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RT

Retina Today

DIABETIC EYE DISEASE: EXPERT DISCUSSIONS ON HOW AND WHEN TO TREAT

A continuing medical education activity provided by
Evolve Medical Education LLC.

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Diabetic Eye Disease:

Expert Discussions on How and When to Treat

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CONTENT SOURCE

This continuing medical education (CME) activity captures content from a virtual roundtable discussion.

ACTIVITY DESCRIPTION

Retinal disorders, including age-related macular degeneration, diabetic eye disease, and retinal vein occlusion can result in vision loss if not treated early and continuously. Prevent Blindness America has found the total health care costs of vision problems in the United States in people older than 40 years to reach almost \$139 billion annually. Retina specialists must be continuously educated on the latest advances relating to the management of these diseases to allow for the best possible care for their patients.

TARGET AUDIENCE

This certified CME activity is designed for retina specialists and eye care professionals involved in the medical management of patients with retinal disorders.

LEARNING OBJECTIVES

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

- **Identify** the current treatment options available for the management of common retinal diseases (neovascular age-related macular degeneration, diabetic eye disease, retinal vein occlusion).

- **Summarize** how treatment paradigms have evolved over time and how they relate to current treatment options.
- **Identify** the relationships between disease characteristics, drug, treatment frequency, visual and anatomic outcomes
- **Implement** best practices using individualized patient treatment plans to ensure optimal outcomes for patients.
- **Recognize** the growing importance of imaging for use in disease management.

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DIGITAL EDITION

This supplement is part of a full curriculum with multiple activities. To view the additional activities, please visit <https://evolvemeded.com/course-group/state-of-retina/>.

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1. Please rate your confidence in your ability to implement individualized patient treatment plans to ensure optimal outcomes for patients (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 the relationships between retinal disease characteristics, drug, treatment frequency, visual and anatomic outcomes.
 - a. Not at all confident
 - b. Not very confident
 - c. Neutral
 - d. Confident
 - e. Very confident
3. At how many weeks did the EARLY analysis of DRCR Protocol I find an association with early response and long-term visual response?
 - a. 4 weeks
 - b. 12 weeks
 - c. 20 weeks
 - d. 36 weeks
4. Which of the following statements is false?
 - a. Prolonged delay in treatment of macular edema from branch retinal vein occlusion (BRVO) is associated with less improvement in visual acuity (VA).
 - b. Minimal data is available on the differential effectiveness of the various anti-VEGF agents for BRVO related macular edema.
 - c. Dexamethasone implant trials have shown more rapid improvement in VA compared with sham injections.
 - d. There is clear evidence that combination therapy is superior to monotherapy in retinal vein occlusion patients with macular edema.
5. What were the treatment groups in DRCR.net Protocol V?
 - a. Eyes were randomized to anti-VEGF, laser, or observation for the duration of the study.
 - b. Eyes were randomized to anti-VEGF or observation with anti-VEGF in the latter group if VA decreased from baseline by at least 10 letters (≥ 2 lines on an eye chart) at any visit or by 5 to 9 letters (1-2 lines) at two consecutive visits.
 - c. Eyes were randomized to anti-VEGF, laser, or observation with anti-VEGF in the last two groups if VA decreased from baseline by at least 10 letters (≥ 2 lines on an eye chart) at any visit or by 5 to 9 letters (1-2 lines) at two consecutive visits.
 - d. Eyes were randomized to anti-VEGF, laser, or observation with anti-VEGF in the last group if VA decreased from baseline by at least 10 letters (≥ 2 lines on an eye chart) at any visit or by 5 to 9 letters (1-2 lines) at two consecutive visits.
6. Which study analyzed intravitreal ranibizumab versus intravitreal triamcinolone?
 - a. DRCR Protocol B
 - b. DRCR Protocol I
 - c. MEAD
 - d. FAME
7. The treatment burden for diabetic macular edema with current therapies is greatest during which period?
 - a. The first 12 months
 - b. The second 12 months
 - c. All time points
 - d. All of the above
8. A 35-year-old woman with a history of type 2 diabetes presents with marked hemorrhages in four quadrants, exudates and thickening of the macula, and some evidence of neovascularization elsewhere present in the left eye. All of the following are evidenced-based approaches to the patient EXCEPT?
 - a. The patient may benefit from an ultrawide field fluorescein angiography to evaluate for proliferative diabetic retinopathy.
 - b. The patient likely has severe nonproliferative diabetic retinopathy. Close observation is warranted.
 - c. The patient has proliferative diabetes and therefore anti-VEGF or panretinal photocoagulation is indicated.
 - d. The patient should be investigated for signs of neuropathy and nephropathy.
9. In a newly diagnosed patient with nonproliferative diabetic retinopathy, center-involving diabetic macular edema, and 20/70 vision, what is the first line of treatment?
 - a. Focal laser
 - b. Proliferative diabetic retinopathy
 - c. Intravitreal Steroids
 - d. Anti-VEGF
 - e. SubTenon's steroids

Diabetic Eye Disease: Expert Discussions on How and When to Treat

In the United States, estimates from 2015 indicate that more than 30 million people have diabetes, which is nearly 10% of the population.¹ Caring for patients with diabetic macular edema (DME) comprises a large part of our practices as retina specialists. The following discussion summarizes a meeting of experts in the field of retina in private practice and university settings. We discuss our individual approaches to diagnosis, disease management, and patient care based on clinical studies and our unique experiences.

— Jorge Fortun, MD, Moderator

TREATMENT OF DIABETIC MACULAR EDEMA

Q | JORGE FORTUN, MD: Let's discuss a disease that represents a significant portion of our practices, which is the treatment of DME. In age-related macular degeneration (AMD), optical coherence tomography (OCT) was the initial treatment and monitoring tool. Is the same true for you with DME? Is there any ancillary testing outside of OCT that you employ in patients with diabetic retinopathy (DR) and DME?

MITUL MEHTA, MD: I always start my examination of diabetic patients with fluorescein angiography (FA) because I want to know the status of their ischemia as well as the status of their edema and leakage. I like to use widefield angiography. We have an Optos machine at our locations, and that provides really good peripheral views so you can get an idea about peripheral ischemia as well. To me, that drives the conversation of treating DME with injections of anti-VEGF or with steroids or adding laser as well. I get an FA once a year, even though it is sort of an old-school way of practicing. But we have a large proportion of patients with severe diabetes, so I believe that getting the FA at least once a year is something worth doing. For the most part, I do agree with also performing an OCT because it is very useful to me.

HEMANG PANDYA, MD: Widefield angiography has helped in terms of educating patients. It gives us a lot of information about the ischemic status of the peripheral retina. I think FA has a great utility when it comes to DR. I believe ischemic load definitely contributes to patients' overall prognosis. I definitely use wide-field angiography to help direct treatment for patients with DME. OCT is our guideline, but the great thing about widefield angiography is that it helps to educate the patient and their family. It stands out as to the drop-out of the vasculature in the ischemic areas, so it hammers home a point. Especially in some of those diabetic patients who have what we call "featureless retinas," where things look quite normal—no dot and blot hemorrhages, but they're so ischemic that

they don't have hemorrhage in the periphery, and the FA can help the patient understand why he or she needs treatment.

