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Applying New Data to Refine the Management of Retinal Venous Occlusion

Allen C. Ho, MD: More data on treatments for retinal venous occlusive disease (RVO) were released in 2009 than have been in a decade for central retinal vein occlusion (CRVO) and two decades for branch retinal vein occlusion (BRVO). What is the current status of understanding about these retinal diseases?

Peter A. Campochiaro, MD: RVO is the second most common retinal vascular disease after diabetic retinopathy, with approximately 180,000 cases in the United States; 80% of cases are BRVO.[1] Further, the incidence of hypertension and diabetes, which are risk factors for RVO, is increasing, so RVO will become more common over time. As the treatment options expand, so will clinicians' realization of the widespread nature of this disease.

Dr. Ho: What percentage of patients with BRVO and CRVO have visually significant macular edema?

David M. Brown, MD: Most patients who present to a retina specialist with BRVO will have significant macular edema; it is difficult to detect if vision is good. Patients with CRVO are often asymptomatic. For example, approximately 30% of patients in the CVOS (Central Vein Occlusion Study) had visual acuity better than 20/40.[2,3]

Robert L. Avery, MD: Retina specialists are seeing more patients with RVO and better vision. This is largely due to the fact that it is increasingly common for optometrists to utilize widefield retinal cameras and optical coherence tomography (OCT) machines in their practices. As a result, patients are being referred to us earlier than they were 20 years ago.

Dr. Ho: As our experience with these patients grows and we gain a better understanding of the natural history of RVO, we will have a better sense of the natural history of RVO. As Dr. Avery indicated, we are seeing these patients earlier in many cases, and so often we have patients who fall outside of the boundaries of our treatment guidelines from the BVOS (Branch Vein Occlusion Study) and CVOS.

Dr. Campochiaro: In the BVOS, patients were generally observed for 3 months after they presented because of the natural history of spontaneous improvement.[4-6] If after 3 months the hemorrhages had cleared, the patients received grid laser photocoagulation.

Dr. Ho: Why should a treating physician be concerned about applying laser photocoagulation when macular hemorrhage is present? Further, how much hemorrhage is considered too much for laser?

Dr. Campochiaro: When laser photocoagulation is done in an eye with few or no retinal hemorrhages, the light energy passes through the retina and is absorbed by the retinal pigment epithelium (RPE),where it is converted to heat, which burns the adjacent photoreceptors. The inner retina, including the nerve fibers that run along the surface of the retina, are spared. Photoreceptors are the cells that consume the most oxygen in the retina, and their destruction by laser reduces oxygen demand and increases its supply. This ameliorates hypoxia in the inner retina. When laser photocoagulation is done in an eye with retinal hemorrhages, the light energy is absorbed by the blood pigment, which generates heat at the surface of the retina, which burns nerve fibers creating scotomata. In addition, photoreceptors are not burned and oxygen demand is not decreased.

Determining whether the amount of retinal hemorrhages

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TARGET AUDIENCE

Retina Specialists and Ophthalmologists

ACTIVITY DESCRIPTION

The goal of this activity is to introduce physicians to the latest clinical trial results from two phase 3 studies of antivascular endothelial growth factor (anti-VEGF) in macular edema secondary to CRVO and BRVO. Recently, the intravitreal dexamethasone implant (Ozurdex, Allergan, Inc) was approved by the Food and Drug Administration for the treatment of macular edema secondary to BRVO and CRVO. This recent approval was based on two multicenter, double-masked, randomized, parallel studies. Study one included 403 patients and study two included 450 patients.

STATEMENT OF NEED

These developments are the first of any magnitude in this disease state in 25 years; it is crucial that retinal specialists be educated to newly available treatment modalities. This is truly a revolutionary time in the history of retinal disease therapies.

LEARNING OBJECTIVES

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

- Describe the epidemiology, pathogenesis, and pathophysiology of RVO, CRVO, and BRVO, including the impact of systemic disease.
- Discuss the current and emerging clinical data, such as from SCORE, BRAVO, and CRUISE trials, evaluating the use of anti-VEGF agents, and the newly approved dexamethasone implant for macular edema secondary to RVO, as well as the clinical trial results the FDA approval was based upon
- Explain the pathogenesis and current/future epidemiology of RVO (CRVO/BRVO), including the impact of systemic disease
- Review the most frequent clinical approaches to CRVO/BRVO management and the shortcomings and advantages of each and discuss strategies to use the agents in practice
- Explain how early, targeted treatment in the typical RVO patient could greatly improve quality of life
- Discuss the role of VEGF as a therapeutic target in macular edema secondary to RVO; eg, VEGF is present at higher levels in the vitreous in RVO
- Describe how the use of steroids and anti-VEGF agents will change retinal practice dynamics and how surgeons can prepare to incorporate these new treatment modalities into their daily clinic.

