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# Advancements in AMD: Optimizing Outcomes With Emerging Therapies



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## MODERNOPTOMETRY

# Advancements in AMD: Optimizing Outcomes With Emerging Therapies



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## Content Source

This continuing education (CE) activity captures content from a roundtable discussion.

## Activity Description

This supplement summarizes a discussion on neovascular age-related macular degeneration, including real-world outcomes, new and emerging therapies, and the patient populations that will benefit from these therapies.

## Target Audience

This certified CE activity is designed for optometrists.

## Learning Objectives

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

- **Summarize** the current treatments and barriers to optimizing medical management of patients with diabetic eye diseases and neovascular AMD in clinical settings
- **Discuss** future therapies and their implications for patient outcomes
- **Identify** patients who may benefit from the next generation of retinal disease therapies

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# PRETEST QUESTIONS

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1. Please rate your confidence in your ability to discuss current and future therapies for optimizing medical management of patients with neovascular age-related macular degeneration (nAMD; 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. Please rate your confidence in your ability to identify patients who may benefit from the next generation of retinal disease therapies (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

3. An 86-year-old woman presents to your office for routine evaluation. On examination, you find pigment epithelial abnormalities and large drusen and thickening in the macula of her right eye. Optical coherence tomography (OCT) shows the presence of fibrovascular pigment epithelial detachment (PED), drusenoid PEDs, and overlying cystic intraretinal fluid. Which treatment option is the next best step for this patient?

- A. Intravitreal ranibizumab
- B. Intravitreal aflibercept
- C. Intravitreal off-label bevacizumab
- D. Any of the above

4. Which of the following statements about the correlation between anti-VEGF injection frequency in nAMD and vision is true?

- A. More frequent injections correlates with better vision
- B. Less frequent injections correlates with better vision
- C. Vision is not correlated to injection frequency
- D. We do not have enough data to determine this

5. You are seeing your 75-year-old patient with nAMD for follow-up. He has received 1 year of monthly injections with ranibizumab and is increasingly frustrated with his treatment burden. He is requesting a different treatment modality. Which of the following is a reasonable treatment option for this patient?

- A. Offer photodynamic therapy
- B. Offer treatment with intravitreal corticosteroids
- C. Offer treatment with intravitreal bevacizumab
- D. Offer treatment with the port delivery system (PDS)

6. According to studies, how much higher is the risk of endophthalmitis with intravitreal ranibizumab versus PDS?

- A. One-fold higher
- B. Two-fold higher
- C. Three-fold higher
- D. Four-fold higher

7. Your 75-year-old patient with nAMD calls the emergency triage line. He had a PDS implanted in his right eye 6 months ago and has been doing well. However, he suddenly developed a red eye and foreign body sensation in the right eye a few hours ago. What is the next best course of management?

- A. Reassurance, this is likely due to irritation from the PDS
- B. Reassurance, foreign body sensation is an expected symptom after PDS implantation
- C. Close follow-up, explain to the patient this is likely normal, but if this persists he should be seen in 2-3 weeks
- D. See the patient immediately, as this could be due to device exposure and lead to endophthalmitis if untreated

8. Faricimab is a first-in-class bispecific antibody that blocks \_\_\_\_.

- A. VEGF-A and Ang-2
- B. VEGF-B and Ang-2
- C. VEGF-A and Ang-1
- D. VEGF-B and Ang-1

9. You are seeing your 65-year-old patient who has exudative nAMD and is currently on monthly aflibercept. He is increasingly frustrated with his treatment burden and wants to discuss alternative treatment options. All of the following might be reasonable treatment options for this patient, EXCEPT:

- A. Observation
- B. Switch to intravitreal ranibizumab
- C. Switch to intravitreal faricimab
- D. Discuss implantation of the PDS

10. What molecules are blocked by OPT-302?

- A. VEGF-A and VEGF-B
- B. VEGF-A and VEGF-C
- C. VEGF-C and VEGF-D
- D. VEGF-B and VEGF-D

11. A 78-year-old Caucasian man with a history of nonexudative AMD presents to your office for follow-up. He notes acute vision loss and metamorphopsia in his right eye. Fluorescein angiogram transiting his right eye shows leakage in a classic choroidal neovascularization pattern, and OCT shows drusenoid PEDs and cystic intraretinal fluid. What is the best management of this patient?

- A. Start intravitreal steroid therapy
- B. Start intravitreal anti-VEGF therapy
- C. Start oral steroid therapy
- D. Perform photodynamic therapy

12. You are evaluating your 67-year-old patient who has exudative macular degeneration. He has been on monthly aflibercept injections for 13 months, but still has persistent fluid and subretinal hemorrhage. All of the following are reasonable treatment options, EXCEPT:

- A. Switch to intravitreal faricimab
- B. Switch to higher dose aflibercept injections (off-label)
- C. Switch to more frequent aflibercept injections (off-label)
- D. Discontinue anti-VEGF therapy and consider corticosteroid therapy



# ADVANCEMENTS IN AMD: OPTIMIZING OUTCOMES WITH EMERGING THERAPIES

**T**he development of anti-vascular endothelial growth factor (VEGF) therapy was a major advance in treating common retinal diseases, particularly neovascular age-related macular degeneration (nAMD). Ranibizumab, aflibercept, and bevacizumab were the first generation of anti-VEGF agents, which continue to have excellent safety and efficacy. We are very familiar with and comfortable using these agents. However, they exact an extremely high treatment burden, which can often translate into worse visual and anatomic outcomes in the real world compared to clinical trials. Our field has been trying to bridge this efficacy gap by exploring alternative disease pathways or modes of drug delivery. Recently, two novel, durable therapies were approved for the treatment of nAMD: faricimab and the port delivery system (PDS). Our panel of experts recently convened to discuss the need for such therapies and the clinical trials that led to their approval. Most importantly, we discussed how optometry and retina can collaborate to alleviate the treatment burden and ensure these therapies improve real-world outcomes.