VEERAL SHETH, MD, MBA, FACS: I agree with the main point made by Drs. Mehta and Pandya. I definitely start these patients off when they're new in my clinic with widefield angiography. I'm also treating severe nonproliferative diabetic retinopathy (NPDR), even without DME, a lot more aggressively these days. I think a lot of it has to do with the fact that I have a very compliant patient population, and so I found myself using a lot less laser and a lot more intravitreal anti-VEGF therapy for these patients. I have found that showing these patients their angiograms and the progression or improvement over time has helped them understand their condition and the importance of treatment. When you have patients who have good visual acuity (VA) to start, these images are what guide the therapy and help them understand what we're trying to accomplish.

Q | DR. FORTUN: In terms of diagnostic information, how much weight do you place on other information? Are you looking at biomarkers such as disorganization of retinal inner layers (DRIL) or other features on the OCT or initial FA that determine the prognosis or treatment strategy in the future?

DR. SHETH: On the FA, I look for diffuse leakage, almost like a vasculitic appearance to the retina because, in some of these patients, I do end up using a combination of anti-VEGF and intravitreal steroid. I find that the FA helps me figure out who these patients might be a little earlier on in the process.

DR. FORTUN: I do the same thing. I use that sort of gestalt sense of how much vascular leakage is present. Justis Ehlers, MD, and colleagues from Cleveland Clinic, as well as others, have published on this.² The data show there may be a biomarker that points to

(Continued on page 9)

CASE STUDY

Monthly Anti-VEGF Injections for DME Resolve Fluid; Exudates Remain

By Jeremy D. Wolfe, MD, MS

A 51-year-old Hispanic male with an 8-year history of diabetes presented to my office. He had not been taking systemic medications for his diabetes for the past 6 months and his A1C was 9.1%. His visual acuity (VA) was 20/63 in his right eye and 20/80 in his left eye.

During this visit, I captured several images. The fundus photos showed numerous retinal hemorrhages and lipid exudates in both eyes (Figure 1), and mid-phase ultrawide fluorescein angiography (UWFA) showed areas of capillary nonperfusion in both eyes, with extensive microvascular changes (Figure 2).

The late/recirculation phase UWFA showed diffuse late leakage in both eyes without obvious neovascularization (Figure 3).

Optical coherence tomography (OCT) demonstrated intraretinal fluid in both eyes, and subretinal fluid (SRF) was noted in the right eye (Figure 4).

One week after being treated with bilateral anti-VEGF injections (right eye, ranibizumab 0.3 mg; left eye was part of the YOSEMITE trial and received either aflibercept or study drug [faricimab]), the patient's OCT showed some fluid resolution in both eyes (Figure 5). At 1 month after his initial visit, both eyes had improved. His VA with correction (VAcc) was 20/50 in his right eye and 20/32 in his left eye; his intraocular pressure (IOP) was 15 mm Hg in his right eye and 13 mm Hg in his left eye. The OCT at 1 month showed the SRF had resolved completely in his right eye (Figure 6).

At month 2, his VAcc in his right eye was 20/50 and 20/32 in his left eye. IOP was 18 mm Hg in his right eye and 16 mm Hg in his left eye. His OCT showed continued improvement during this visit and also at month 3, when his VAcc was 20/32-1 in his right eye and 20/32 in his left eye. His IOP in his right eye was 16 mm Hg and 14 mm Hg in his left eye. OCT at 3 months showed intraretinal fluid and exudate in his right eye while the left eye revealed no demonstrable fluid.

At month 4, his VAcc was 20/40 in the right eye and 20/25-1 in the left eye, with an IOP of 17 mm Hg in both eyes. Fundus images showed improvement in hemorrhages, but with significant exudates still present in both eyes (Figure 7) and areas of capillary nonperfusion that persisted in both eyes (Figure 8). However, continued improvement was noted in OCT of the right eye.

By month 5 of receiving monthly injections, the patient's OCT showed continued improvement (Figure 9) and his VAcc was 20/40 in his right eye and 20/40 in his left eye, with IOPs of 15 mm Hg and 18 mm Hg, respectively.

The patient continued receiving bilateral anti-VEGF treatment for 1 year, with the right eye receiving ranibizumab 0.3 mg and the left eye receiving

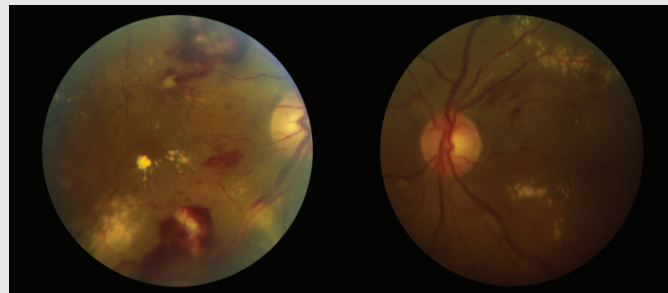


Figure 1. Retinal hemorrhages and lipid exudates are visible in both eyes.

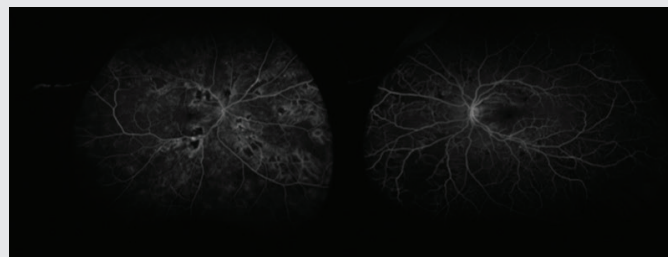


Figure 2. Areas of capillary nonperfusion with extensive microvascular changes are visible in both eyes.

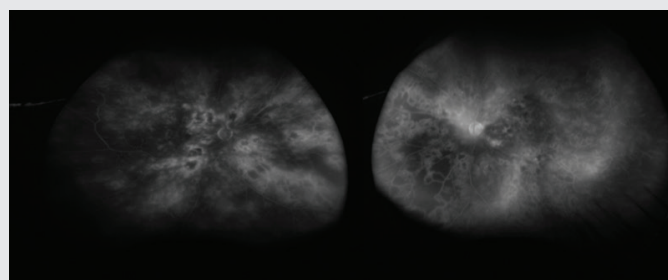


Figure 3. Diffuse leakage without obvious neovascularization is visible in both eyes.

