She has a complex ocular history with a corneal transplant for keratoconus and pseudophakia in the right eye. She also has an early cataract in the left eye with a history of a single dexamethasone intravitreal implant injection in the left eye at an outside retina practice.

Driving is a particular concern in diabetic patients, as these individuals are usually younger than our AMD patients. These working-age patients with diabetes need to maintain their independence. Real-world data indicates that the probability of maintaining driving vision more than 4 years is 72% in patients with DME.[18] Critically, the frequency of anti-VEGF injections is directly correlated to the probability of being able to drive. Patients who receive more anti-VEGF injections have the highest chance of maintaining their driving vision, whereas those who receive fewer injections, generally one to five annually, have the lowest chance of maintaining driving vision for more than 4 years (63%).[18] This data drives home the point that more frequent therapy leads to better outcomes.

This patient presented with 20/100 VA in the right eye in 20/50 in the left. You can see on Figure 6 that there's a thickened central fovea with large cystic changes in the right eye, and the left eye has trace DME. There is some vitreomacular adhesion without traction in the right eye and mild drusen in both eyes.

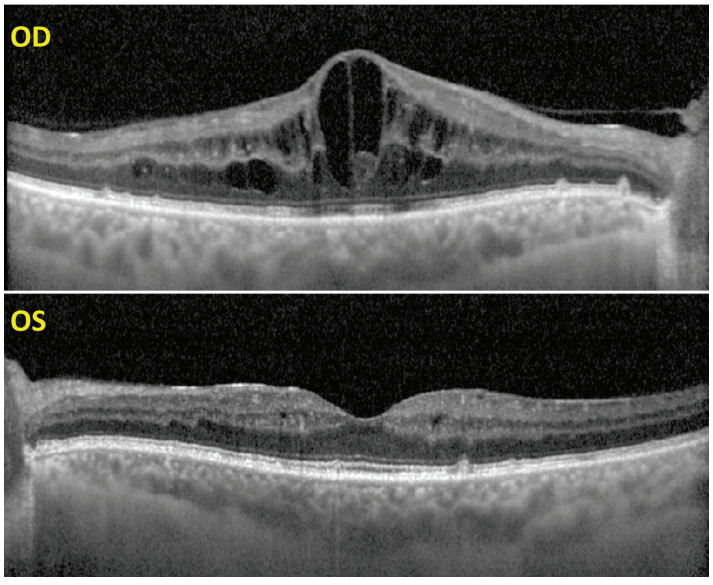

Figure 6. Baseline OCT.

Initially, I treated this patient monthly with aflibercept 2 mg and observed that extension failure occurred in that right eye at 8 weeks. Interestingly, you'll see on the right side of Figure 7 that the left eye's macular edema fluctuated with concurrent treatment in the right eye. The patient also had a significant amount of edema in September 2021, but I held off on treatment at that visit (Figure 7). On the next visit, she had no fluid at all. Dr. Regillo, have you experienced this bilateral effect of anti-VEGF treatment?

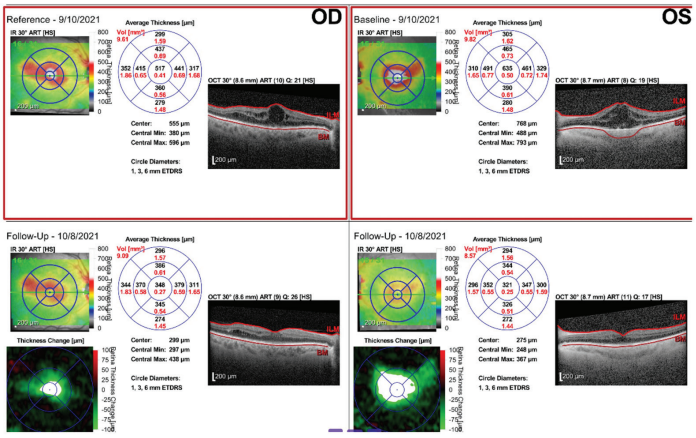

Figure 7. Reference, baseline, and follow-up imaging.

Dr. Regillo: I've seen DME naturally fluctuate small degrees, but never that much. There have been reports of injecting one eye and seeing effects in the other. Neovascularization can be exquisitely sensitive to anti-VEGF. The initial reports of a contralateral effect was indeed regression of neovascularization of the disc in the fellow eye. But it's very unusual with bilateral DME.

Dr. Adam: I agree; typically, the fluctuations are smaller. This is certainly an unusual case. We continue treating the patient monthly with aflibercept 2 mg. We've administered eight injections so far. I extend out 5 or 6 weeks, and we see failure. The left eye eventually has a significant drop in vision, so we administer aflibercept 2 mg in that eye. Overall, the patient does have good control; if I treat her every 4 to 5 weeks, there is a marked improvement in anatomy and vision. However, she has a busy schedule, and coming in every 4 to 5 weeks isn't a realistic option. Dr. Regillo, what would you do in this situation? Would you continue to push for every 4- to 5-week maintenance with aflibercept 2 mg, or would you consider another option?

Dr. Regillo: Two years ago, continuing with aflibercept 2 mg would have been an option. Aflibercept 2 mg is the best drying drug of the first-generation agents (eg, aflibercept 2 mg, bevacizumab, and ranibizumab). That was proven in Protocol T.[8,9] Selecting upfront aflibercept 2 mg to dry the macula as quickly as possible with the fewest treatments was a good choice. It's working, but it's frequent treatment. Corticosteroids are another option for suboptimal responders or as a way to extend durability.[19] You can get about 3 months or so with off-label intravitreal triamcinolone or an on-label intravitreal dexamethasone implant. That doesn't diminish the treatment burden, because the patient has to return so you can monitor IOP.

Now, we have second-generation agents (eg, brolucizumab, faricimab, and high-dose aflibercept) that either last longer, dry better, or both.[16,20,21] Faricimab is the first and only dual-acting agent.[22] High-dose aflibercept was the most recent FDA approval in DME.[23] Brolucizumab dries well, but there are safety

issues.[24,25] My next selection for this patient would be faricimab. We have a lot of experience with it because it's been FDA approved for 2 years.

Dr. Adam: I agree. My approach was similar to yours. I switched the patient to faricimab, and she had relatively good control at a 4- to 5-week interval. The left eye is doing well and maintains good vision. The right eye has some mild fluctuations in fluid but, overall, is doing well. However, after extending the patient with faricimab to 6 to 7 weeks, the right eye begins to fail (Figure 8). The left eye seems to be a better responder, perhaps due to the Ang-2 component in faricimab. I ultimately switched the right eye to the dexamethasone implant. After 6 weeks, the patient responded quite well and didn't require additional anti-VEGF treatment (Figure 9). The left eye is responding well to faricimab. Because the patient's left eye was phakic and still had accommodation, I decided not to treat it with an intravitreal steroid, which may cause a cataract. She's very appreciative that we've reduced her in-office burden in both eyes with two different approaches.