— Carl D. Regillo, MD, FACS, Program Chair

## FIRST-GENERATION ANTI-VEGF THERAPIES AND REAL-WORLD OUTCOMES

**Q | Dr. Regillo:** What are our current treatments for nAMD?  
**Roger A. Goldberg, MD, MBA:** Intravitreal anti-VEGF injections are the current mainstay of treatment. For almost a decade, ranibizumab, aflibercept, and off-label bevacizumab were the only commercially available agents. They all inhibit VEGF, which is the key driver of retinal neovascularization and leakage of the blood vessels of the choroidal neovascular membrane, which is the hallmark of nAMD. In 2019, brolucizumab was approved; although its use was relatively short-lived due to reports of intraocular inflammation (IOI) and safety concerns.<sup>1</sup> For now, it remains a niche player. Ranibizumab, aflibercept, and off-label bevacizumab are injected every 1 to 3 months depending on disease characteristics and the patient's needs. While the pivotal trials used monthly or 2-monthly dosing regimens, most of us now use the treat-and-extend (T&E) algorithm for nAMD. This involves monthly injections until patients are dry on optical coherence tomography (OCT) scans, ie, no intraretinal or subretinal fluid. If we can achieve this, we start to extend the interval—I typically use 2-week steps, ie, extend to 6 weeks, and if they remain dry, then extend to 8 weeks, and so on. If I see fluid reappear at any point,

it's an indication that the durability of that agent is starting to wane, and I'll shorten the interval back down.

**Q | Dr. Regillo:** I want to ask our optometry colleagues – what do you hear from patients with nAMD about the tolerability of these therapies? What would they want to see improved in the way we manage nAMD?

**Reecha Kampani, OD:** The number of visits is a big burden for patients. In the beginning, at least, we need monthly visits to gauge disease progression. After this phase, visits can be spread out; however, the logistics of attending regular appointments can still be burdensome. A lot of patients don't like getting injections, but they know they must endure them. There are a lot of other factors that aren't related to the disease itself, eg, dealing and coping with vision loss and depression.

**Mohammad Rafieetary, OD:** Many of these patients must rely on family members or caregivers to take them to their visits. Some may live in assisted living and have limited schedules that affect their follow-up care. Lapses in follow-up and treatment negatively impact their outcomes, as we all know. However, overall, I think patients with nAMD have better compliance with their follow-up care than patients with diabetic eye disease. The poorer adherence in the latter is partly due to the stability of their insurance coverage, work schedule, care of comorbidities, etc.

**Rebecca Miller, OD:** My background is in cataract surgery. Usually after surgery, the patient's vision is much improved, and he or she is very happy. When I then refer patients to a retina specialist for nAMD care, oftentimes they'll return and say, "I'm not getting better." I have to explain that our goal is to prevent worsening of disease and achieve stability, rather than aim for improvement, which can be challenging for the patient to hear, but helpful to set expectations.

**Dr. Rafieetary:** I would recommend all patients undergoing cataract surgery have a preoperative OCT. If or when macular disease is discovered after cataract surgery, it can be frustrating for a patient who expected better postoperative vision.

**Dr. Miller:** I completely agree. Obtaining a macular OCT prior to cataract surgery is standard of care for our practice. It's incredible



how much pathology we pick up. The OCT can often “see” the earliest signs of nAMD, which ensures patients get treatment quickly. Based on the patient’s response to treatment (most commonly, injections) we make the best possible intraocular lens (IOL) suggestion by working with our retina specialists.

**Dr. Regillo:** You’ve all raised great points. Patients tolerate the injections but don’t like them and prefer not to get them. Well over half of these patients are accompanied by family, friends, or other caregivers, whether due to comorbidities or transportation issues, which poses a burden for everyone. As a chronic disease, nAMD requires lifelong management and all these things can take a toll, leading to depression in many of our patients.

The anti-VEGF clinical trials showed visual gains in the “induction phase” and maintenance for the first 2 years. There weren’t appreciable differences in efficacy between the three anti-VEGF agents for nAMD, and durability and drying ability were relatively comparable. Most people respond to these agents, and importantly, the earlier we catch the disease, the better the results.

**Q | Dr. Modi, can you shed some light on the real-world outcomes, beyond these first 2 years?**

**Yasha Modi, MD:** Looking at all the clinical trials, we must remember that a select group of patients are enrolled. They have a narrow window of vision, typically 20/40-20/400, and are willing to come in monthly for intensive imaging and spend double the amount of time in a clinical office relative to patients undergoing standard-of-care therapy. On average, patients gain 7-10 letters in these trials. They logged around 12-13 visits a year, with monthly checkups even if they were only dosed every 4-12 weeks.

Real-world studies look at the larger population and the number of injections received.<sup>2-5</sup> Uniformly, we saw that patients came in less frequently and, on average, received three to five injections. Comparatively, in clinical trials, they received 12-13 injections on a monthly dosing regimen or eight to nine injections, if the interval was longer, in that first year. Unfortunately, visual outcomes reflected this lower frequency of visits and injections and were worse. From baseline, we didn’t see the typical 5-10-letter gain in visual acuity. Rather, there was a flatline and after 1 year, their visual acuity was worse. In the retina community, we struggle with distinguishing between underevaluation due to fewer or missed visits (remember, classical PRN treatment involves monthly evaluations) versus undertreatment due to less frequent anti-VEGF administration. While we still can’t answer that, we know that if patients were encouraged to visit us more frequently, we could affect better long-term visual outcomes. Home OCT monitoring is an interesting pipeline technology that could facilitate more personalized treatment intervals and minimize visit burden; however, for now, we need more consistency in patient follow-ups.

**Dr. Regillo:** The anti-VEGF therapies we’ve been using over the years are highly effective, but they’re not very durable. The average durability is 8 to 9 weeks, with a range of 4 to 12 weeks.

Even with the T&E regimen, most of us arbitrarily stop extending at 12 weeks. Some patients could probably be further extended; however, studies indicate that we’ll see an exponential rise in recurrence rates and setbacks if we push the treatment interval with these drugs much beyond 12 weeks.

With a mean durability of 8 weeks, ideally, we should be averaging six injections during the maintenance phase. Of course, we don’t, and therefore vision declines over time, on average. The CATT trial showed that relative undertreatment was a setup for fibrosis and, consequently, decreased vision.<sup>6</sup> Atrophy also becomes a contributor to visual decline in some of our patients with nAMD undergoing treatment over time. At this time, that is not treatable.

**Dr. Goldberg:** What’s interesting is that Ciulla et al showed this undertreatment in the first year.<sup>3</sup> There is a clear correlation between the number of injections and the vision gained, ie, more injections in the first year led to higher vision gains. These aren’t long-term outcomes or vision loss due to fibrosis and atrophy. This may be an area where optometrists, general ophthalmologists, and retina specialists could collaborate more efficiently. Retina specialists may not feel like patients are undertreated, but we don’t see the patients that we don’t see. We primarily see our monthly or adherent patients. Occasionally we may see patients who have missed several appointments over the pandemic, and now present with vision loss due to active disease. It is remarkable, however, that undertreatment happens even in the first year.