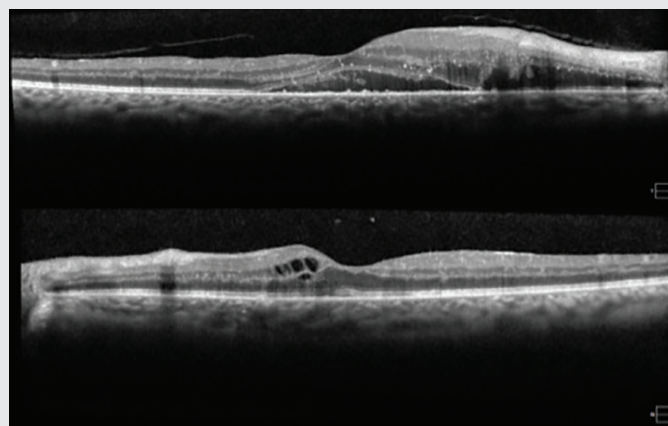


Figure 4. The OCT demonstrated intraretinal fluid in both eyes. SRF was noted in the right eye.

either aflibercept or faricimab as part of the YOSEMITE phase 3 clinical trial. During that time, there was improvement in his diabetic macular edema, diabetic retinopathy, and best corrected VA in both eyes. The patient's most recent best corrected VA was 20/40 in his right eye and 20/25 in his left eye (Figures 10-12).

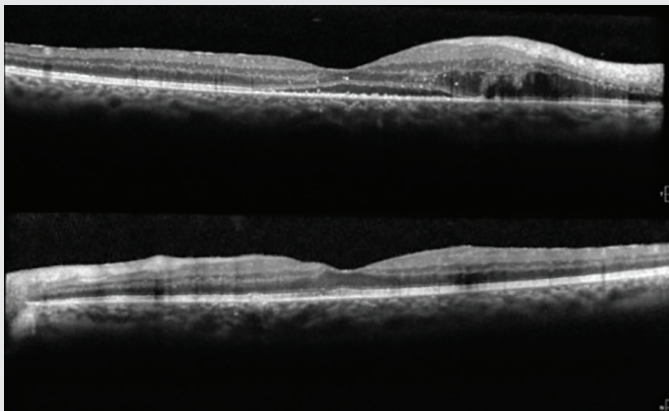


Figure 5. Some fluid resolution can be seen in both eyes.

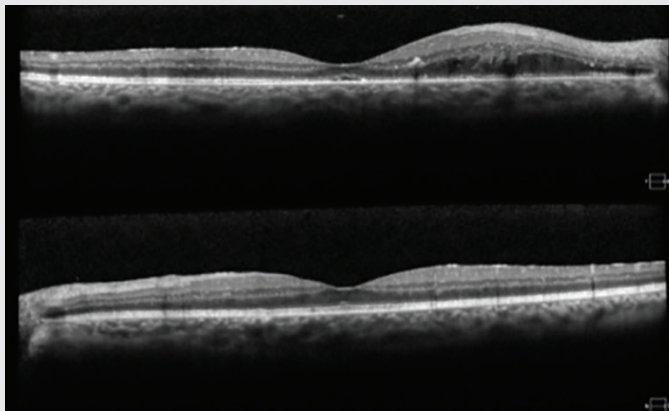


Figure 6. The SRF has resolved completely in his right eye.

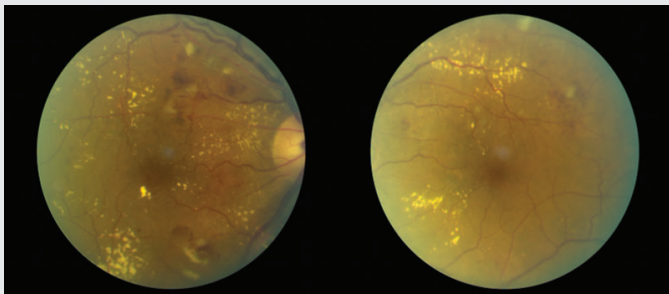


Figure 7. The hemorrhages have improved but significant exudates are still present in both eyes.

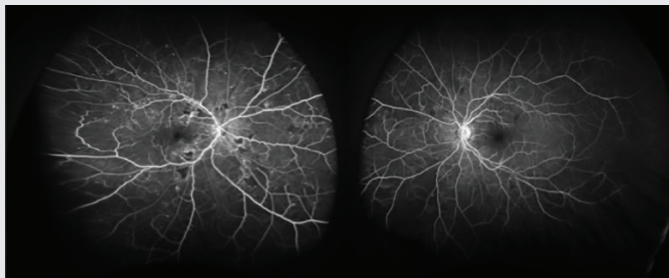


Figure 8. Areas of capillary nonperfusion persist.

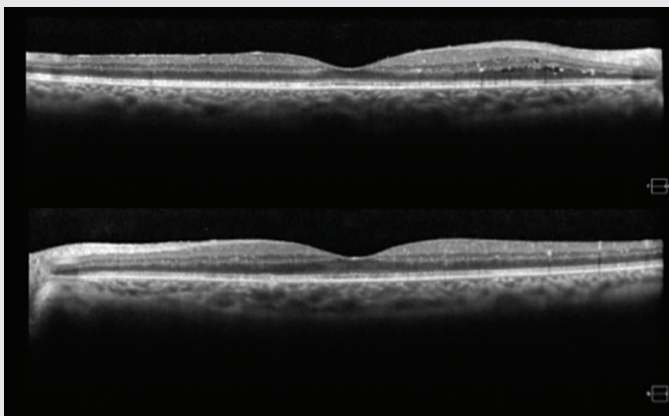


Figure 9. The patient's OCT showed continued improvement.

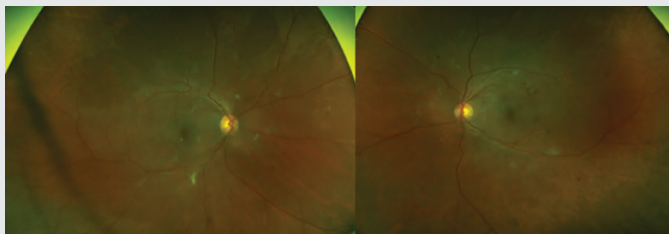


Figure 10. Fundus images at 1 year following monthly injections.

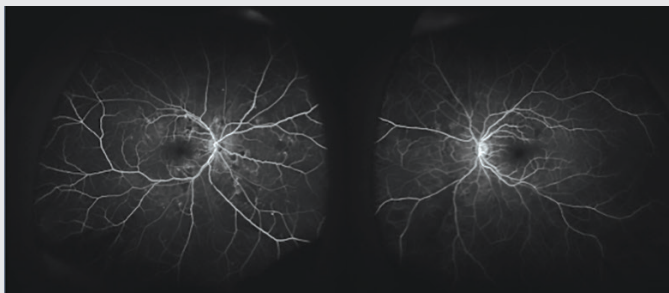


Figure 11. FA demonstrates continued improvement with near resolution of diffuse vessel leakage.

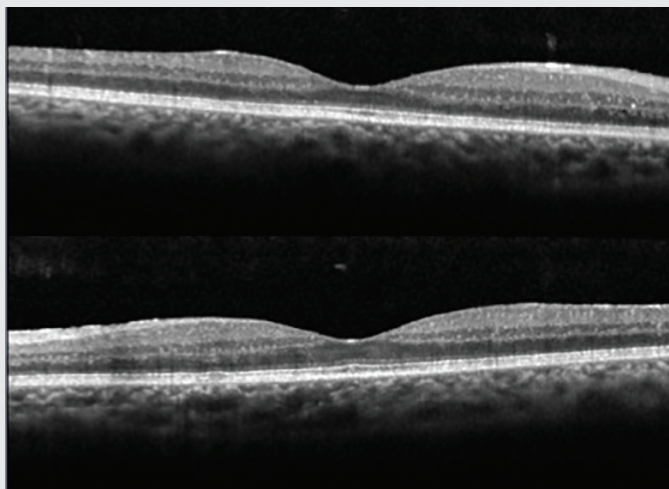


Figure 12. Marked improvement in the patient's OCT compared with baseline.