FACULTY

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ACCREDITATION

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of The National Retina Institute (NRI) and *Retina Today*. NRI is accredited by the ACCME to provide continuing medical education for physicians.

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Method of Participation: There are not fees for participating and receiving CME credits for this activity. During the period of February 1, 2010 to February 1, 2011, participants must:

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makes laser dangerous is an important decision and when in doubt, laser should be deferred.

Dr. Ho: What has been our clinical experience with CRVO?

Dr. Avery: The standard clinical practice for CRVO has been to watch the vein occlusion for development of neovascularization and then to apply laser upon its occurrence. In the past few years, however, off-label bevacizumab (Avastin, Genentech, Inc.) has become widely accepted as a treatment for macular edema secondary to CRVO.

ANTI-VEGF AGENTS FOR RVO

Dr. Ho: The 2009 American Society of Retina Specialists Patterns and Trends (PAT) survey reported that an overwhelming number of physicians are utilizing off-label intravitreal bevacizumab as first-line therapy for both CRVO and BRVO.[7] Recently, the results from a number of trials investigating the efficacy of alternative therapies to laser for macular edema in CRVO and BRVO have been made available to us. Dr. Campochiaro, can you summarize these results?

Dr. Campochiaro: The BRAVO trial (A phase 3, multicenter, randomized, sham injection-controlled study of the efficacy and safety of ranibizumab injection compared with sham in patients with macular edema secondary to BRVO) was designed to compare ranibizumab to focal/grid laser. Patients were randomized to receive either monthly injections of 0.3 mg ranibizumab (Lucentis, Genentech, Inc.), 0.5 mg ranibizumab, or sham injection for 6 months. Rescue laser was allowed after 3 months if the macular edema showed little or no improvement, vision was 20/40 or worse, and central subfield thickening was 250 µm or worse.

The 6-month results that were released at the 2009 Retina Congress[8] were impressive. The mean gain in visual acuity at day 7 was 7.6 letters for the patients in the 0.3 mg group and 7.4 letters in the 0.5 mg group, compared with 1.9 letters in the sham injection group. At the primary endpoint of 6 months, the improvement was between 15 and 18 letters in patients treated with ranibizumab, compared with 7.3 letters in the sham group—a rapid and substantial improvement in mean visual acuity.

Fifteen to 20% of patients treated with ranibizumab gained three or more lines at week 1. By 6 months, more than 50% of patients in both of the ranibizumab groups (55.2% in the 0.3 mg group and 61.1% in the 0.5 mg group) gained 15 letters of best corrected visual acuity compared with 28.8% in the sham group. The rapidity and the magnitude of the effect on visual acuity show that ranibizumab is an effective treatment for BRVO.

The results for CRUISE (A phase 3, multicenter, randomized, sham injection-controlled study of the efficacy and safety of ranibizumab injection compared with sham in patients with macular edema secondary to CRVO) are equally impressive.[9] The visual acuity improvements in the ranibizumab groups almost mirror those in the BRAVO trial, although patients in the sham group did not do as well as the sham group in BRAVO. In CRUISE, 46% to 47% of the patients in the ranibizumab groups were three-line gainers compared with only 16.9% of patients in the sham injection group. At day 7, the mean gain in the 0.3 mg group was 8.8 letters and 9.3 letters in the 0.5 mg group, compared with 1.1 letters in the sham injection group. At the primary endpoint, ranibizumab-treated patients had a mean gain of 12.7 and 14.9 letters compared to 0.8 in sham-treated patients.

Dr. Ho: Regarding the 0.3 mg dose and 0.5 mg dose of ranibizumab, do the results of these trials give us reason to believe that one dose is better than the other?

Dr. Avery: No. BRAVO and CRUISE were not powered to determine this. Based on the results, however, we can probably assume that there is not a significant difference between the two doses.