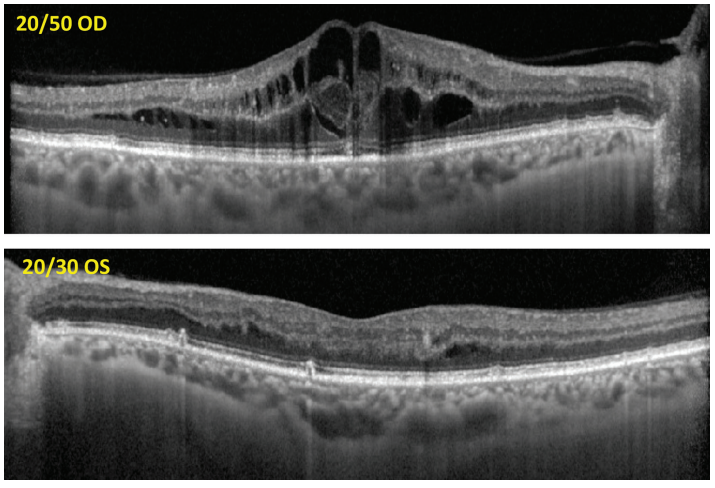

Figure 8. Follow-up imaging after faricimab extension.

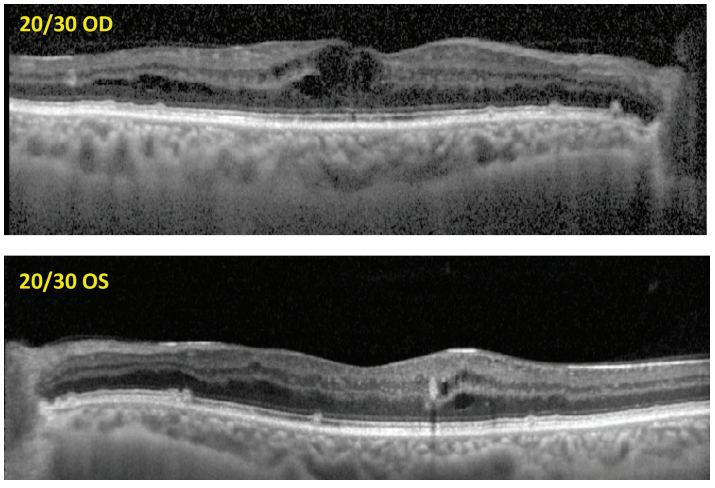

Figure 9. Follow-up imaging 6 weeks after dexamethasone (OD) and faricimab (OS).

Dr. Regillo: I liked the way you managed this case. You're obtaining a good benefit and good vision outcomes with the least burden possible. Faricimab has better drying and more durability, which is exactly what my experience is in practice, too. This case illustrates that durability well.

CASE 3: A 46-YEAR-OLD WOMAN WITH TYPE 1 DIABETES WHO NEEDS FREQUENT TREATMENT

Dr. Adam: Our next case is a 46-year-old woman with type 1 diabetes, diagnosed at the age of 25 years. She presents with blurred vision in both eyes. She's had a renal transplant and has peripheral neuropathy, which are all systemic biomarkers of advanced diabetic disease. The vasculature of the eye and the vasculature of the nephron are very similar in terms of caliber. When we see those changes in renal function, we always worry about the eye.

She has a history of pseudophakia and has had panretinal photocoagulation (PRP) in both eyes to control her proliferative diabetic retinopathy. She presented with a history of chronic anti-VEGF treatment every 4 weeks for DME at an outside retina practice and came to us due to an insurance change. She also had a history of epiretinal membrane (ERM) in both eyes. However, as we know from prior studies, suboptimal DME responders are 3.8 times more likely to have an ERM.[26] Has that been your clinical experience, Dr. Regillo?

Dr. Regillo: It's definitely a confounding factor. I think it does play a role in cases where it looks like it's a suboptimal response or in patients who may require more frequent treatment to dry the macula. Sometimes, when a patient with DME responds well to treatment, the ERM will form later, which then contributes to the need to change the management strategy.

Dr. Adam: Figure 10 shows the right and left eyes, and the pucker that we see on the right side is not that impressive. This patient had no insurance authorization for treatment with aflibercept 2 mg, so we decided to wait 2 weeks. Two weeks later, you can see a subtle increase of her macular thickening (Figure 11).

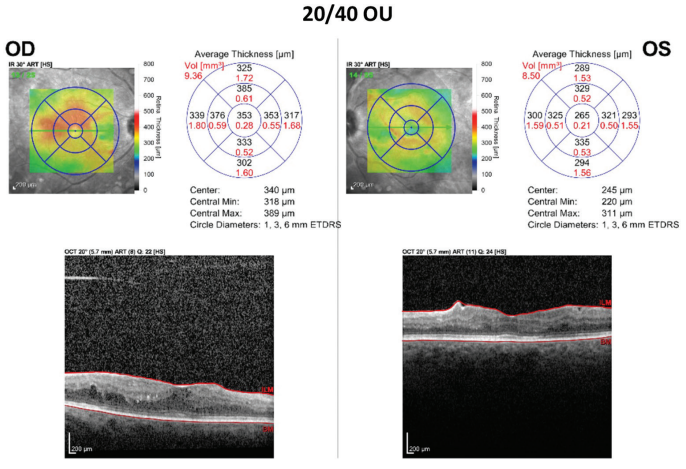

Figure 10. Baseline imaging.

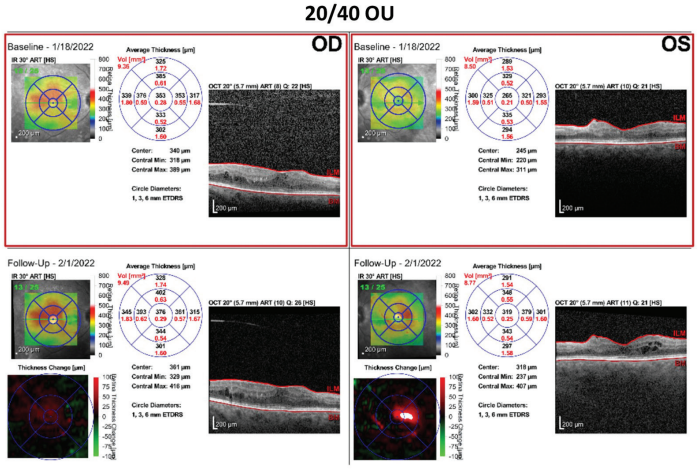

Figure 11. Two-week follow-up imaging waiting for insurance authorization.

Dr. Adam: Clearly this patient has chronic, recurrent DME at a 6-week interval, or longer. Following 3 monthly injections of aflibercept 2 mg, I attempted to extend her to 6 weeks again and was unsuccessful (Figure 12). On the left side, the fovea is threatened with DME. The right eye has a plateau effect upon the fovea from diffuse DME. However, when we return to a 4- to 5-week interval, the patient does well (Figure 12). As you can see on the left side of Figure 12, the right eye foveal contour is missing despite the good visual acuity. In the left eye, we see good foveal contour and equal vision. Therefore, the pucker is playing a role with regard to macular anatomy, but perhaps not much in terms of visual function. This is a high-need patient with chronic disease we are treating with monthly aflibercept 2 mg. With the persistent macular thickening in the right eye despite monthly treatment, would you consider surgery to relieve macular traction from the ERM, Dr. Regillo?