CASE STUDY

Beyond Anti-VEGF in the Management of DME

By Jorge Fortun, MD

A 69-year-old male transferred care to our practice at Bascom Palmer Eye Institute. He reported mild worsening of vision since his last visit to an eye care provider, but he had no other symptoms or complaints.

His primary medical history included diabetes, hypertension, and hyperlipidemia. His ocular history included treatment with multiple lasers and injections, but he did not share any diagnoses. The patient had cataract extraction and a posterior chamber intraocular lens was placed in both eyes. The patient reported taking aspirin, rosuvastatin, insulin lispro, and insulin glargine.

Clinical examination revealed corrected visual acuity (VAcc) was 20/50 in his right eye and 20/30 in his left eye with intraocular pressure (IOP) of 15 mm Hg in his right eye and 10 mm Hg in his left eye. Pupils were equal, round, and reactive to light (PERRL) with no afferent pupillary defect, and visual field was tests full to confrontation. There was full movement of the extraocular muscles. The rest of the clinical examination was unremarkable.

The color fundus photos (Figure 1) showed previously applied focal laser scars throughout the macula of both eyes and optical coherence tomography (OCT) showed center involving diabetic macular edema in both eyes (Figure 2).

A review of his records sent from his previous retina specialist revealed he had received several intravitreal injections of bevacizumab and ranibizumab but had a “poor response.” He also had received intravitreal triamcinolone and sub-Tenon intravitreal 40-mg triamcinolone with steroid response.

I treated the patient with intravitreal aflibercept, and his OCT showed slight improvement at his next three follow-up visits, each 5 weeks apart (Figure 3). His VAcc improved from 20/50 in his right eye and 20/30 in his left eye during this first follow-up visit to 20/40 and 20/25 at his third follow-up.

After five injections with aflibercept resulted in a poor response in his right eye, I switched to the dexamethasone implant. The edema resolved, and at 12 weeks following the dexamethasone implant injection the patient was observed. At his follow-up visit, now 20 weeks after the initial dexamethasone implant was injected, the edema recurred. At this time another dexamethasone implant was injected with resolution of edema sustained at 16 weeks postinjection (Figure 4).

In the left eye (Figure 5), the patient responded well to intravitreal injection of aflibercept, however, a recurrence of edema occurred with extension beyond 6 weeks. There was recurrence of the edema at 18 weeks after injection of the implant.

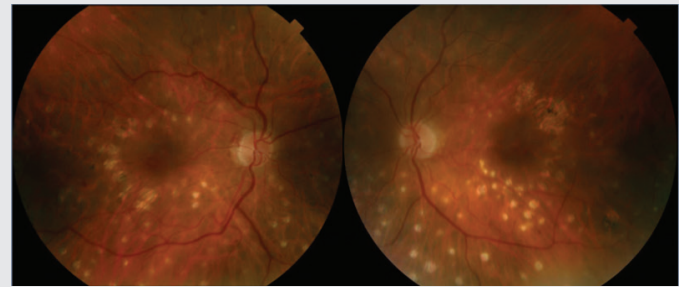


Figure 1. The color fundus photos show focal laser scars throughout the macula of both eyes.

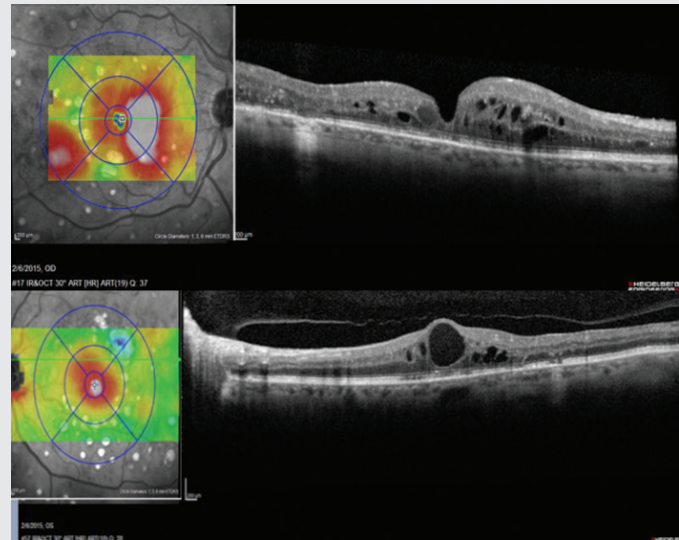


Figure 2. OCT showed center involving DME in both eyes.

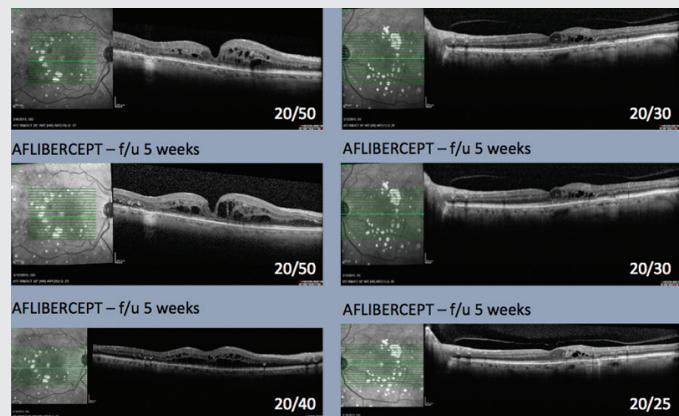


Figure 3. OCT showed slight improvement at his next three follow-up visits, each 5 weeks apart.

Both eyes have remained fluid free with q16 week dexamethasone implants over a period of 3 years. Of note, there was an initial steroid-induced rise in IOP in both eyes after the first dexamethasone implant. Treatment with a combination drop of dorzolamide and timolol was initiated, and the eyes remain normotensive.