Dr. Ho: Based on the similarity in efficacy of the 0.3 mg and 0.5 mg doses of ranibizumab, would it be fair to say that the lower dose would be better?

Dr. Brown: In my opinion, no. When injected monthly, the difference between 0.3 and 0.5 mg ranibizumab does not make that a significant difference; if one exists, it likely dissipates within a few days. BRVO and CRVO, however, are driven more strongly by vascular endothelial growth factor (VEGF) than is age-related macular degeneration (AMD). Because of this, I think that some of our RVO patients will require higher doses of anti-VEGF. We have seen macular edema rebound in some cases with high amounts of ischemia, suggesting the need for more anti-VEGF.

That said, I do not think that there is much difference between 0.3 mg and 0.5 mg, but I think that differences between 0.3 mg vs 2.0 mg will be shown to be significant.

Dr. Campochiaro: Additionally, 2.0 mg will last longer in the eye and will stay above the level needed to suppress VEGF for a longer period of time. We are currently recruiting patients in a study that will compare 0.5 mg ranibizumab with and without laser to ranibizumab 2.0 mg with and without laser for macular edema due to RVO.

STEROIDS FOR RVO

Dr. Ho: Dr. Brown, can you summarize the SCORE data?

Dr. Brown: In the SCORE-BRVO study, there were no differences in efficacy seen between laser outcomes and steroids through the first year.[10] The steroid used in SCORE was a preservative-free triamcinolone acetonide (Trivaris,

Allergan, Inc.) hybrid gel formulation that is not commercially available. The benefit of the gel formulation is that it does not disperse like crystalline steroid particles in preserved triamcinolone acetonide (Kenalog, Bristol-Myers Squibb), which may provide a more sustained release.

Going into the trial, the popular thinking was that steroids would be a "home run" for BRVO. Over the long-term, however, it became apparent that the steroid effect does not last; after 1 year, laser produced better results. In sum, SCORE-BRVO reconfirmed the results of the 1985 BVOS. Laser remains the standard of care for BRVO.

In SCORE-BRVO, however, patients were treated with triamcinolone every 4 months, so an argument can be made that patients were underdosed. Initial visual acuity gains, especially for patients who were administered 4.0 mg, dropped off, similar to what we saw with ranibizumab in PIER (A Phase IIIb, Multicenter, Randomized, Double-Masked, Sham Injection-Controlled Study of the Efficacy and Safety of Ranibizumab in Subjects with Subfoveal Choroidal Neovasularization with or without Classic CNV Secondary to Age-Related Macular Degeneration)[11] and SAILOR (Safety Assessment of Intravitreal Lucentis for AMD)[12] with underdosing.

The SCORE-CRVO study resulted in a recommendation that the standard of care for CRVO, which is observation, should be adjusted to allow treatment with steroids.[13] The interesting thing about this study, however, is that the patients in the natural history cohort fared worse than those in the natural history cohorts of the CVOS, the sustained-release dexamethasone implant (Ozurdex, Allergan, Inc.), and the CRUISE studies. Patients in the natural history cohort of SCORE-CRVO lost six to eight letters by month 4. The mean visual acuities and the edema were the same as those for patients in the CVOS, sustained-release dexamethasone implant study, and CRUISE; however, more patients had capillary nonperfusion in SCORE-CRVO.

Dr. Ho: What about the expected side effects that we anticipated with corticosteroids in terms of intraocular pressure (IOP) elevation and cataract formation or progression?

Dr. Brown: Forty percent of patients who received the 4.0 mg dose of triamcinolone acetonide required IOP-lowering medication. Cataracts were also present in high numbers—in 20% to 30% of patients who received steroid. These results were typical of what one might expect with steroids.

The conclusions and recommendations of the SCORE-BRVO study were based on the risk:benefit ratio. How many patients will be helped with a steroid more than laser vs the risk associated with steroid?

In comparison, in the BRAVO study, we found that one would have to give 2,000 to 3,000 injections of ranibizumab before encountering a complication of endophthalmitis or a retinal tear. A rough estimate is that anti-VEGF injections will benefit eight out of nine patients with BRVO. And, as earlier suggested, it is my opinion that a higher dose of ranibizumab could increase that ratio to nine out of nine.

In my clinical experience, I have not yet seen any RVO patient in whom macular edema did not improve early on with anti-VEGF therapy.