Dr. Regillo: This patient is a good responder, but she needs frequent treatment. Surgery is a last resort. A vitrectomy will decrease the durability of any future anti-VEGF agent. I'd consider switching her to one of the second-generation agents with better drying power. I'd use faricimab because we have more experience with it, but high-dose aflibercept could also be a good option.

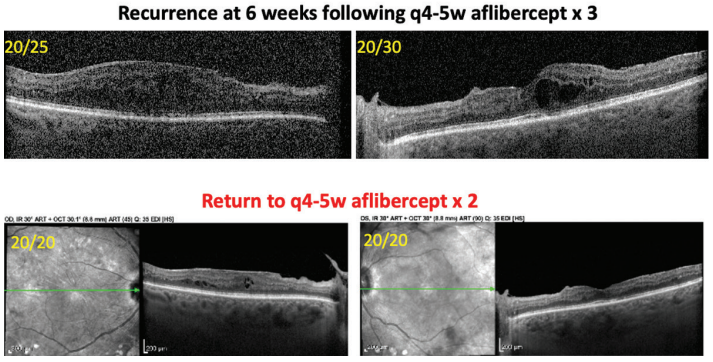

Figure 12. Imaging 6-week vs 4- to 5-week extension with aflibercept 2 mg.

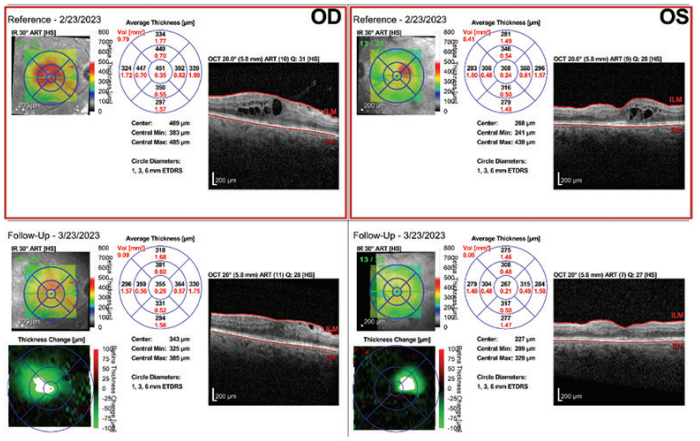

Figure 13. Faricimab switch OD and maintenance aflibercept 2 mg OS.

Dr. Adam: I agree. I decided to try faricimab first and scheduled a vitrectomy with membrane peeling as a backup plan. She had an excellent anatomic response to faricimab after a single treatment, showing that the impact of her ERM may have not been as significant as we previously thought (Figure 13). We cancelled her surgery, and she was very happy with this outcome. I'm maintaining her on every 5- to 6-week faricimab in both eyes. We noticed some recurrence at 7 weeks, but she's maintaining between 20/20 and 20/40 VA in the right eye. The left eye VA was 20/25 at her last visit.

CASE 4: A SYMPTOMATIC PATIENT WITH NEW-ONSET NEOVASCULAR AMD

Dr. Regillo: Our fourth case is a 77-year-old woman who presents with new-onset neovascular AMD (nAMD). She is symptomatic with 3 weeks of distortion and blur OS. The FA shows occult CNV, and the corresponding OCT shows signs of exudation with central subretinal fluid OS (Figure 14). The elevation at the level of the RPE is consistent with type 1 CNV. Her VA is 20/60 in the left eye. The right eye has dry AMD with 20/25 VA and no symptoms.

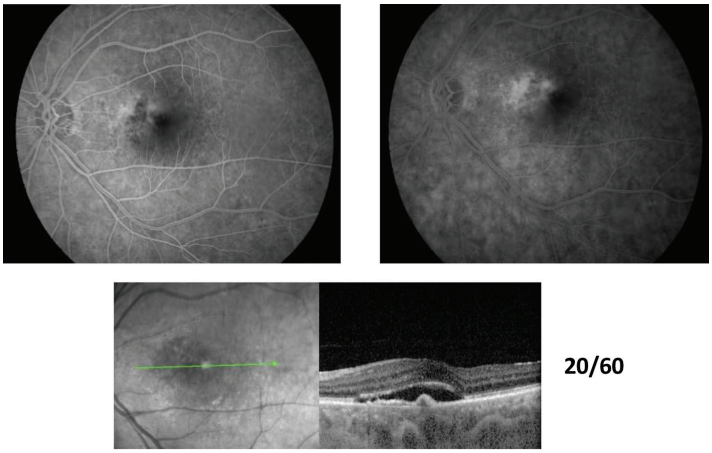

Figure 14. Baseline FA and OCT.

I started her on intravitreal aflibercept 2 mg. The subretinal fluid began to improve after one injection, and her VA improved to 20/40. A month after the second injection, all signs of exudation have mostly resolved. Some incidental vitreomacular adhesion (VMA) is present, but I don't think it is affecting her in any way (Figure 15). Evidence does suggest that if you have VMA, it's more likely to result in the need for more frequent treatment.[27,28] I attempted to extend her by 2 weeks. Six weeks after the third aflibercept 2 mg injection, her treated eye has a dry macula and 20/30 VA. I attempted to extend to 8 weeks, and we then ran into some difficulties (Figure 16). At 8 weeks, it's almost as if we reverted to baseline. There's about the same amount of subretinal fluid with this recurrence as there was before treatment, and her VA is now 20/50. Is this subretinal fluid we can tolerate?

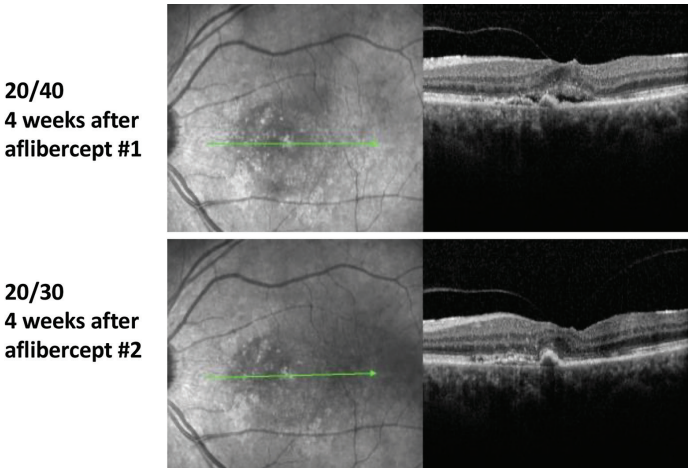

Figure 15. Initial treatment course.