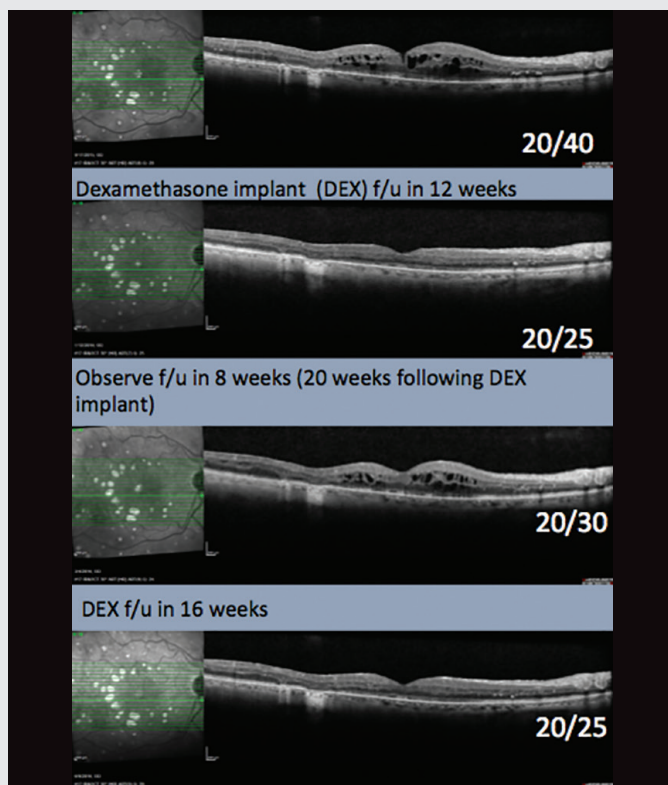


Figure 4. Another dexamethasone implant was injected with resolution of edema sustained at 16 weeks postinjection.

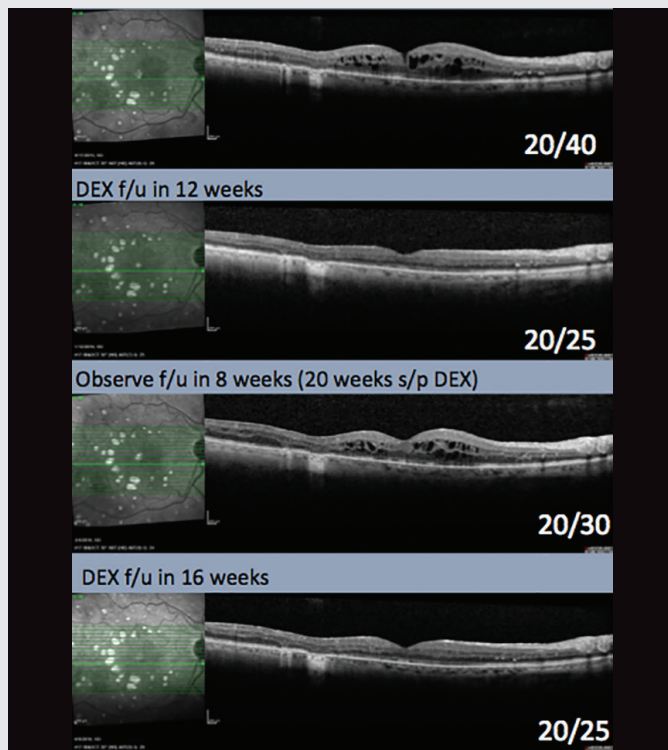


Figure 5. The patient responded well to intravitreal injection of aflibercept in the left eye. However, a recurrence of edema occurred with extension beyond 6 weeks.

(Continued from page 5)

perhaps a greater inflammatory component in these patients, and that the use of steroids may likely be indicated in the future course of their disease. Does anyone else have comments to share about baseline imaging?

DR. MEHTA: One other thing I would add is that if the central macular thickness is greater than 500 microns, I use steroids much earlier than if not. The thickness of the retina impedes the efficacy of anti-VEGFs for patients with DME. I definitely use that for not only prognosis but also guiding my treatment, especially because a lot of these patients are younger or phakic. We're always hesitant to cause a cataract, but as we all know, cataracts can be removed, and macular ischemia is not as easily treatable. We want these patients to be able to see for as long as they can, and if that means causing a cataract and they need cataract surgery, in my opinion, it's not really that terrible of an outcome because we will save the long-term vision.

DR. PANDYA: I agree with what everyone said regarding the OCT changes. One thing I look at is presence of SRF localized from the edema. That makes me feel like even though I generally start with an anti-VEGF, I will, as you've all mentioned, consider intravitreal steroids much sooner because there's a lot more going on.

DR. FORTUN: It seems most of us are using some of these initial imaging tests and looking at some of these biomarkers to perhaps consider the pathogenesis of the disease and if there may be a more inflammatory component, or maybe more of an exuberant vascular leakage that may need steroids.

DME DOSING STRATEGIES

Q | DR. FORTUN: We talked about the myriad treatment strategies that are implemented in the treatment of nAMD, and the same treatment strategies exist and are implemented in DME. However, DME is such a different disease, so let's discuss what treatment strategies you implement in these patients, the different dosing strategies you use, and what leads to that determination.

DR. PANDYA: With diabetes, it's still variable based upon the patient's chronic blood sugar levels and comorbid conditions, and that is directed by their social factors. I obviously try to communicate well with their primary care physicians and endocrinologists, to try to get them in touch with some of those physicians to make sure they are covered. My treatment modality is this: if they're well-controlled and we can extend the time between doses, that's always optimal. Based on the results of the DRCR.net Protocol T study,³ I believe that for patients with VA worse than 20/50, I do prefer to use aflibercept. Obviously, those patients have a lot more SRF and a lot more chronic edema. I think combined treatment with anti-VEGF and an intravitreal steroid is optimal. But if their blood sugar and hypertension aren't controlled, it's like pouring a little bit of water on

(Continued on page 11)

CASE STUDY

Retinal Vein Occulsion

By Veeral Sheth, MD, MBA, FACS

A 78-year-old woman with hypertension and hypercholesterolemia presented to my office with painless loss of vision in her left eye. Her past ocular history included stable primary open-angle glaucoma in both eyes for which she was administering timolol twice daily. Her vision was 20/20 in her right eye and 20/400 in her left eye, and her intraocular pressure (IOP) was 15 mm Hg in both eyes.

Her anterior segment exam was remarkable for pseudophakia, and she had 0.8 cup/disc ratio with stable visual field changes. She had a posterior chamber intraocular lens.

Her right eye retinal exam was remarkable for some arteriovenous crossing changes. Her left eye exam was remarkable for engorged vessels, swollen optic nerve, and four quadrants of intraretinal hemorrhage with macular edema (Figure 1).

OCT was performed as the initial imaging in this patient. OCT demonstrated significant retinal thickening and edema with some disorganization (Figure 2).

Fluorescein angiography was ordered and demonstrated delayed but progressive venous fill and blockage from the intraretinal hemorrhages plus vascular engorgement and tortuosity (Figure 3). Peripheral nonperfusion is also evident, in addition to late macular leakage and leakage at the nerve (Figure 4).

I chose to manage this patient with intravitreal bevacizumab on the initial visit as well as on repeat visit 1 month later. Her vision improved to 20/200 in her left eye, and her imaging demonstrated significant resolution of the edema but early atrophic changes (Figure 5).

After three monthly injections of bevacizumab, the patient returned for her next monthly visit and her vision was 20/200 (Figure 6). During this visit, she requested a pause in treatment because she had only seen a slight improvement in her vision. Given the overall guarded prognosis, we decided to pause the injection schedule, but she was asked to return 1 month later to determine if the retina remained dry or if she had a recurrence of macular edema.