Dr. Ho: Regarding the possibility that patients in both of the SCORE studies may have been underdosed, would more frequent dosing also increase the overall incidence of side effects and, therefore, maintain a similar risk:benefit ratio?

Dr. Brown: That is possible.

Dr. Ho: What information do we have on the sustained-released dexamethasone implant?

Dr. Brown: The sustained-released dexamethasone implant is injected with a 22- or 23-gauge needle. It then gives high levels of steroid for at least 2 months but then tapers off. The 6-month results for both BRVO and CRVO showed that a significant number of patients with the implant gained three lines of visual acuity compared with the control group.[14] At 2 months, 29% of patients with the implant (combined BRVO and CRVO) gained three lines. This robust effect was no longer seen at 6 months. Complication rates were low in the trial; fewer than 10% of patients developed glaucoma, and the incidence of cataract formation was low. The 6-month data that were reported have a limitation in that it is well known that the second year is when many of the side effects of steroid are seen.

Dr. Ho: The main differences between the results of the sustained-released dexamethasone implant trial vs the SCORE trials could be related to several factors. In terms of efficacy, particularly with respect to BRVO, there could be an argument for underdosing in both the sustained-release dexamthasone and SCORE studies. In terms of safety and side effects, the difference in steroid preparation (dexamethasone vs triamcinolone acetonide) may be significant, and certainly, comparisons should be made at similar point in time.

CASE 1

Dr. Ho: Now that we have these data available to us, how will we apply them to treating our patients? How frequently are we following these patients? For example, patients with RVO can have varying responses to a VEGF agent at different time points, so how can we be sure we are getting an accurate assessment of a patient's response?

A 55-year-old man presents with a superior BRVO, is symptomatic, and has associated macular edema. What is your initial management of this patient?

Dr. Avery: It depends on how long the patient has had symptoms. I am more aggressive than many clinicians in that I sometimes treat the patient with an anti-VEGF agent on the first visit, especially if he or she has had symptoms for a month or longer. The recommendations from the BVOS tell us to wait 3 months to see if it spontaneously resolves,[4-6] but now that we have anti-VEGF agents available, we have a safe option for earlier treatment. I treat only if macular edema is present, and then I treat frequently—every 4 to 6 weeks until the edema and blood are gone. If edema reccurs as I extend out the intervals of treatments, I will apply light laser along with anti-VEGF therapy. I try to taper the anti-VEGF agent using a treat-and-extend protocol.

Dr. Ho: Dr. Campochiaro, how would you manage this patient?

Dr. Campochiaro: My management would depend on the amount of edema present and the visual acuity. If, for example, the edema is not severe and the visual acuity is better than 20/40, I would consider waiting. I do not, however, see any downside to immediate treatment. Any treatment that we offer comes with a risk of complications, so I consider the patient's individual needs and decide accordingly. If there is substantial macular edema seen on OCT, and the patient's vision is 20/40 or worse, the patient may be at risk for permanent visual loss. For this patient, I will treat with anti-VEGF immediately. Over time, my management is similar to Dr. Avery's treat-and-extend protocol.

Dr. Avery: For patients who are asymptomatic or have good vision, I also tend not to treat immediately with anti-VEGF. I do not think that much is lost in waiting for 1 month in such a case. I may offer treatment, but often I find it helpful to follow the patient for 1 month. If macular edema or visual acuity worsens, the patient is often more psychologically prepared for initiating treatment. When I do initiate anti-VEGF injections, I use my OCT scans as tools to engage patients as partners in their treatment.

Dr. Brown: I follow a similar protocol, except that I use combination therapy with laser more frequently—not immediately, but for patients with at least 3 months of history. I typically treat with an anti-VEGF agent followed by grid laser 1 week later, eliminating the edema with the anti-VEGF and adding laser in hopes that it will address the ongoing VEGF drive. Rather than applying the 100-µm to 200-µm spots that were used in the BVOS, I use 50-µm or 75-µm sized spots with the PASCAL Photocoagulator (OptiMedica, Santa Clara, CA).