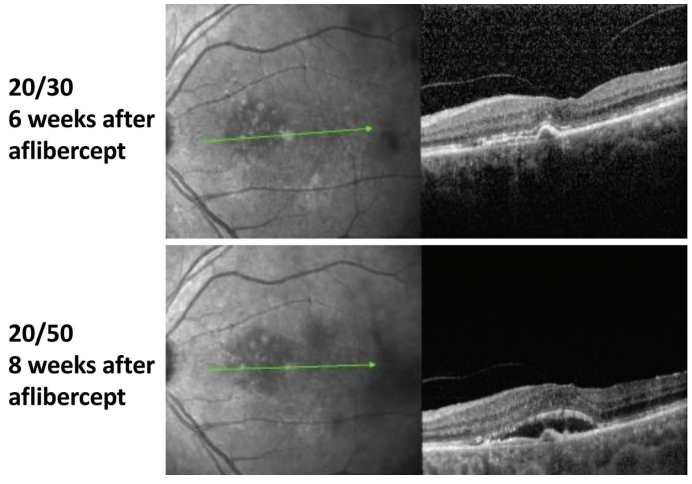

Figure 16. Treatment extension to 6 and 8 weeks.

Dr. Adam: Evidence suggests that short-term subretinal fluid is not particularly detrimental to visual acuity outcomes for patients with this condition.[29] Macular edema is much more concerning, and we should be aggressive with treatment when we see persistent macular edema. My take is that better fluid control in the beginning of treatment leads to the best visual outcomes. In my opinion, a little subretinal fluid in the short term with mild fluctuations are reasonable. In the long term, patients will likely have better visual outcomes if we are tighter with our injection intervals and more vigilant with resolving subretinal fluid.

Dr. Regillo: I agree. Small amounts of stable or minimally fluctuating fluid is often fairly well tolerated and can be acceptable but, in general, we should still try to achieve and maintain the driest macula possible. When I'm treating patients in that 4- to 6-week interval, I will sometimes extend and decrease that interval by a week. The goal is to minimize the treatment burden while achieving the best possible vision outcomes. With the first-generation agents (bevacizumab, ranibizumab, and aflibercept 2 mg), median durability in the maintenance phase in nAMD is about 8 weeks (range, 4 to 12 or so weeks). About 75% of patients can extend 8 weeks or more in between injections. This case represents those 25% of patients who can't extend that far. This patient has a few options: we can continue aflibercept 2 mg every 6 weeks, continue the aflibercept 2 mg and extend the treatment interval to 8 weeks, switch to a more durable anti-VEGF agent, or add PDT. What would you select?

Dr. Adam: I'd switch the patient to a more durable anti-VEGF agent, assuming insurance approved it. We know from the high-dose aflibercept trials that 80% of patients can extend 12 weeks longer based on phase 3 clinical trial data.[14] Generally, my goal is to extend patients to 8 weeks or longer. AMD incidence is increasing in our population. Extending treatment intervals will be important to maintain scheduling availability of retina specialists and treatment adherence for patients.

Dr. Regillo: This case occurred before second-generation anti-VEGFs became available, so I didn't have that option. I had to continue with every 6 weeks of aflibercept 2 mg for quite a while, and I didn't want to re-extend to 8 weeks. Adding PDT seems to be most helpful in polypoidal choroidal vasculopathy cases, but not this type of case. Now that we have second-generation anti-VEGFs available, I think faricimab or high-dose aflibercept would be a good option.

CASE 5A: SWITCHING FROM RANIBIZUMAB TO BROLUCIZUMAB

Dr. Regillo: For our next cases, I will share a few switching examples. The first is a patient who could not extend beyond 4 weeks with ranibizumab. The affected eye looks great at week 4 after an injection with good control. This is not a suboptimal responder case; it is case with a good response that needs very frequent treatment to maintain optimal disease control. Five weeks after the injection, the effect is wearing off with a drop in vision and recurrent intraretinal edema (Figure 17). After switching this patient to brolucizumab, I was able to extend the injection interval to 6 weeks with adequate control. The patient is on brolucizumab to this day and doing well.

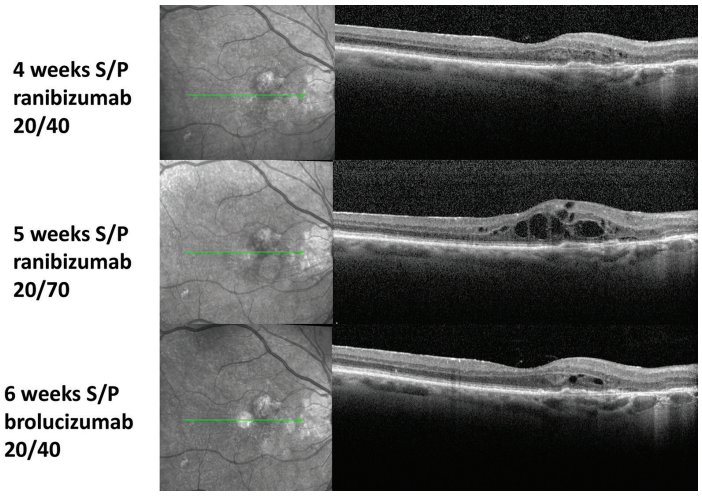

Figure 17. Outcomes after switching from ranibizumab to brolucizumab.

CASE 5B & 5C: SWITCHING FROM AFLIBERCEPT TO FARICIMAB

Dr. Regillo: Our next example is a patient whose right eye continued to have edema 4 weeks after an aflibercept 2 mg injection. The patient's VA was 20/40, but disease control was not ideal. I switched this patient to faricimab and achieved better vision (Figure 18) and was able to extend the treatment interval to 6 weeks. In another example, I had a patient whose treatment in the affected right eye was able to be extended to 6 weeks on ranibizumab, which was great. However, I was able to get up to 11 weeks with faricimab (Figure 19). What has been your experience switching from first- to second-generation agents?

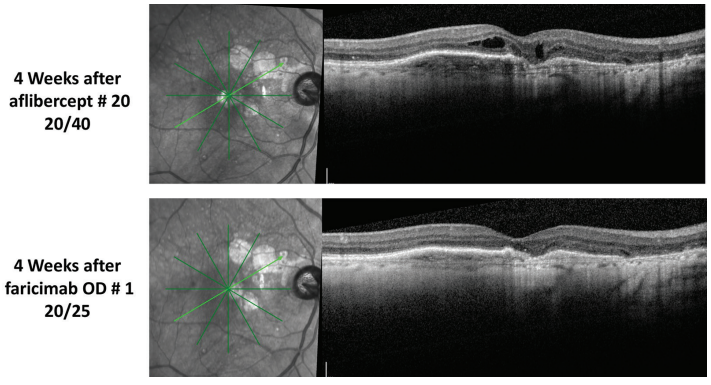

Figure 18. Outcomes after switching from aflibercept 2 mg to faricimab.