One month later, and 2 months since her last intravitreal bevacizumab, she presented with significant central thickening/edema and vision drop to 20/400 (Figure 7).

Bevacizumab injections were resumed at this time. One month after resuming treatment, her edema improved and her vision improved to 20/200. She maintained this anatomy and vision for more than 6 months on a reduced schedule with bevacizumab injections every 6 weeks.

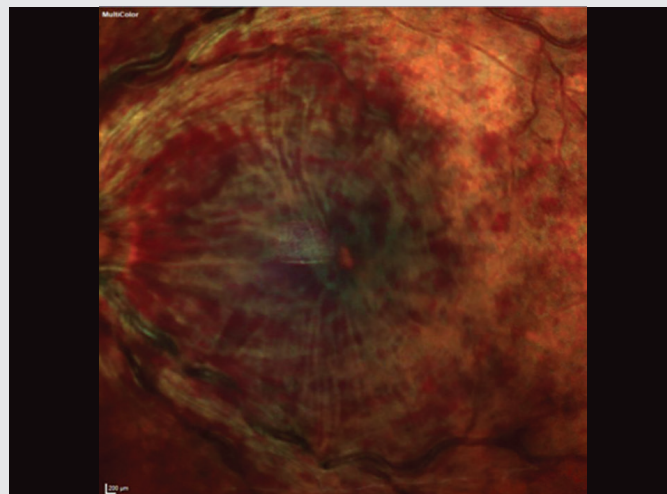


Figure 1. Engorged vessels, swollen optic nerve, and four quadrants of intraretinal hemorrhage with macular edema can be seen in this image of the left eye.

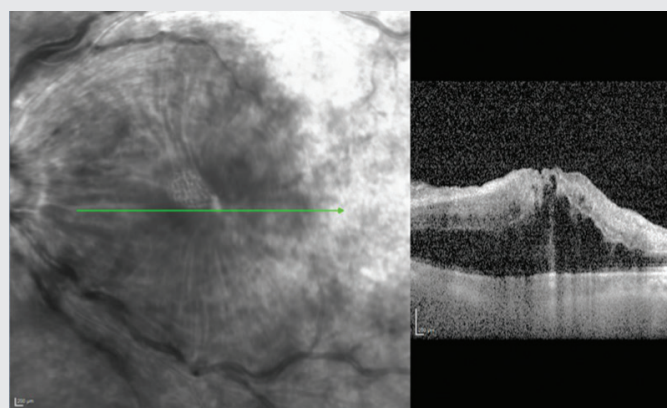


Figure 2. OCT shows significant retinal thickening and edema with some disorganization.

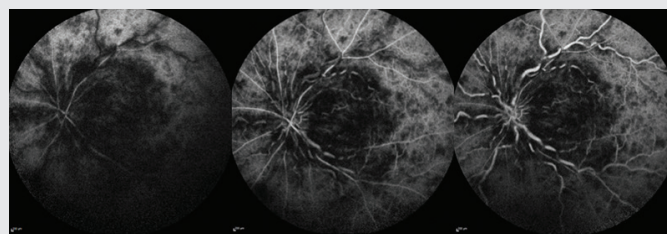


Figure 3. Progressive venous fill and blockage from the intraretinal hemorrhages plus vascular engorgement and tortuosity.

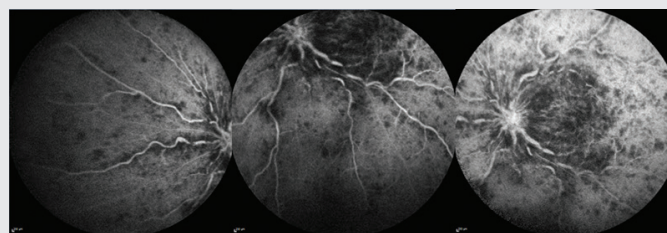


Figure 4. Peripheral and leakage at the nerve.

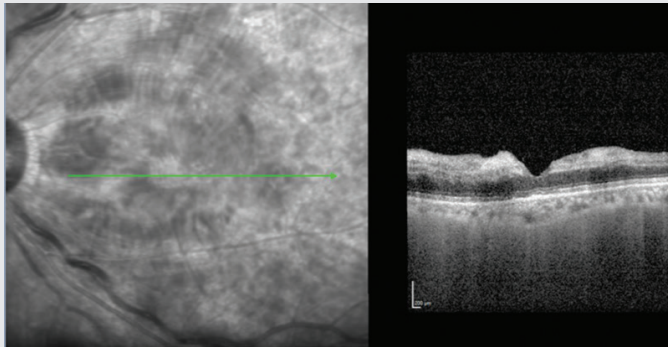


Figure 5. Imaging demonstrates significant resolution of the edema but early atrophic change.

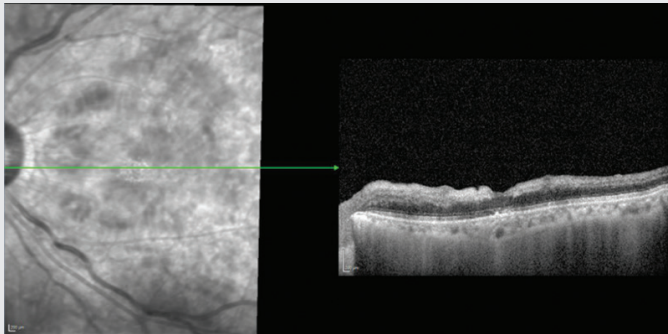


Figure 6. After three monthly injections of bevacizumab, the patient returned for her next monthly visit and her vision was 20/200.

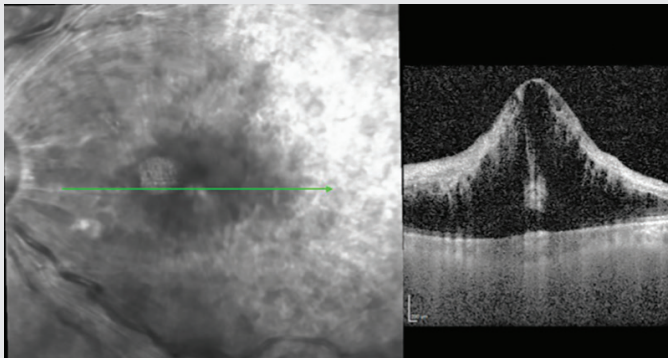


Figure 7. Significant central thickening/edema and vision drop to 20/400.

(Continued from page 9)

a forest fire; it is not going to help. You have to control all the systemic factors as well. That really drives my decision making.

DR. SHETH: I agree with that statement, and the only thing I'd add is that for patients with better VA—for example, 20/20 or 20/25—I am finding myself watching these patients a little more, based on some of the DRCR.net data. I'm not sure if some of the other DR data that is coming out will change my mind and cause me to once again intervene earlier in these patients, but I think that's one change I've seen in my practice. I am confident that we're not going to see them slide downhill quickly—assuming these are compliant patients.

DR. MEHTA: I agree with Dr. Sheth. I'm definitely watching many more 20/20 patients, and not as many with center-involved DME (CI-DME).