More leeway exists in RVO than in AMD because RVO is an inner retinal disease. The photoreceptors stay dry due to a retinal epithelial pigment (RPE) pump, and this is why the patient can have 700 µm of edema and still be able to see. The "wiring" in the system becomes damaged with edema in RVO; we know from our experience with glaucoma that a patient can lose half of his optic nerve and retain good vision. AMD, on the other hand, is an outer retinal disease that involves RPE dysfunction and photoreceptor damage that causes permanent visual acuity loss. I also apply a treat-and-extend protocol with my anti-VEGF agent, but I am more comfortable letting patients have occasional edema than I am when treating a patient with AMD. For AMD, I aggressively address any fluid in the eye.

Dr. Ho: I think we all agree that we would take a fluorescein angiogram (FA) for this patient. Would you want to also take a widefield angiogram?

Dr. Brown: Yes. FA is only 30°—a small part of the functioning retina that leads to the VEGF drive. If I see massive areas of peripheral capillary nonperfusion on a widefield angiogram, I am more likely to apply scatter panretinal photocoagulation (PRP).

Dr. Ho: When would you schedule the follow-up visit after the first injection?

Dr. Campochiaro: I would have the patient come back to the office 1 month after the injection. Although the maximum effect may be at 1 week, I am able to discern whether the drug had effect at 1 month; I do not think it is worthwhile to make a patient come back at 1 week.

Dr. Brown: I have the patient come back in 1 week for two reasons. First, the patient has never had an injection before, so I want to check them carefully for any signs of endophthalmitis or retinal tears. I also take the opportunity to show the patient the OCT so that they can visualize the effect of the injection. After the 1-week visit, I see them again in 1 month.

CASE 2

Dr. Ho: What is your course of action for a patient with BRVO for whom you injected anti-VEGF, and at the 1-month follow-up visit edema is still present (eg, reduced from 600 µm to 450 µm), and the vision has declined by 1 line or so to 20/50?

Dr. Avery: I talk to the patient to elicit whether the vision improved initially after the injection and then declined as the effect wore off. I will not hesitate to give them a second injection, but this time I will see them 1 or 2 weeks later, rather than waiting a full month.

Dr. Campochiaro: I would give another injection. I generally tell patients at the outset that they should expect to

receive several injections before seeing a measurable improvement.

Dr. Brown: Would you add laser at this point?

Dr. Avery: It would depend on whether blood is present. Anti-VEGF speeds up the resolution of hemorrhaging quickly, and for an under- or nonresponding patient who has significant edema even after one injection, I will consider laser if there is no blood. If there is blood, however, which is common 1 month after the first injection, I will continue to inject and apply light laser after the blood has cleared.

Dr. Ho: Assuming the conditions are favorable (symptomatic loss of vision, minimal macular hemorrhage) would you consider combination therapy with laser after your first injection of anti-VEGF agent?

Dr. Campochiaro: I am open to combination therapy; however, I am more inclined to hold off on laser at this point. I look at laser as not only a long-term solution, but also as something I cannot take back. I do not think that we yet know the full extent of the visual consequences of laser. Thus, I am not eager to use laser photocoagulation on patients. In fact, some of my patients have received three of four injections of ranibizumab and resolved to the point where laser is not required. I prefer this scenario.

One of the factors that has yet to be determined is whether scatter laser photocoagulation in the periphery is more beneficial than grid laser for RVO. I think that scatter laser may be a more rational approach. We know that there are many patients to whom we give grid laser who continue to need additional therapy. I suspect that we can do more for patients by applying laser to nonperfusion in the periphery.

CASE 3

Dr. Ho: A 65-year-old man complains of visual loss for 2 months. The patient is 20/200 with nonischemic CRVO and swollen macula at 600 µm. What would be your approach?

Dr. Brown: In CRVO I want to know the extent of the ischemia and capillary dropout. Hayreh et al[15] showed that CRVOs are not simply ischemic and nonischemic but that they all have some relative amount of ischemia. Severe ischemia and capillary dropout are important to detect because, although we can eliminate the edema with an anti-VEGF agent, the patient is still at risk for neovascular glaucoma and neovascularization in the posterior segment. In the RAVE (Rubeosis Anti-VEGF [RAVE] Trial for Ischemic Central Retinal Vein Occlusion) study, some patients developed neovascularization as late as 35 months after presentation and 18 months after the last anti-VEGF injection.

The more severe cases will require paretinal photocoagulation if they are not followed closely for the development of neovascularization.