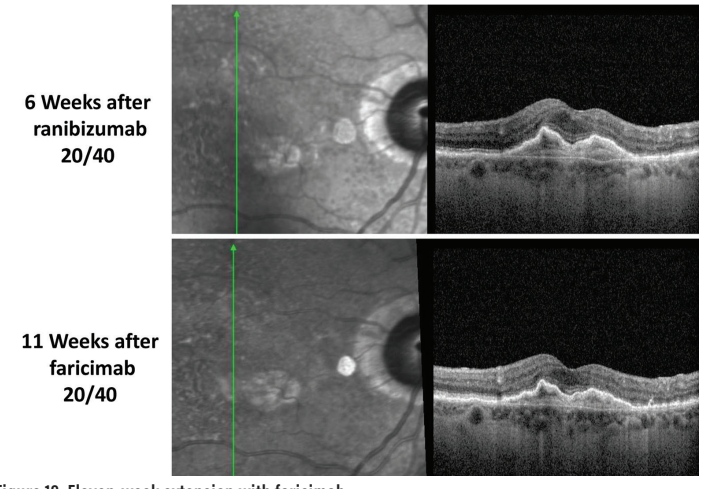

Figure 19. Eleven-week extension with faricimab.

Dr. Adam: My experience switching from first- to second-generation agents has been largely with faricimab because it's been on the market over 2 years; high-dose aflibercept has only been available until much more recently. I'm using faricimab in high-need patients and suboptimal responders. For those patients, we are achieving 2 additional weeks of extension, on average. Some patients have amazing results with faricimab. A patient I saw this week has been on 4- or 5-week aflibercept 2 mg for 6 years. We switched them to faricimab about 12 months ago, and we're now extending 3 months between treatment intervals. Previously, if I tried to extend to 6 weeks with aflibercept 2 mg, this patient would have recurrent subretinal fluid. Additionally, this patient is functionally monocular. In this patient, minimizing treatment burden and risk to the eye while maintaining his prior vision gains has been a huge benefit of utilizing second-generation therapies.

Dr. Regillo: That's been my experience, too; second-generation agents provide 2 additional weeks on average in high-need, previously treated scenarios. Our impressions are supported by real-world data. The TRUCKEE study found a trend for improved anatomy after three injections when patients were switched to faricimab.[17] One injection of faricimab may not provide a huge improvement in a suboptimal responder; it may take a few treatments to see the full effect. FARETINA-AMD is a retrospective real-world study using data from the IRIS Registry that's also been presented at our major congresses.[30] It shows that we're obtaining a 1- or 2-week extension in the majority of patients when switching to faricimab. There is no doubt that we are obtaining greater durability.

CASE 6: A PATIENT WITH BRVO-RELATED MACULAR EDEMA

Akshay S. Thomas, MD, MS, FASRS: This is a 42-year-old patient presenting with branch retinal vein occlusion (BRVO)-related macular edema (Figure 20). The OCT shows classic intraretinal fluid. His VA is 20/60. I started him on monthly bevacizumab. He had a good response, with a dry and healthy-appearing macula. His VA improved to 20/20. However, every time I attempted to extend him, even by a week, fluid recurred. Given that we now have more durable agents, when would you consider switching an eye like this?

Avni P. Finn, MD, MBA: This patient has done well on bevacizumab. However, now that we have second-generation agents, I would favor switching patients who require monthly injections with first-generation agents to a second-generation agent. This patient is 42 years old and likely in the workforce; due to the high treatment burden in his case, it is important to try to decrease the treatment burden to make the follow-up more sustainable in the long term.

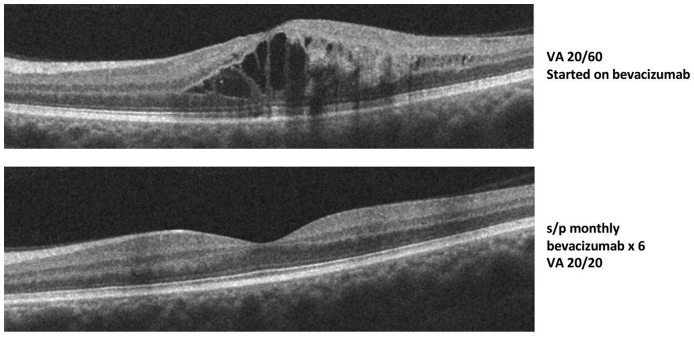

Figure 20. Baseline and follow-up OCT.

Dr. Thomas: I agree. This patient had a significant recurrence extending him 5 weeks on bevacizumab, and his VA declined to 20/25. I switched him to aflibercept 2 mg, and he was able to extend to 6 weeks (Figure 21). However, when I extend him to 7 weeks, he experienced a recurrence of fluid and a decline in vision (Figure 22). How do we define treatment failure or a failure to extend? This patient was able to extend 2 additional weeks with aflibercept 2 mg. Is that enough?

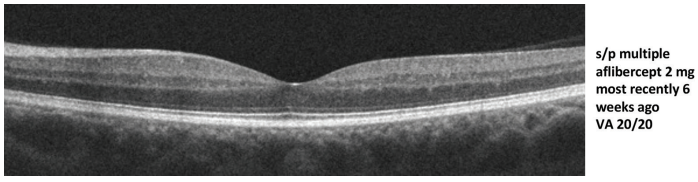

Figure 21. Six-week extension with aflibercept 2 mg.

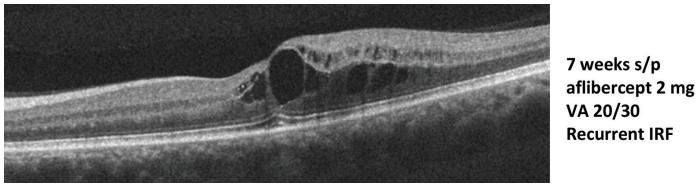

Figure 22. Seven-week extension with aflibercept 2 mg.

Dr. Finn: There's no right answer, and it is important to individualize care. We should consider a couple of question and steps. I'd start by having a conversation with the patient. Is it difficult for him to come into the office? How well does he tolerate injections? Is he happy with the 6-week interval? This patient is young and probably phakic, so I wouldn't want to administer corticosteroids. Before I consider a corticosteroid, I would use one of our newer therapeutic agents.

Dr. Thomas: One challenge we face is insurance-mandated step therapy. Do we continue to cycle through these first-generation agents, which may provide savings on direct health care costs versus going straight to an agent with improved drying capabilities and durability thus providing savings in indirect costs such as missing work, transportation, etc? I don't have the answer, but what we do is often dictated by insurance.

Dr. Finn: Yes, we are often asked to step through each therapy by the insurer, and these decisions are taken out of our hands. In this patient's case, there's not much that can steer us to choosing one agent or another. We have data from the DRCR Network for DME about who may have better outcomes with certain therapies,[9,31] but we have very little data related to macular edema in the setting of BRVO. We're still learning about this. As more and more therapeutic agents are approved, we'll need to assess for imaging biomarkers to see what we can glean to help us make those decisions.