I've been thinking a lot more about systemic treatment because we are physicians. We are supposed to manage care for the entire patient, and ultimately, if we don't help them manage their underlying diseases and conditions like diabetes, high blood pressure, and elevated cholesterol, then we're not really going to have long-term success. One of the best things I can do for these patients is refer them to an endocrinologist. Many times patients will tell me they are seeing their primary care doctor, but in reality, because of the way their insurance is structured, they only have a few short visits, and they don't get all of their questions answered because they have a lot of problems. However, endocrinologists tend to have nutritionists and dieticians in their offices who can help patients establish a fundamental understanding of their disease and what is necessary to gain control. I have found that to be incredibly helpful in lowering A1C levels and gaining control of their blood pressure and cholesterol. It really changes their lives, and often can lead to better success for the patient in the long run.

DR. FORTUN: These are excellent points on how and when we initiate therapy. We discussed how oftentimes patients with good vision and a small amount of edema can be observed based on recent Protocol V data.⁴ The point was also made that, unlike some of the other retinal and choroidal vascular diseases that we treat, DME is a systemic disease that does and can respond to optimization of systemic factors, such as glycemic control, hypertension, and cholesterol levels.

MANAGING RVO

DR. SHETH: There are two major ways my treatment approach for RVO differs from my approach to AMD. The first is that the number of patients that end up needing only a short or defined course of treatment is higher than with AMD, so I am willing to switch to PRN more quickly in these patients to determine who these patients might be. In other words, where I may use a treat-and-extend approach for my AMD patients, I am more likely to use PRN in my RVO patients. The other difference in management is that I end up using targeted PRP in my RVO patients who have significant nonperfusion on their angiography because I think it lowers the risk of neovascular sequelae and may reduce overall treatment burden.

WHAT ABOUT THE FLUID?

Q | DR. FORTUN: If you look specifically at the Protocol T data³ and other trials, we are leaving a lot of fluid on the table, so to speak. In Protocol T, nearly 44% of patients in the aflibercept arm and almost 70% of patients with the bevacizumab arm had some persistent DME at 2 years. That begs the question: when do you consider a patient to be a suboptimal responder as was described in the secondary analysis in Protocol I⁵ from Susan Bressler, MD? And when do you consider switching, which is something that was looked at in the EARLY analysis⁶ by Pravin Dugel, MD, and colleagues? As far as switching to combination therapy or perhaps another anti-VEGF agent, what do you look for? When do you look for it? And what goes into that consideration of making a treatment switch?

DR. MEHTA: Compared with patients with AMD, I definitely give patients with DME more time before I switch to another anti-VEGF. Sometimes just giving a patient six bevacizumab injections is what they need to get under control long enough for the bevacizumab to work for them. Especially if there's a small amount of fluid that's persistent. If it's a lot of fluid that's persistent after three or four injections, I typically switch them or add a steroid. Usually I'll add a steroid before I switch the anti-VEGF agent, but it depends on how much fluid is present. If there's very little fluid, I may switch the agent instead of adding a steroid, but if there's a lot of persistent fluid, I'll add a steroid early.

DR. SHETH: I take the same approach. I think when retina specialists talk about switching, most of the time they're referring to a switch within a class. But I agree with Dr. Mehta, and I don't even call it a switch. I just call it combination therapy, because I'm adding, in a lot of those cases, an intravitreal steroid.

DR. PANDYA: I agree about adding a steroid. Especially in those patients who really have poor systemic control of their disease.

Q | DR. FORTUN: From what I'm hearing, even though the statistical endpoint and the top line data of Protocol U⁷ showed there was really no added benefit to combination therapy when you combined the dexamethasone implant with ranibizumab, from a VA standpoint, a greater percentage of those patients did not have a decrease of three lines. And the OCT data showed greater turgescence of the retina. I think we're all in agreement that combination therapy is a valuable tool for the recalcitrant or suboptimal responding patient. Let us talk about what goes into your discussion with patients when you're adding steroids. How do you explain the side effects? Do you discuss with them? What steroids do you use?

DR. PANDYA: With regard to intravitreal steroids, I primarily use the intravitreal dexamethasone implant. In terms of side effects, I review the side effects in the same manner I would with any intravitreal injection. But in particular, I let them know that in my hands about one of every five or six patients develops mild ocular hypertension. If they're phakic, I advise them they will develop a cataract sooner rather than later because the steroid injection will accelerate that process. If they're pseudophakic, I inform them this would have been an issue, but they don't have that complication. The biggest concern is letting them know their ocular pressure may be elevated and they may have to instill an eye drop to keep the pressure under control. I also advise them that in a worst-case scenario, they may need to see a glaucoma specialist. I do keep a very low threshold for sending to glaucoma specialists in these cases, just to ensure that we're not missing anything. The exam begins at the slit lamp and then proceeds with a look at the optic nerve. If they have a suspicious optic cup-to-disc ratio, then I tend to stay away from steroids in those patients.

DR. FORTUN: Any other comments on the intraocular pressure with the use of steroids? Any other considerations?

DR. MEHTA: I also use the intravitreal dexamethasone implant most frequently, but I will sometimes use the 0.19-mg fluocinolone acetonide intravitreal implant, which is a longer acting steroid implant. I discuss steroids as a possibility before I administer the first anti-VEGF injection. At the patient's first visit, I tell them that because they're diabetic and have poorly controlled disease, that's why they're seeing me. I also inform them that although they would likely develop a cataract as a natural part of the aging process, this treatment is going to make that process happen faster. The priority is fixing the retina to assure long-term vision.

I use the longer acting fluocinolone implant because I have a lot of patients who travel. From the social aspect, a lot of diabetic patients tend to be younger and still working, so this fits their schedule because making it to multiple visits can be difficult. Therefore, I like to use longer-acting treatments whenever I can. I do think, for the most part, pressure issues are blown out of proportion. I find, for the most part, the occasional dexamethasone implant pressure spikes really aren't bad, and most patients can be managed with eye drops. There are now five different classes of pressure-lowering drops we can use before they go to surgery, and there's microinvasive glaucoma surgery if necessary. So I really think there are so many options to treat high pressures that it tends not to concern me too much; unless the pressure spikes are extreme, in which case I'll set them up with a glaucoma specialist.

DR. FORTUN: We've covered quite a few topics, and obviously we can't discuss everything in depth, but I think that this discussion summarizes what we do in your practices and how to incorporate evidence-based medicine into real-world retinal disease management.

Some of the take-away points include that we have a variety of imaging modalities and it's important to consider all of them. We still rely heavily on OCT for initial evaluation and guiding our treatment. There are several different treatment protocols, and we can consider them all, but in the end, the data only helps to guide us, and the treatment must be individualized to each patient. ■

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2. Ehlers JP, Wang K, Vasanji A, et al. Automated quantitative characterization of retinal vascular leakage and microaneurysms in ultra-widefield fluorescein angiography. *Br J Ophthalmol*. 2017;101(6):696–699.