**Dr. Regillo:** In the real world, we appear to undertreat both early and later on in the course of therapy. That first year is so crucial to getting optimal visual acuity improvement and then, in subsequent years, it is mainly about maintaining those early visual gains. Our optometry colleagues can certainly be valuable in helping us motivate our patients to keep coming to the office to get the treatments needed to achieve the best long-term visual outcomes. That’s a key difference between clinical trial and real-world patients. Clinical trial patients are more willing and able to keep up with frequent visits and treatments and, ultimately, derive the best results from a course of anti-VEGF therapy. That being said, I am still surprised to see how much relative undertreatment there is in practice.

**Dr. Rafieetary:** It is somewhat unfair to compare a real-world patient with a clinical trial patient. Clinical trial staff are diligent about capturing patients within the windows they need to be seen. If a patient cannot attend scheduled appointments for any reason, the clinical trial staff ensure they are seen the next day. However, in the real world, if an appointment is missed, the patient may receive the next available slot, eg, a month and a half later, because the receptionist may not understand the gravity of the disease. That’s part of the problem in comparing these patient populations. I’ve always thought of clinical trial patients as high rollers in a casino—they have handlers. However, most real-world



patients are handled by general clinic staff who are not familiar with every case situation.

**Dr. Regillo:** That's right. There's a completely different algorithm for each.

## EMERGING THERAPIES FOR nAMD

**Dr. Regillo:** We know the major unmet need with anti-VEGF therapies is for greater durability. Fortunately, there's been progress for the treatment of nAMD with the recent FDA approval of the PDS in October 2021, and faricimab in January 2022.

**Q** | The PDS is approved for patients who have had at least two anti-VEGF injections, based on the phase 2 and 3 trials. Can you tell us about the PDS?

**Dr. Goldberg:** The PDS is a surgically implanted reservoir placed into the sclera, underneath the conjunctiva and covered by Tenons. It's hidden underneath the upper eyelid. It can be refilled every 6 months with a high concentration of ranibizumab, which is designed to be released into the vitreous cavity over an extended period. In the phase 2 LADDER trial, patients were allowed to go longer than 6 months but in the phase 3 ARCHWAY study, which led to approval, patients were refilled every 6 months.<sup>7,8</sup> Compared to monthly ranibizumab injections, the results were excellent. The visual acuity and anatomic (central subfield thickness; CST) outcomes were comparable. Not surprisingly, they had a different set of safety issues associated with the surgical procedure. The LADDER study demonstrated issues with vitreous hemorrhage during the time of implantation. Once they revised the surgical technique, the incidence of vitreous hemorrhage significantly decreased. Most of the acute postoperative complications were conjunctiva-related, primarily erosion of the conjunctiva and exposure of the septum used to refill the reservoir. If left unaddressed, this could lead to IOI. There is a warning on the label which specifies a three-fold higher risk of endophthalmitis compared to monthly intravitreal ranibizumab injections.<sup>9</sup> However, with good conjunctival management, most of these complications can be effectively mitigated.

**Dr. Regillo:** The PDS also requires special training for the implantation. There is a lot of nuance to the surgical procedure. Although not many have been implanted yet in practice, it's coming and we're relying on every eye care provider to recognize the potential problems associated with the device. The per patient rate of endophthalmitis is about 2%, which is higher than a course of intravitreal injections.<sup>8</sup> Our practice staff must be aware that if a patient with the PDS complains of a red or irritated eye, discharge, or foreign body sensation at any time, even long after the surgical implantation, this could be due to device exposure. As this is a setup for endophthalmitis, such symptoms should be promptly evaluated. The PDS is underneath the eyelid in the superotemporal quadrant, so the examiner should make sure to lift the lid and examine the area.

Otherwise, conjunctival issues like erosion or retraction, which need surgical repair, will be missed.

**Dr. Rafieetary:** One factor affecting the rollout of the PDS is the cost of device to the ambulatory surgical centers and insurance coverage. However, an advantage of the PDS is the sustained release of ranibizumab, versus the peaks and troughs of monthly injections.<sup>8</sup>

**Dr. Regillo:** Absolutely. We discuss the safety issues for good reason—they're unique, new problems. However, we now have 4-year data with the PORTAL study extension program.<sup>10</sup> Patients who had a baseline VA of 20/40, having already had anti-VEGF injections before getting the device, can maintain this visual acuity with a stable OCT even after 4 years with the device. It's amazing. No previous nAMD study has shown this degree of disease control for this long of a time frame. This is the potential answer to those poor long-term visual outcomes seen in the real world.

**Dr. Goldberg:** This durability will be the key to offsetting the increased risk of PDS implantation. The open-label HORIZON study, which followed patients in the ANCHOR and MARINA trials, for 2 more years demonstrated that vision returned to baseline levels at 4 years.<sup>11</sup> The real-world SEVEN-UP study then followed these patients for another 3 years and most of them actually lost vision.<sup>12</sup> It will be interesting to see whether the PDS can prevent fluid recurrence and maintain vision in the longer term.

**Dr. Kampani:** Invariably, safety remains an issue for the PDS. However, over the years, we will see these patients for various other reasons. If we take a more collaborative approach, communicate with each other, and monitor them closely, we can keep these patients at very low risk.

**Dr. Miller:** I completely agree. A 6-month refill means lower cost and time burden for patients, caregivers, and physicians. It can make access to care a lot easier and presents an opportunity for collaboration. We could prioritize high-risk patients for the surgeon's office and divide imaging between the OD and MD office. Maybe ODs take on more routine OCT monitoring and develop communication systems to facilitate this division of burden. I was excited to learn about the PDS, and I look forward to more retina specialists integrating the treatment. From the referring doctor's side, it seems like a home run for the patient and the retina specialists.

**Dr. Regillo:** Our retina colleagues may be hesitant because of the potential complications and higher rates of infection. There's a lot of comfort with performing intravitreal injections. However, most patients with the PDS prefer it to monthly injections,<sup>8</sup> even if they still need to come to the office for frequent checkups. This collaboration with optometry will be very important for continued success with the PDS. You can help us monitor disease activity, conjunctival integrity, and identify whether





retreatment may be needed. It is an exciting technology and with additional modifications and enhancements in the surgical approach, we can reduce complications and improve the safety profile. Granted, these complications can be perioperative or occur years later in some of our patients. This is another source of hesitancy amongst some of our retina colleagues. There is the concern that the patient will become less adherent to monitoring visits because they know they likely won't require retreatment for at least 6 months.