CASE 7: A 62-YEAR-OLD WITH DME AND PERSISTENT INTRARETINAL FLUID

Dr. Finn: Our final case is a 62-year-old man with moderate nonproliferative diabetic retinopathy. The patient has DME with cystic intraretinal fluid, and we start him on bevacizumab injections. After four injections, he is unchanged (Figure 23) and his vision has remained about the same, and he still has persistent intraretinal fluid. We are already treating him monthly. What are the next steps for this patient? Are four injections enough? Should we proceed with the same agent, or should we consider switching agents?

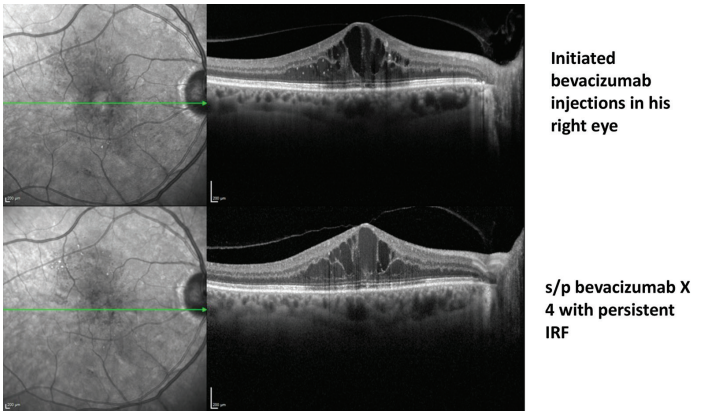

Figure 23. Baseline and follow-up OCT after four bevacizumab injections.

Dr. Thomas: Based on the imaging characteristics, he is a nonresponder. Does he simply need stronger VEGF inhibition? Do we choose a steroid, or do we try one of our stronger agents? I tend to cycle through at least two anti-VEGF agents before using a steroid. At this point, I would switch to either aflibercept 2 mg or faricimab.

Dr. Finn: This patient was switched to faricimab. He had a good response after one injection with decreased intraretinal fluid (Figure 24). He experienced a steady improvement in vision with each injection of faricimab. After seven injections, he had a small amount of persistent fluid just temporal to the fovea, but his VA has improved dramatically from 20/80 to 20/40. That fluid improved dramatically from where it started with only small cystic spaces at this point. Dr. Thomas, what are your thoughts on the hypotheses that faricimab can decrease macular leakage? Is it the Ang-2 effect playing a part, or is it the higher dose of VEGF helping this patient?

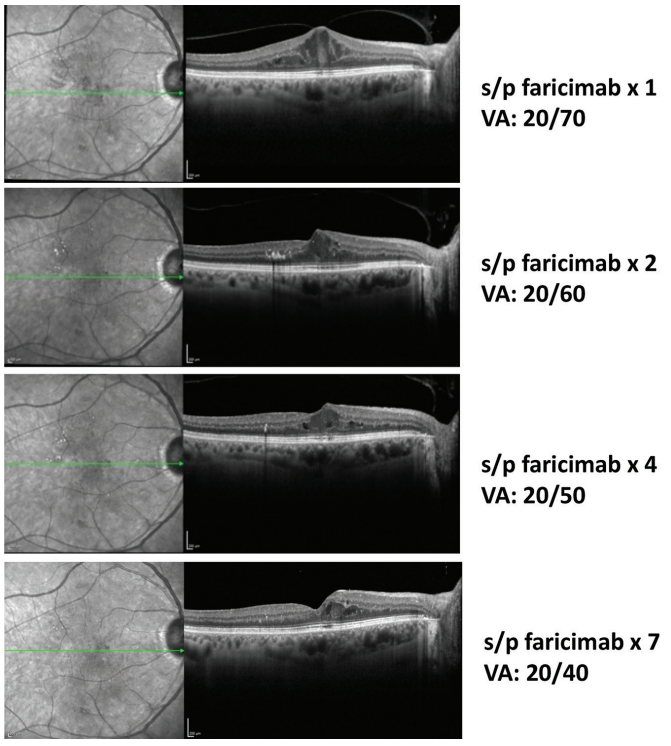

Figure 24. Visual improvements with faricimab.

Dr. Thomas: It's anyone's guess. It would be ideal if we had an organized way to quantify vascular leakage beyond subjective improvement. It's certainly plausible that we're seeing an Ang-2 effect. The other interesting aspect of this case is after the second injection of faricimab, I noticed a small amount of VMT release. It may be unrelated, but some clinicians in our field think that tractional components play a role in persistent edema. In this case, it's probably the swollen retina moving away from the vitreous and not faricimab, but I wonder if that release of traction helped resolve the edema.

Dr. Finn: There are those who hypothesize that VMT in the presence of DME can play a large part in the persistence of that DME. However, patients need to be considered on a case-by-case basis. Ranibizumab was tested in the READ-3 trial to look at DME response in patients with VMA and those patients had an equivalent response to ranibizumab.[32] In some patients, there may be a tractional component from an ERM or VMT that can contribute to that persistent macular edema.

Dr. Thomas: Would you continue to treat this patient monthly to dry or would you extend him and tolerate some fluid if it doesn't worsen?

Dr. Finn: This patient has dramatically improved. I would slowly extend them. As long as their vision is stable, a small amount of fluid is reasonable in these patients, especially if I've been treating them monthly for some time. For young patients, it's a balance between the treatment burden and maintaining a long-term treatment regimen potentially for the rest of their life. ■