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6. Dugel PU, Campbell JH, Kiss S, et al. Association between early anatomic response to anti-vascular endothelial growth factor therapy and long-term outcome in diabetic macular edema. An independent analysis of Protocol I study data. *Retina*. 2019;9(1):88–97.

7. Maturi RK, Glassman AR, Liu D, et al. Effect of adding dexamethasone to continued ranibizumab treatment in patients with persistent diabetic macular edema. A DRCR Network phase II randomized clinical trial. *JAMA Ophthalmol*. 2018;136(1):29–38.

DIABETIC EYE DISEASE: EXPERT DISCUSSIONS ON HOW AND WHEN TO TREAT

Release Date: May 2020
Expiration Date: June 2021

INSTRUCTIONS FOR CREDIT

To receive credit, you must complete the attached 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 visit <https://evolvemeded.com/online-courses/1922-supp2>. If you are experiencing problems with the online test, please email us at info@evolvemeded.com. Certificates are issued electronically; please be certain to provide your email address below.

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

Name _____ ☐ MD/DO participant ☐ OD ☐ non-MD participant

Phone (required) _____ ☐ Email (required) _____

Address _____

City _____ State _____ Zip _____

License Number _____

OE Tracker Number _____

DEMOGRAPHIC INFORMATION

Profession	Years in Practice	Patients Seen Per Week (with the disease targeted in this educational activity)	Region	Setting	Models of Care
___ MD/DO	___ > 20	___ 0	___ Northeast	___ Solo Practice	___ Fee for Service
___ OD	___ 11-20	___ 1-15	___ Northwest	___ Community Hospital	___ ACO
___ NP	___ 6-10	___ 16-30	___ Midwest	___ Government or VA	___ Patient-Centered Medical Home
___ Nurse/APN	___ 1-5	___ 31-50	___ Southeast	___ Group Practice	___ Capitation
___ PA	___ <1	___ 50+	___ Southwest	___ Other	___ Bundled Payments
___ Other				___ I do not actively practice	___ Other

LEARNING OBJECTIVES

DID THE PROGRAM MEET THE FOLLOWING EDUCATIONAL OBJECTIVES?

Identify the current treatment options available for the management of common retinal diseases (neovascular age-related macular degeneration, diabetic eye disease, retinal vein occlusion).

AGREE NEUTRAL DISAGREE

Summarize how treatment paradigms have evolved over time and how they relate to current treatment options.

Identify the relationships between disease characteristics, drug, treatment frequency, visual and anatomic outcomes.

Implement best practices using individualized patient treatment plans to ensure optimal outcomes for patients.

Recognize the growing importance of imaging for use in disease management.

POSTTEST QUESTIONS

Please complete at the conclusion of the program.

- 1. Based on this activity, please rate your confidence in your ability to implement individualized patient treatment plans to ensure optimal outcomes for patients (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 the relationships between retinal disease characteristics, drug, treatment frequency, visual and anatomic outcomes.**
 - a. Not at all confident
 - b. Not very confident
 - c. Neutral
 - d. Confident
 - e. Very confident
- 3. At how many weeks did the EARLY analysis of DRCR Protocol I find an association with early response and long-term visual response?**
 - a. 4 weeks
 - b. 12 weeks
 - c. 20 weeks
 - d. 36 weeks
- 4. Which of the following statements is false?**
 - a. Prolonged delay in treatment of macular edema from branch retinal vein occlusion (BRVO) is associated with less improvement in visual acuity (VA).
 - b. Minimal data is available on the differential effectiveness of the various anti-VEGF agents for BRVO-related macular edema.
 - c. Dexamethasone implant trials have shown more rapid improvement in VA compared with sham injections.
 - d. There is clear evidence that combination therapy is superior to monotherapy in retinal vein occlusion patients with macular edema.
- 5. What were the treatment groups in DRCR.net Protocol V?**
 - a. Eyes were randomized to anti-VEGF, laser, or observation for the duration of the study.
 - b. Eyes were randomized to anti-VEGF or observation with anti-VEGF in the latter group if VA decreased from baseline by at least 10 letters (≥ 2 lines on an eye chart) at any visit or by 5 to 9 letters (1-2 lines) at two consecutive visits.
 - c. Eyes were randomized to anti-VEGF, laser, or observation with anti-VEGF in the last two groups if VA decreased from baseline by at least 10 letters (≥ 2 lines on an eye chart) at any visit or by 5 to 9 letters (1-2 lines) at two consecutive visits.
 - d. Eyes were randomized to anti-VEGF, laser, or observation with anti-VEGF in the last group if VA decreased from baseline by at least 10 letters (≥ 2 lines on an eye chart) at any visit or by 5 to 9 letters (1-2 lines) at two consecutive visits.
- 6. Which study analyzed intravitreal ranibizumab versus intravitreal triamcinolone?**
 - a. DRCR Protocol B
 - b. DRCR Protocol I
 - c. MEAD
 - d. FAME
- 7. The treatment burden for diabetic macular edema with current therapies is greatest during which period?**
 - a. The first 12 months
 - b. The second 12 months
 - c. All time points
 - d. All of the above
- 8. A 35-year-old woman with a history of type 2 diabetes presents with marked hemorrhages in four quadrants, exudates and thickening of the macula, and some evidence of neovascularization elsewhere present in the left eye. All of the following are evidenced-based approaches to the patient EXCEPT?**
 - a. The patient may benefit from an ultrawide field fluorescein angiography to evaluate for proliferative diabetic retinopathy.
 - b. The patient likely has severe nonproliferative diabetic retinopathy. Close observation is warranted.
 - c. The patient has proliferative diabetes and therefore anti-VEGF or panretinal photocoagulation is indicated.
 - d. The patient should be investigated for signs of neuropathy and nephropathy.
- 9. In a newly diagnosed patient with nonproliferative diabetic retinopathy, center-involving diabetic macular edema, and 20/70 vision, what is the first line of treatment?**
 - a. Focal laser
 - b. Proliferative diabetic retinopathy
 - c. Intravitreal Steroids
 - d. Anti-VEGF
 - e. SubTenon's steroids

ACTIVITY EVALUATION

Your responses to the questions below will help us evaluate this CME 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 opportunity (patients)

Other. Please specify: _____

____ Lack of consensus or professional guidelines

____ Reimbursement/insurance issues

____ Lack of administrative support

____ Lack of resources (equipment)

____ Lack of experience

____ Patient compliance issues

____ Lack of time to assess/counsel patients

____ No barriers

The design of the program was effective for the content conveyed.

____ Yes ____ No

The content was relative to your practice.

____ Yes ____ No

The content supported the identified learning objectives.

____ Yes ____ No

The faculty was effective.

____ Yes ____ No

The content was free of commercial bias.

____ Yes ____ No

You were satisfied overall with the activity.

____ Yes ____ No

Would you 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

____ Medical Knowledge

____ Practice-Based Learning and Improvement

____ Interpersonal and Communication Skills

____ Professionalism

____ System-Based Practice

Additional comments:

____ I certify that I have participated in this entire activity.

This information will help evaluate this CME activity; may we contact you by email in 3 months to see if you have made this change? If so, please provide your email address below.