**Dr. Modi:** It's worthwhile to extrapolate lessons learned about long-term inflammation control with local devices. In uveitis, long-term follow-up is 10 to 15 years and those receiving long-term local therapies (fluocinolone acetonide intravitreal implant), did worse over 7 years relative to those receiving systemic therapies.<sup>13</sup> The rationale for this outcome was undertreatment in the local therapy arm from not replacing the implant. To avoid a similar outcome in the retina space, it's important to realize that the PDS doesn't absolve patients of regular follow-up. As retina specialists, we'll also have to learn when to refill and develop monitoring strategies to determine this interval in the real world. Long-term compliance is an issue that requires scrutiny.

**Dr. Rafieetary:** On the one hand, not all patients require lifelong anti-VEGF therapy. On the other hand, for many that do, long-term treatments such as the PDS are a reasonable option. Implantable devices such as IOLs and glaucoma shunts have been around for decades and are well-tolerated. For patients, this is a relatable concept when discussing the PDS as a treatment option.

**Dr. Kampani:** Exactly. We're used to watching these patients regularly, examining blebs, and monitoring for infection. As soon as I know a patient has had a surgical procedure, I'm always on high alert. I pay attention to that red eye right away. As long as the communication is on point, we can sort that out.

**Dr. Regillo:** I agree. This will help the adoption.

**Dr. Goldberg:** In some parts of the country, an optometrist is often much closer to the patient who may need to travel very long distances to see a retina specialist. The PDS lends itself very nicely to a collaborative approach between retina and optometry here. They can do a lot of the follow-up and routine monitoring.

**Dr. Regillo:** Being truly sustained release means that when we get any fluid recurrence, we know that it's not likely to worsen rapidly, as it might between bolus intravitreal injections. We're used to the latter mindset. However, there is more latitude with the PDS. For example, an optometrist who is monitoring such a patient doesn't necessarily need to get the patient to see the retina specialist the next day for a refill or supplemental injection. The patient may be able to wait 2 to 3 weeks or so.

**Dr. Rafieetary:** For patient education, I find it useful to compare the PDS to insulin pumps, a device that helps avoid repeat injections.

**Dr. Regillo:** Good point. What's more, pump users usually have better HbA1C levels. It's great technology, truly novel.

**Q | Dr. Modi, can you tell us about the other new therapy that was approved—faricimab? Most of us consider it a second-generation anti-VEGF, but it's more than that.**

**Dr. Modi:** Faricimab is a first-in-class bispecific antibody that blocks VEGF-A and angiopoietin-2 (Ang-2). In the normal retina, Tie-2 stabilizes endothelial cells; however, in the ischemic or inflamed retina, there are higher levels of the Tie2 antagonist, Ang-2. This leads to instability and leaky blood vessels. With faricimab, we not only block the VEGF pathway but also counteract the actions of Ang-2 to improve endothelial stability.

The phase 3 TENAYA and LUCERNE trials led to FDA approval for faricimab for the treatment of nAMD.<sup>14</sup> The trials had a unique design whereby patients were extended between 8-16 weeks depending on how they fared with monthly injections.<sup>15</sup> Along with the HAWK and HARRIER trials, 16 weeks is the longest interval that has been trialed and succeeded.<sup>16</sup> Faricimab was demonstrated to be noninferior to aflibercept administered every 8 weeks, which is impressive given the longer treatment intervals for the majority of patients on faricimab.<sup>14</sup> The CST reduction, which is the primary parameter guiding re-treatment decisions, was also improved with faricimab compared to aflibercept, at some timepoints. This agent is not only durable but also has anatomic efficacy. Faricimab also demonstrated similar levels of safety as aflibercept.<sup>14</sup> We've seen reports of occlusive retinal vasculitis with brolocizumab<sup>1</sup> and now have a heightened awareness of this with new agents, but no such episodes were reported in TENAYA or LUCERNE.

**Dr. Regillo:** The faricimab phase 3 program is the largest set of nAMD clinical trials to date, so we're confident in the data. There were slightly higher rates of IOI in the faricimab arms compared to aflibercept; however, these differences were small. Faricimab has only been available for a few months. Have you started using it? Where do you think it fits in?

**Dr. Modi:** The interval extensions in TENAYA and LUCERNE were 4 weeks, which is quicker than what we might practice in the real world, ie, 1 to 2 weeks. Four weeks seems like a leap of faith, but we now have some very good phase 3 data to support this.

In choosing patients who might receive faricimab, I would first try those who aren't doing well on aflibercept or cannot be extended beyond 4 to 8 weeks but want a longer extension. It's interesting that in clinical practice, we usually try these new agents on patients who have previously received therapy. However, TENAYA and LUCERNE both enrolled treatment-naïve patients. Once we start learning more about new therapies and see how they stack up against the current stalwarts, we can expand the patient pool.





**Dr. Rafieetary:** Once again, insurance coverage also plays a big role in the delivery of various agents.

**Dr. Regillo:** Exactly. That tends to slow the adoption of any therapy because patients want to be fully covered or minimize their out-of-pocket expenses. It does take a few months to get those systems in place and for insurers to recognize the product. The J-code should come sometime this year and then it'll be logistically easier to prescribe. Dr. Modi made a great point about the accelerated extension. I know I'll consider that, especially if we can achieve less frequent treatment faster, and with equivalent outcomes.

**Dr. Kampani:** Neither faricimab nor PDS are on our formulary yet; however, I'm excited for them. I often wonder whether patients who are doing well on a first-generation anti-VEGF agent could be doing better or just how much we could extend that treatment interval.

**Dr. Regillo:** Some of our colleagues are only willing to let patients go 2 to 3 months between visits. Part of the reason for this is that we're also checking the fellow eye, which often has dry AMD and is at higher risk of converting to nAMD. We know we achieve better outcomes when we catch this conversion from dry to wet AMD early. This is where comanagement and collaboration is useful to help keep a watch on that fellow eye, if there is any dry AMD.

**Dr. Kampani:** That was one of my concerns with the PDS. Patients might think it's a free pass, and new changes or progression may be missed along the way if follow-up visits are spaced too far apart.

**Dr. Rafieetary:** This is where we might leverage not only the Home OCT device for the treated eye but also the ForeseeHome device for the fellow eye, to make sure it doesn't progress to advanced AMD.