1. Almony A. Disease burden of neovascular age-related macular degeneration and diabetic macular edema. *Am J Manag Care.* 2023;29(6 Suppl):S75-S80.
2. Flaxel CJ, Adelman RA, Bailey ST, et al. Age-related macular degeneration preferred practice pattern® [published correction appears in Ophthalmology. 2020;127(9):1279]. *Ophthalmology.* 2020;127(1):P1-P65.
3. Flaxel CJ, Adelman RA, Bailey ST, et al. Diabetic retinopathy preferred practice pattern® [published correction appears in Ophthalmology. 2020;127(9):1279]. *Ophthalmology.* 2020;127(1):P66-P145.
4. Anguita R, Tasiopoulou A, Shahid S, Roth J, Sim SY, Patel PJ. A review of aflibercept treatment for macular disease [published correction appears in Ophthalmol Ther. *Ophthalmol Ther.* 2021;10(3):413-428.
5. Comparison of Age-related Macular Degeneration Treatments Trials (CATT) Research Group, Martin DF, Maguire MG, et al. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. *Ophthalmology.* 2012;119(7):1388-1398.
6. Wells JA, Glassman AR, Ayala AR, et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema: two-year results from a comparative effectiveness randomized clinical trial. *Ophthalmology.* 2016;123(6):1351-1359.
7. Nguyen QD, Brown DM, Marcus DM, et al. Ranibizumab for diabetic macular edema: results from 2 phase III randomized trials: RISE and RIDE. *Ophthalmology.* 2012;119(4):789-801.
8. Glassman AR, Wells JA 3rd, Josic K, et al. Five-year outcomes after initial aflibercept, bevacizumab, or ranibizumab treatment for diabetic macular edema (Protocol T extension study). *Ophthalmology.* 2020;127(9):1201-1210.
9. Cai S, Bressler NM. Aflibercept, bevacizumab or ranibizumab for diabetic macular oedema: recent clinically relevant findings from DRCR.net Protocol T. *Curr Opin Ophthalmol.* 2017;28(6):636-643.
10. Pham B, Thomas SM, Lillie E, et al. Anti-vascular endothelial growth factor treatment for retinal conditions: a systematic review and meta-analysis. *BMJ Open.* 2019;9(5):e022031.
11. Mettu PS, Allingham MJ, Cousins SW. Incomplete response to Anti-VEGF therapy in neovascular AMD: Exploring disease mechanisms and therapeutic opportunities. *Prog Retin Eye Res.* 2021;82:100906.
12. Khanani AM, Patel SS, Ferrone PJ, et al. Efficacy of every four monthly and quarterly dosing of faricimab vs ranibizumab in neovascular age-related macular degeneration: the STAIRWAY Phase 2 randomized clinical trial [published correction appears in JAMA Ophthalmol. 2020 Sep 1;138(9):1006]. *JAMA Ophthalmol.* 2020;138(9):964-972.
13. Heier JS, Khanani AM, Quezada Ruiz C, et al. Efficacy, durability, and safety of intravitreal faricimab up to every 16 weeks for neovascular age-related macular degeneration (TENAYA and LUCERNE): two randomised, double-masked, phase 3, non-inferiority trials. *Lancet.* 2022;399(10326):729-740.
14. Lanzetta P, Korobelnik JF, Heier JS, et al. Intravitreal aflibercept 8 mg in neovascular age-related macular degeneration (PULSAR): 48-week results from a randomised, double-masked, non-inferiority, phase 3 trial. *Lancet.* 2024;403(10432):1141-1152.
15. Dugel PU, Singh RP, Koh A, et al. HAWK and HARRIER: Ninety-six-week outcomes from the phase 3 trials of brolucizumab for neovascular age-related macular degeneration [published correction appears in Ophthalmology. 2022;129(5):593-596]. *Ophthalmology.* 2021;128(1):89-99.
16. Wykoff CC, Abreu F, Adamis AP, et al. Efficacy, durability, and safety of intravitreal faricimab with extended dosing up to every 16 weeks in patients with diabetic macular oedema (YOSEMITE and RHINE): two randomised, double-masked, phase 3 trials. *Lancet.* 2022;399(10326):741-755.
17. Khanani AM, Aziz AA, Khan H, et al. The real-world efficacy and safety of faricimab in neovascular age-related macular degeneration: the TRUCKEE study - 6 month results. *Eye (Lond).* 2023;37(17):3574-3581.
18. Emami-Naeini P, Garmo V, Boucher N, Fernando R, Menezes A. Maintenance of vision needed to drive after intravitreal anti-VEGF therapy in patients with neovascular age-related macular degeneration and diabetic macular edema. *Ophthalmol Retina.* 2024;8(4):388-398.
19. Chi SC, Kang YN, Huang YM. Efficacy and safety profile of intravitreal dexamethasone implant versus antivascular endothelial growth factor treatment in diabetic macular edema: a systematic review and meta-analysis. *Sci Rep.* 2023;13(1):7428.
20. Brown DM, Emanuelli A, Bandello F, et al. KESTREL and KITE: 52-week results from two phase iii pivotal trials of brolucizumab for diabetic macular edema. *Am J Ophthalmol.* 2022;238:157-172.
21. Brown DM, Boyer DS, Do DV, et al. Intravitreal aflibercept 8 mg in diabetic macular oedema (PHOTON): 48-week results from a randomised, double-masked, non-inferiority, phase 2/3 trial. *Lancet.* 2024;403(10432):1153-1163.
22. Genentech. VABYSMO Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761235s000lbl.pdf. Revised January 2022. Accessed May 29, 2024.
23. Regeneron. Eylea HD. https://www.regeneron.com/downloads/eyleahd_fpi.pdf. Revised December 2023. Accessed May 29, 2024.
24. Baumal CR, Spaide RF, Vajzovic L, et al. Retinal vasculitis and intraocular inflammation after intravitreal injection of brolucizumab. *Ophthalmology.* 2020;127(10):1345-1359.
25. Saba NJ, Walter SD. Efficacy, safety, and durability of brolucizumab: an 8-month post-marketing surveillance analysis. *Clin Ophthalmol.* 2023;17:2791-2802.
26. Han YE, Jo J, Kim YJ, Lee J. Factors affecting intensive aflibercept treatment response in diabetic macular edema: a real-world study. *J Diabetes Res.* 2023;2023:1485059.
27. Mayr-Sponer U, Waldstein SM, Kundi M, et al. Influence of the vitreomacular interface on outcomes of ranibizumab therapy in neovascular age-related macular degeneration. *Ophthalmology.* 2013;120(12):2620-2629.
28. Houston, SK, 3rd, et a. Influence of vitreomacular interface on anti-vascular endothelial growth factor therapy using treat and extend treatment protocol for age-related macular degeneration (Vintrex). *Retina.* 2015;35(9):1757-1764.
29. Guymer RH, Markey CM, McAllister IL, et al. Tolerating subretinal fluid in neovascular age-related macular degeneration treated with ranibizumab using a treat-and-extend regimen: FLUID study 24-month results. *Ophthalmology.* 2019;126(5):723-734.
30. Borkar, DS, et al. FARETINA-AMD- Early treatment patterns and outcomes in patients with neovascular age-related macular degeneration initiating faricimab: an IRIS RegistryTM analysis. *Investigative Ophthalmology & Visual Science.* 2023;64(8):2218-2218.
31. Baker CW, Glassman AR, Beaulieu WT, et al. Effect of initial management with aflibercept vs laser photocoagulation vs observation on vision loss among patients with diabetic macular edema involving the center of the macula and good visual acuity: a randomized clinical trial. *JAMA.* 2019;321(19):1880-1894.
32. Sadiq MA, Soliman MK, Sarwar S, et al. Effect of vitreomacular adhesion on treatment outcomes in the ranibizumab for edema of the macula in diabetes (READ-3) study. *Ophthalmology.* 2016;123(2):324-329.

REAL-WORLD CHALLENGES MANAGING RETINAL DISEASES:
NEW SOLUTIONS WITH FEWER INJECTIONS

Release Date: July 2024
Expiration Date: August 2025

INSTRUCTIONS FOR CREDIT

To receive credit, you must complete the attached **Pretest/Posttest/Activity Evaluation/Satisfaction Measures** Form and mail or fax to Evolve Medical Education LLC, 353 West Lancaster Avenue, Second Floor, Wayne, PA 19087; Fax: (215) 933-3950. To answer these questions online and receive real-time results, please go to https://evolvemeded.com/course/2347-supp. If you experience problems with the online test, email us at info@evolvemeded.com. *NOTE: Certificates are issued electronically.*

Please type or print clearly, or we will be unable to issue your certificate.