**Dr. Regillo:** We'd all like to see more ForeseeHome use for eyes with dry AMD, especially the fellow eyes. However, it is a little challenging and time consuming for patients. It requires more patient motivation, and we've struggled with that.

**Dr. Miller:** I think retina specialists may be quicker to adopt a familiar treatment pattern than a new surgical procedure. I'm optimistic about what this can mean for patient care. I do agree that we don't want patients to develop a false sense of security that can lead to a decline. Anything that can extend the treatment burden but keep patients in the office for close monitoring is ideal.

**Dr. Goldberg:** Obeid et al showed that patients with proliferative diabetic retinopathy, who were treated with panretinal laser

photocoagulation and given longer follow-up, had higher rates of loss-to-follow-up than those treated with anti-VEGF injections and given shorter follow-up.<sup>17</sup> It will be interesting to see how these longer-acting therapies for nAMD will fare.

**Dr. Rafieetary:** We always counsel patients with longer treatment intervals to alert us when their vision deteriorates. We also explain that stable vision doesn't always equate to stable disease. This may be one of the reasons for loss-to-follow-up. Your eyesight should not be the measuring stick by which you decide not to keep up with follow-up appointments.

## THERAPEUTICS THAT COULD BE AVAILABLE IN THE NEXT FEW YEARS

**Dr. Regillo:** There are a few therapies in the pipeline that I want to discuss. Aflibercept is being tested at a high dose of 8 mg in phase 3 studies. The phase 2 CANDELA trial hinted at better drying and durability.<sup>18</sup> Whether it will be comparable to faricimab is yet to be determined. Even when the phase 3 PULSAR data are available, we won't really know until we have a true head-to-head study.<sup>19</sup>

OPT-302 is a unique anti-VEGF agent because it's a fusion protein that blocks VEGF-C and VEGF-D. It won't be a monotherapy; it'll be injected in combination with either ranibizumab or aflibercept. It's currently in phase 3 trials—in SHORE, the comparator and combination treatment are ranibizumab, and in COAST, it's aflibercept.<sup>20,21</sup> The goal here is not added durability, but rather better vision outcomes. Admittedly, this is a high bar, and we might need to wait at least another year before we see any data.

KSI-301 is an anti-VEGF-A monoclonal antibody covalently bound to an inert, large biopolymer, which effectively doubles its half-life in the vitreous cavity. While the large open-label phase 1 study demonstrated promising results, the phase 3 data recently showed that KSI-301 did not meet its primary endpoint of being noninferior to aflibercept (dosed on-label).<sup>22</sup> Its durability was really pushed to the limit; dosed every 3 to 5 months. Perhaps more frequent dosing could have led to a different outcome.

**Dr. Rafieetary:** Do you think that pushing for durability sacrificed efficacy?

**Dr. Regillo:** Most patients did well when dosed every 5 months.<sup>22</sup> It is certainly impressive in its durability. However, it may not be good enough for high-need patients, either in terms of higher anti-VEGF levels or dosing frequency. I presented the data from the phase 3 trial at the ARVO meeting in May 2022. The question remains: is KSI-301 still in the running for a future therapy?

**Dr. Goldberg:** I think KSI-301 has a tough road ahead. For one, it's anti-VEGF-A monotherapy, which is not a new mechanism of action. It needs to be a better drying agent or more durable to compete in this already crowded space. Even



in the Phase 1 open-label studies, it looked to be a slightly weaker drying agent, but with hints of longer durability. Do we need another 1- to 3-month anti-VEGF-A agent? I don't think there's a lot of enthusiasm.

**Dr. Regillo:** To me, KSI-301 is like a sustained-release drug, which works well for many, but maybe not all patients, at least in an extended-dosing fashion. It is reminiscent of the results we're seeing with tyrosine kinase inhibitors (TKI), such as EYP-1901 or OTX-TKI. These are small molecule-containing sustained-delivery biodegradable implants. The phase 1, and some phase 2, data suggest good anti-VEGF-like effects, which is reasonable given that TKIs can block the VEGF receptor, and good durability in some patients for around 6-9 months.<sup>23,24</sup> However, it may not be powerful enough to control disease in all patients much beyond 4 months. It's still early in the course of the TKI clinical trials and so more information is coming.

**Q** | Let's delve into the two gene therapies because I think these are intriguing. Dr. Modi, what can you tell us about RGX-314?

**Dr. Modi:** RGX-314 is an adeno-associated viral (AAV) vector containing a gene encoding for a ranibizumab-like molecule, administered via either the subretinal or suprachoroidal route (both in testing). To inject it subretinally, we would perform a vitrectomy and then administer the gene therapy via a 38-gauge cannula under the retina. Once injected, it would initiate local production of an anti-VEGF molecule to control the disease. The dose-escalating phase 1 study enrolled patients receiving frequent anti-VEGF therapy and administered one dose of RGX-314.<sup>25</sup> They then looked at the number of rescue treatments that were required. In the high-dose arms, very few rescue injections were needed. As a proof-of-concept, we now know gene therapy works! However, some aspects of the treatment are still being investigated. For example, will this be a one-and-done treatment where patients will never require another injection? What are the AAV-associated inflammatory complications that may occur?

**Dr. Regillo:** As with the PDS, RGX-314 also aims to maintain steady levels of anti-VEGF therapy. However, this may or may not suffice for all patients and supplemental injections may be needed. We have over 3 years of data for the subretinal approach. There were some safety issues with peripheral subretinal pigmentary alterations at the high doses with macula involvement and vision loss in one patient. Surgical modifications have since been made and this latest technique for subretinal delivery is now in phase 3 and should be safer.<sup>26,27</sup> The suprachoroidal approach is in phase 2 now,<sup>28</sup> and it looks promising with both efficacy and safety, but it's still early in the clinical trial.

**Dr. Rafieetary:** Dr. Modi, as a uveitis specialist, do you think there's a difference between the delivery methods, based on their immunoprivileged status?

**Dr. Modi:** Patients receiving intravitreal gene therapy generally have higher rates of inflammation than those receiving subretinal therapy. The suprachoroidal approach allows delivery without a surgical procedure and could have an even better safety profile. Inflammation also depends on the viral vector that's utilized.

**Q** | **Dr. Regillo:** Speaking of intravitreal gene therapy, Dr. Goldberg, what can you tell us about ADVM-022?

**Dr. Goldberg:** Yes, it's an AAV vector that encodes an aflibercept-like molecule. It's also a single intravitreal injection, which has the advantage of being familiar, comfortable, and highly consistent for retina specialists. We know exactly where 100% of the dose is injected. However, with the subretinal approach, there may be surgical complications and some reflux from the subretinal space into the vitreous cavity. Similarly, with suprachoroidal injections, there can be reflux into the subconjunctival space. Clinically, we cannot be certain we're delivering the exact dose.

The phase 1 OPTIC study had very promising results and has shown up to 2 years of durability in previously treated patients with nAMD.<sup>29</sup>

Two different doses were tested along with different regimens of steroid prophylaxis or treatment to control inflammation issues that were prevalent throughout the study. The company halted a similar program in diabetic macular edema due to more serious safety signals that occurred in this patient cohort. Whether this was related to the viral vector dose, steroid

Courtesy of Reecha Kampani, MD

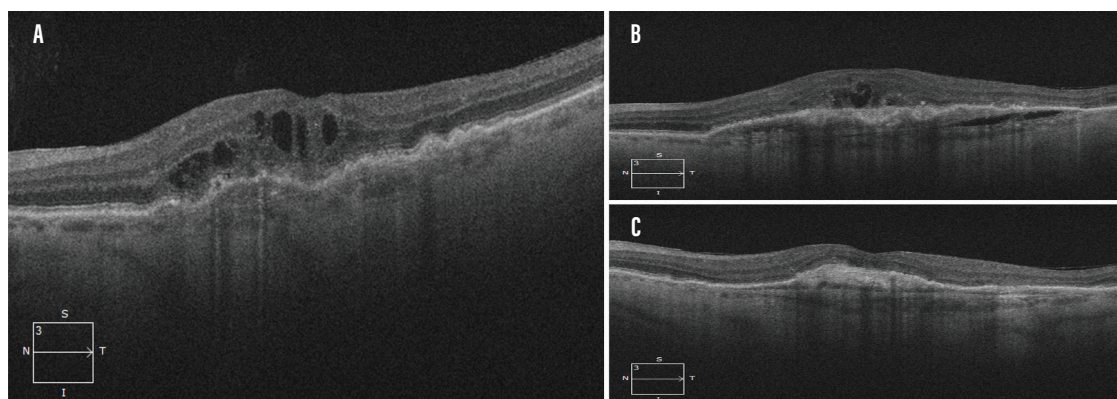


Figure 1. Presenting OCT image of left eye of a 78-year-old patient with 20/200 VA and metamorphopsia (A). OCT image taken prior to fourth aflibercept injection, at 20/70 VA (B). OCT image taken prior to 13th aflibercept injection, at 20/40-2 VA (C).



regimen, or inherent differences in the pathologies of diabetic retinopathy versus nAMD is being investigated. For the phase 2 nAMD program, they are testing lower doses and instituting an aggressive anti-inflammatory approach to strike a balance between generating enough anti-VEGF molecules and reducing the risk of sustained inflammation.

**Dr. Regillo:** The inflammation was dose-dependent in these programs and lower doses are now being used. The intravitreal gene therapy worked well in many of the patients, but patients often needed one or two daily steroid eyedrops to keep inflammation in check. Would it be a viable, long-term approach for patients?

**Dr. Kampani:** I am concerned that we're treating one problem but potentially causing another, eg, intraocular pressure (IOP) increases for steroid-responders. There could be a trade-off in burdens. If there were a lower risk, that would be ideal.

**Dr. Rafieetary:** It depends if there's a real need for it. If they don't comply with the eyedrops, what are the consequences of that? Would it be detrimental? From a long-term standpoint, we maintain several patients on long-term steroids, on a case-by-case basis. Adverse effects are always a concern, but a risk/benefit assessment dictates our decisions.

**Dr. Miller:** The majority of the patients who I manage are comfortable using eyedrops as a treatment modality. I acknowledge that strong steroids increase IOP concerns with glaucoma and, along with long-term inflammation management, these are significant issues. However, looking for the sunshine in the rain clouds, many of these patients are more mature and potentially dealing with dry eye. Steroids can be helpful for managing dry eye symptoms. If we had a milder corticosteroid medication placed in a comfortable vehicle, that also hydrated the ocular surface, we may not see the IOP spikes that are more common with stronger steroids. Patients may even appreciate the eyedrops. We do try to minimize the burden of every treatment and disease course, but with some of these new pathways, we can get creative.

**Dr. Regillo:** There will most likely be patients with nAMD who could be good candidates for each of these approaches. It's exciting to see all of these different choices and know that patients will have more options. It will be hard to choose between them.

**Dr. Rafieetary:** It's Darwinian—survival of the fittest. Attrition by either expense, misuse, or efficacy. But it is good to have options.

## CASE 1: HITTING THE CEILING

**Dr. Kampani:** This is a case of a 78-year-old white man I comanage with one of our retina specialists. His right eye has

been severely affected by nonexudative AMD and geographic atrophy. In February 2021, his VA was 20/25 in his left eye, but he had a history of nonexudative AMD, with high-risk characteristics of soft confluent drusen. He presented 2 months later with acute vision loss at 20/200 and metamorphopsia (Figure 1A). He received his first aflibercept injection and showed a great response at the 4-week follow-up, with a VA of 20/50. Center thickness was much improved, but a pigment epithelial detachment (PED) was developing. He continued to receive monthly aflibercept injections, but VA fluctuated and decreased to 20/70 in July (Figure 1B). He was given a fourth aflibercept injection, and we recommended a strict monthly schedule. By September, the patient regained some vision at 20/50+2 and was up to aflibercept number eight. We continued with monthly dosing and by January 2022, the patient had stable vision. After the 10th injection was given, we considered extending him to 5 weeks. However, we took a conservative approach, given his right eye was 20/200 eccentric, and maintained monthly dosing. His most recent OCT in April 2022 showed good disease control and VA improvement to 20/40-2 (Figure 1C).

Overall, he's received 13 aflibercept injections and is responding well, even though he hasn't achieved preconversion visual acuity. However, we haven't been able to extend his intervals for over 1 year. Going forward, my concerns would be tachyphylaxis and/or the ceiling effect, ie, will additional injections have an effect? That's where these new therapies and delivery systems become interesting. We could take the safe approach and start him off on high-dose aflibercept before considering a new therapy. This patient is really motivated to attend clinic visits. He comes in for monthly injections, and sometimes even more frequently if he wants to track his vision. He wants to try to obtain his driver's license, he's dealing with occasional depression, and has a huge treatment burden. This case highlights the need for new treatments, especially for patients like this who are motivated but are hitting these roadblocks.