Full Name_____ DOB (MM/DD): _____

Phone (required) _____ Email (required*) _____

Address/P.O. Box_____

City _____ State/Country _____ Zip _____

License Number:_____OE Tracker Number:_____National Provider ID:_____

*Evolve does not share email addresses with third parties.

DEMOGRAPHIC INFORMATION

Profession
___ MD/DO
___ OD
___ NP
___ Nurse/APN
___ PA
___ Other

Years in Practice
___ >20
___ 11-20
___ 6-10
___ 1-5
___ <1

Patients Seen Per Week
(with the disease targeted
in this educational activity)
___ 0
___ 1-15
___ 16-30
___ 31-50
____ >50

Region
___ Midwest
___ Northeast
___ Northwest
___ Southeast
___ Southwest

LEARNING OBJECTIVES

Did the program meet the following educational objectives?	**Agree**	**Neutral**	**Disagree**
Assess real-world evidence around the efficacy of traditional anti-VEGF agents for the management of serious retinal diseases (ie, diabetic macular edema [DME], neovascular age-related macular edema [nAMD], retinal vein occlusion [RVO])	_____	_____	_____
Evaluate the latest clinical evidence, including real-world efficacy and safety data, around more durable treatments options for serious retinal diseases (ie, DME, nAMD, RVO)	_____	_____	_____
Integrate management strategies that minimize treatment burden in patients with serious retinal diseases (ie, DME, nAMD, RVO)	_____	_____	_____

POSTTEST QUESTIONS

Please complete at the conclusion of the activity.

1. Based on this activity, please rate your confidence in your ability to manage patients with serious retinal diseases (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).

a. 1
b. 2
c. 3
d. 4
e. 5

2. A 48-year-old patient presents to your office for evaluation. He has a history of diabetic macular edema in his right eye that was initially treated with bevacizumab with only mild resolution of cystic intraretinal fluid. He was switched to aflibercept 2 mg with some improvement, but he still has some resistant cystic intraretinal fluid after 4 monthly injections. All of the following are reasonable management options for this patient EXCEPT?

a. Observation without injections
b. Consider intravitreal steroid therapy
c. Consider faricimab
d. Consider high-dose aflibercept (8 mg)

3. A 42-year-old patient with a history of macular edema secondary to branch retinal vein occlusion has been maintained on monthly bevacizumab with adequate drying of the retina. Unfortunately, this patient reaccumulates fluid whenever bevacizumab is extended beyond 4 weeks. He is becoming increasingly frustrated with his treatment burden. All of the following are reasonable management options for this patient EXCEPT:

a. Switch to aflibercept 2 mg
b. Switch to high-dose aflibercept
c. Switch to faricimab
d. Continue bevacizumab

4. A 77-year-old woman with new onset neovascular age-related macular degeneration presents to your office for consultation. She notes 3 weeks of distortion in her left eye. Her OCT shows central subretinal fluid and elevation at the level of the retinal pigment epithelium. Her fluid resolves after 3 monthly injections of intravitreal aflibercept 2 mg, but her subretinal fluid returns after an 8-week injection holiday. Which of the following is a reasonable treatment option?

a. Switch to a more durable anti-VEGF
b. Consider focal laser
c. Switch to bevacizumab
d. Extend treatment with aflibercept 2 mg to 10 weeks

5. A 74-year-old woman with age-related macular degeneration presents to your office with a large, tall pigment epithelial detachment with overlying intraretinal fluid and adjacent subretinal fluid. You decide to initiate intravitreal anti-VEGF therapy. What is an important risk of treatment to discuss with this patient prior to initiation of treatment?

a. Cataract formation
b. Neovascular glaucoma development
c. Retinal pigment epithelium rip development
d. Iris atrophy

6. According to real-world data, which of the following statements about the ability to drive and diabetic macular edema are TRUE?

a. The probability of maintaining driving vision over 4 years is 72%
b. The probability of maintaining driving vision is higher amongst patients who receive a higher number of anti-VEGF injections per year
c. Both A and B
d. None of the above

7. A 72-year-old man presents to your clinic for evaluation with new vision loss in his right eye. Examination of his right eye shows a pigment epithelial detachment with overlying intraretinal fluid and adjacent subretinal fluid. He has previously been treated with four injections of bevacizumab every 4 weeks, with no significant improvement in fluid. Which of the following is a reasonable next step in management?

a. Switch to faricimab
b. Continue bevacizumab
c. Consider dexamethasone intravitreal implant 0.7 mg
d. Switch to pegcetacoplan

8. A patient with a history of diabetic macular edema presents to your office for evaluation. He has macular edema that is inadequately controlled with bevacizumab injections. Fluorescein angiography shows diffuse leakage in the macula. Which of the following is the next best treatment option?

a. Switch the patient to faricimab and schedule a follow-up for 12 weeks after the first injection
b. Switch the patient to faricimab and perform three loading doses 4 weeks apart prior to extending
c. Perform focal laser photocoagulation
d. Start the patient on topical NSAIDs and steroids

ACTIVITY EVALUATION

Your responses to the questions below will help us evaluate this activity. They will provide us with evidence that improvements were made in patient care as a result of this activity.

Rate your knowledge/skill level prior to participating in this course: 5 = High, 1 = Low____

Rate your knowledge/skill level after participating in this course: 5 = High, 1 = Low____

This activity improved my competence in managing patients with this disease/condition/symptom. _____ Yes _____No

Probability of changing practice behavior based on this activity: _____High _____ Low _____No change needed

If you plan to change your practice behavior, what type of changes do you plan to implement? (check all that apply)

Change in pharmaceutical therapy _____
Change in nonpharmaceutical therapy _____
Change in diagnostic testing _____
Choice of treatment/management approach _____
Change in current practice for referral _____
Change in differential diagnosis _____
My practice has been reinforced _____
I do not plan to implement any new changes in practice _____

Please identify any barriers to change (check all that apply):

_____ Cost
_____ Lack of consensus or professional guidelines
_____ Lack of administrative support
_____ Lack of experience
_____ Lack of time to assess/counsel patients
_____ Lack of opportunity (patients)
_____ Reimbursement/insurance issues
_____ Lack of resources (equipment)
_____ Patient compliance issues
_____ No barriers
_____ Other. Please specify: _____

The design of the program was effective for the content conveyed	___ Yes	___ No
The content supported the identified learning objectives	___ Yes	___ No
The content was free of commercial bias	___ Yes	___ No
The content was relative to your practice	___ Yes	___ No
The faculty was effective	___ Yes	___ No
You were satisfied overall with the activity	___ Yes	___ No
You would recommend this program to your colleagues	___ Yes	___ No

Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced through your participation in this activity:

_____ Patient Care
_____ Practice-Based Learning and Improvement
_____ Professionalism
_____ Medical Knowledge
_____ Interpersonal and Communication Skills
_____ System-Based Practice

Additional comments:

_____

_____

This information will help evaluate this activity; may we contact you by email in 3 months to inquire if you have made changes to your practice based on this activity? If so, please provide your email address below.

_____

_____