**Dr. Regillo:** He's a frequent flyer, a good response but a high need for treatment, who may or may not be extendable beyond 4 to 5 weeks with aflibercept. About 20-25% of our patients hit this 4- to 6-week roadblock, and this is supported by published T&E studies. We know that switching to ranibizumab or bevacizumab won't produce a vastly different result. Brolucizumab is on the table as an option, but the higher IOI risk may not be acceptable for this patient. He's certainly very compliant, but my impression is that he would be a good candidate for one of the newer approved therapies.

**Dr. Kampani:** My only concern with the PDS for him is his comorbidities, ie, diabetes, cardiovascular issues, and the higher risk of endophthalmitis. Moreover, his right eye has poor vision, which only increases the risk for surgery on the left eye.



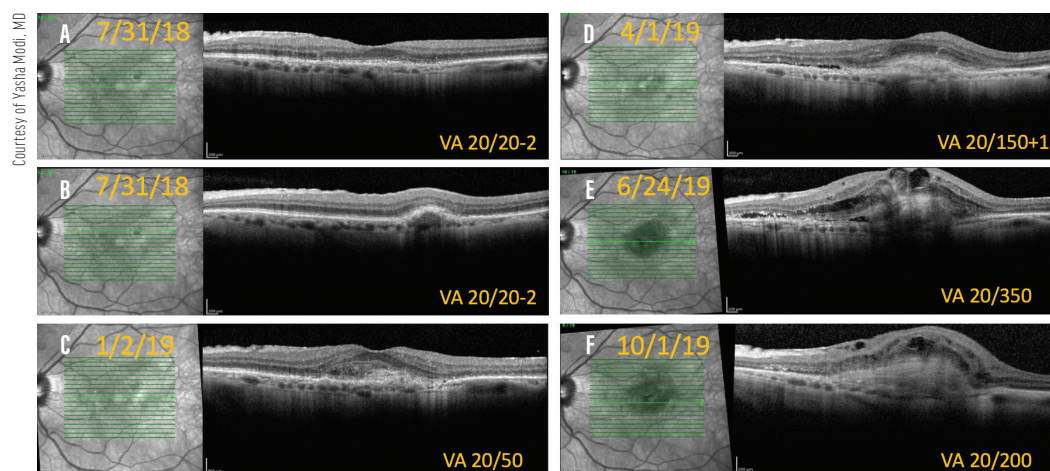


Figure 2. OCT images demonstrating early development of pigmental epithelial detachment and SHRM (A, B). OCT images showing worsening SHRM in the setting of receiving anti-VEGF therapy (C, D). OCT image showing intraretinal and subretinal fluid with associated hemorrhage—type 3 neovascularization (E). OCT image showing intraretinal hemorrhage and fluid over a disciform scar (F).

**Dr. Regillo:** He may not even want surgery or to take on potential risks. Faricimab would be a great option. If not 12 to 16 weeks, you could at least get an 8-week interval.

**Dr. Kampani:** He averages 15 visits in a year, so any extension would be nice!

**Dr. Goldberg:** An incremental improvement still makes a difference in the patient's life. Thank you for taking the time to learn more about the patient. I find that a lot of retina specialists know there's a burden but don't take the time to hear about that how that burden affects the patient, his mental health, and his family. It's therapeutic for him to express that to somebody. Thank you for doing that. I agree that I would probably start with faricimab. I see that the PED is still there but appears fibrotic and is quite broad-based. As we become more comfortable with faricimab, we may even initiate earlier treatment to shrink that PED.

**Dr. Regillo:** These high-need patients are not uncommon. This is a great case.

### CASE 2: UNYIELDING DISEASE WITH AN UNFORTUNATE OUTCOME

**Dr. Modi:** This patient presented with retained lens fragments and aphakia in the left eye, and I performed a vitrectomy and sutured a scleral-fixed IOL in July 2018. She had nonexudative AMD in the right eye and had previously received anti-VEGF for nAMD in the left eye, with 8- to 12-week intervals prior to the vitrectomy. Three weeks after surgery, her uncorrected VA was 20/20- (Figure 2A). However, we started to see a fibrovascular PED and early development of subretinal hyperreflective material (SHRM), so I gave her a bevacizumab injection (Figure 2B).

When she returned in 6 weeks, the amount of SHRM had increased and extended well beyond the hemorrhage into the foveal slice, along with an increase in subretinal fluid (SRF). We discussed the necessity of 4-week intervals going forward, after receiving another bevacizumab injection. At the next visit in October 2018, there was improvement in the SHRM and SRF, but her vision dropped to 20/40-2. I administered another bevacizumab injection, but she returned 6 weeks later (instead of 4), with increasing SHRM and SRF. I wanted to reevaluate the diagnosis with a fluorescein angiogram, but the patient declined, so I switched to

aflibercept instead, deeming this a failure of bevacizumab at a 4- to 6-week interval. Four weeks later, the SHRM improved despite persistent SRF, so she received another injection. In January 2019, she complained of decreased vision (20/50 VA) and we saw increased SRF and SHRM, but also choroidal hypertransmission progressing to atrophy (Figure 2C). I suggested adopting a more aggressive approach (eg, injections every 2 to 3 weeks in an off-label fashion) as the eye was vitrectomized, but she refused another injection.

She returned in February 2019, after receiving two second opinions who advised continued treatment, and was developing a more consolidated area of hyperreflectivity. She was given another aflibercept injection, but we had already lost valuable ground. In March 2019, I saw consolidated fibrosis and because her VA worsened to 20/150, I suggested switching to ranibizumab. She declined as she "had read that aflibercept was the best." By April 2019, she had progressive fibrosis and subretinal hemorrhage (Figure 2D). During the next two 4-week intervals, her SRF continued to increase with larger areas of hemorrhage all whilst receiving monthly aflibercept. In May 2019, she agreed to try ranibizumab. Two weeks after her ranibizumab injection, she came in saying her vision was worse. It was now 20/350 and she progressed to a type 3 neovascularization, with extensive intraretinal hemorrhage, all overlying a disciform scar (Figure 2E). We re-initiated aflibercept therapy. I suggested 2-week intervals, which we do try in some of these patients, but she declined in favor of monthly treatment. Her last visit in October 2019 showed some hemorrhage and intraretinal fluid over the disciform scar, even after 12 aflibercept injections (Figure 2F). Fortunately, her right eye remained stable throughout this ordeal.

This case was the most extreme example of frequent treatment falling short of a favorable outcome, because usually frequent treatments do work for most patients with nAMD. This poses some interesting questions: Were there inherent anatomic



different with this patient? Were we missing a form of aggressive polypoidal choroidal vasculopathy (PCV)? Should we consider increasing the injection frequency in vitrectomized eyes? If she had presented 4 years later, with the more durable treatment options we have now, the outcome may have been different.

**Dr. Rafieetary:** Was the patient an aspirin user?

**Dr. Modi:** Great question. She wasn't on antiplatelet or anticoagulant therapy. Some patients who are on newer anticoagulation medications can have larger hemorrhages if they were to bleed, but the risk of hemorrhage is not greater on these medications.

**Dr. Regillo:** The good news is that this aggressive and downhill course on regular anti-VEGF therapy represents less than 5% of our patients with nAMD. You're right in that the anti-VEGF is cleared faster after vitrectomy and the patient could have benefitted from either more frequent injections or durable/sustained-delivery therapies. Even if there was PCV, it should have responded relatively well to monthly aflibercept, had it not been for the prior vitrectomy. It's interesting to consider how this course would have changed if you'd introduced faricimab, which has a dual mechanism of action and durability. It could have allowed at least 4-week intervals in this patient.

**Dr. Modi:** An update on her case—her right eye progressed to nAMD 3 months ago. She's received two aflibercept injections, with the first faricimab injection last week. Fortunately, she's not vitrectomized in this eye, but we're taking the full-court press strategy and she's on board with that.

**Dr. Regillo:** We know the PDS works in vitrectomized eyes. In the phase 2 LADDER trial, early implantations led to hemorrhages, which required vitrectomies. The PDS still performed well. However, we never implanted the PDS in an already vitrectomized eye, so that ventures into unknown territory.

Novel nAMD treatments are such a dynamic space right now,

with a lot of favorable changes that will hopefully result in better outcomes for our patients. ■

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# ADVANCEMENTS IN AMD: OPTIMIZING OUTCOMES WITH EMERGING THERAPIES

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## 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

**Summarize** the current treatments and barriers to optimizing medical management of patients with diabetic eye diseases and neovascular AMD in clinical settings

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

**Discuss** future therapies and their implications for patient outcomes

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

**Identify** patients who may benefit from the next generation of retinal disease therapies

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_



# POSTTEST QUESTIONS

Please complete at the conclusion of the program.

1. Based on this activity, please rate your confidence in your ability to discuss current and future therapies for optimizing medical management of patients with neovascular age-related macular degeneration (nAMD; 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. Based on this activity, please rate your confidence in your ability to identify patients who may benefit from the next generation of retinal disease therapies (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

3. An 86-year-old woman presents to your office for routine evaluation. On examination, you find pigment epithelial abnormalities and large drusen and thickening in the macula of her right eye. Optical coherence tomography (OCT) shows the presence of fibrovascular pigment epithelial detachment (PED), drusenoid PEDs, and overlying cystic intraretinal fluid. Which treatment option is the next best step for this patient?

- A. Intravitreal ranibizumab
- B. Intravitreal aflibercept
- C. Intravitreal off-label bevacizumab
- D. Any of the above

4. Which of the following statements about the correlation between anti-VEGF injection frequency in nAMD and vision is true?

- A. More frequent injections correlates with better vision
- B. Less frequent injections correlates with better vision
- C. Vision is not correlated to injection frequency
- D. We do not have enough data to determine this

5. You are seeing your 75-year-old patient with nAMD for follow-up. He has received 1 year of monthly injections with ranibizumab and is increasingly frustrated with his treatment burden. He is requesting a different treatment modality. Which of the following is a reasonable treatment option for this patient?

- A. Offer photodynamic therapy
- B. Offer treatment with intravitreal corticosteroids
- C. Offer treatment with intravitreal bevacizumab
- D. Offer treatment with the port delivery system (PDS)

6. According to studies, how much higher is the risk of endophthalmitis with intravitreal ranibizumab versus PDS?

- A. One-fold higher
- B. Two-fold higher
- C. Three-fold higher
- D. Four-fold higher

7. Your 75-year-old patient with nAMD calls the emergency triage line. He had a PDS implanted in his right eye 6 months ago and has been doing well. However, he suddenly developed a red eye and foreign body sensation in the right eye a few hours ago. What is the next best course of management?

- A. Reassurance, this is likely due to irritation from the PDS
- B. Reassurance, foreign body sensation is an expected symptom after PDS implantation
- C. Close follow-up, explain to the patient this is likely normal, but if this persists he should be seen in 2-3 weeks
- D. See the patient immediately, as this could be due to device exposure and lead to endophthalmitis if untreated

8. Faricimab is a first-in-class bispecific antibody that blocks \_\_\_\_.

- A. VEGF-A and Ang-2
- B. VEGF-B and Ang-2
- C. VEGF-A and Ang-1
- D. VEGF-B and Ang-1

9. You are seeing your 65-year-old patient who has exudative nAMD and is currently on monthly aflibercept. He is increasingly frustrated with his treatment burden and wants to discuss alternative treatment options. All of the following might be reasonable treatment options for this patient, EXCEPT:

- A. Observation
- B. Switch to intravitreal ranibizumab
- C. Switch to intravitreal faricimab
- D. Discuss implantation of the PDS

10. What molecules are blocked by OPT-302?

- A. VEGF-A and VEGF-B
- B. VEGF-A and VEGF-C
- C. VEGF-C and VEGF-D
- D. VEGF-B and VEGF-D

11. A 78-year-old Caucasian man with a history of nonexudative AMD presents to your office for follow-up. He notes acute vision loss and metamorphopsia in his right eye. Fluorescein angiogram transiting his right eye shows leakage in a classic choroidal neovascularization pattern, and OCT shows drusenoid PEDs and cystic intraretinal fluid. What is the best management of this patient?

- A. Start intravitreal steroid therapy
- B. Start intravitreal anti-VEGF therapy
- C. Start oral steroid therapy
- D. Perform photodynamic therapy

12. You are evaluating your 67-year-old patient who has exudative macular degeneration. He has been on monthly aflibercept injections for 13 months, but still has persistent fluid and subretinal hemorrhage. All of the following are reasonable treatment options, EXCEPT:

- A. Switch to intravitreal faricimab
- B. Switch to higher dose aflibercept injections (off-label)
- C. Switch to more frequent aflibercept injections (off-label)
- D. Discontinue anti-VEGF therapy and consider corticosteroid therapy

# 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:

\_\_\_\_ I certify that I have participated in this entire activity.

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.