I use FA to image patients with ischemic CRVO—it is instrumental in detecting capillary nonperfusion early on. In the CVOS, 40% of patients had increased capillary perfusion from day 0 to month 4.[2,3] I also take a follow-up angiogram to catch any ischemia that occurs later.

Dr Avery: I sometimes have my photographer pull back and image the iris also, particularly for patients with severe diabetes. This is a simple measure that takes no more than a few frames. When a patient is dilated, it is easy to miss subtle rubeosis or iris neovascularization that the photographer can pick up.

Dr. Campochiaro: The CRUISE study has shown that ranibizumab is extremely effective in CRVO, so I treat these patients quickly and vigorously. Just as with BRVO, we are still trying to sort the endpoint issues, but again, I think that peripheral nonperfusion is important.

Dr. Ho: How would you treat this patient, and when would you schedule a follow-up visit?

Dr. Brown: Because the vision is 20/200 and he has been symptomatic for 2 months, he will need an injection of either ranibizumab or bevacizumab, depending on whether I can get ranibizumab via an access program. Once we determine the agent, we will give him an injection within 1 to 2 weeks.

Dr. Campochiaro: I would inject right away and follow up at 1 month .

Dr. Avery: So would I.

CASE 4

Dr. Ho: What if a patient with CRVO was sent to you from another retina specialist? The clinical scenario is the same: Visual acuity is 20/200, and the macula is swollen to 600 µm. The history, however, includes three bevacizumab injections over the past 3 months. What do you do in this case?

Dr. Campochiaro: This question deals with an important issue: the comparative effects of ranibizumab and bevacizumab. There are currently no good data on this topic to guide our approach, but I would inject with ranibizumab. It is my impression that there may be a difference between the efficacy of ranibizumab and bevacizumab in retinal vascular disease, so I am inclined to use ranibizumab if there is a lack of response to bevacizumab.

Dr. Brown: There are several reasons both biologically and practically why ranibizumab maybe more beneficial in RVO. One is that each vial of ranibizumab has 140 µL of injectable drug, and for RVO I often use more than the 50 µL that is US Food and Drug Administration-approved for AMD.

Dr. Avery: I have had a handful of cases where I have clearly seen a better response to ranibizumab than bevacizumab. I was surprised because I would have thought that, because bevacizumab is a larger molecule, it would linger in the vitreous cavity longer, going straight to the inner retina and having a more robust effect in RVO. This, however, does not seem to be the case.

Dr. Campochiaro: I agree. This is the opposite of what I expected; however, a possible explanation for this might be found in the study that we published recently using a transgenic mouse model to compare the two anti-VEGF agents.[16] We showed that in a model of subretinal neovascularization, bevacizumab had a systemic effect, whereas ranibizumab did not. One reason that bevacizumab has a systemic effect may have to do with the Fc receptors in the ciliary body, which transport full length antibodies out of the eye into the circulation. This may enhance its effects in the choroid and decrease its effects in the retina somewhat. Also, the smaller size of ranibizumab may allow it to penetrate into the retina better than is the case for bevacizumab.

Dr. Avery: I share your concern about possible systemic absorption, which could be mediated by the Fc receptor on bevacizumab. In addition to your animal model, there are increasing reports of fellow eye effects in patients following bevacizumab injection.[17,18] A difference in systemic absorption may have clinical relevance in certain high-risk patients such as those with retinopathy of prematurity.[19]

Dr. Ho: It is clear from our discussion that the treatment of RVO requires a varied approach, depending on the case. There seems to be a consensus among the faculty that anti-VEGF agents can be used with success as first-line therapy for CRVO and BRVO and in combination with laser. It remains to be seen whether there is a difference in the effects of ranibizumab and bevacizumab but currently, the most extensive data that we have available are regarding the use of ranibizumab from the BRAVO and CRUISE trials. Treatment endpoints continue to evolve.

New generation corticosteroid delivery systems have improved the safety profile of intravitreal sustained-release low-dose steroids, and they may be important tools in the treatment of RVO, particularly for recalcitrant disease.

Although there may be a role for corticosteroids, the data for both injected triamcinolone and sustained-release dexamethasone monotherapy are not as impressive as those with ranibizumab with respect to both safety and efficacy.

Dr. Campochiaro: We have to keep in mind the argument that in these studies, steroids may not have gotten a fair test. Additionally, the mechanism of action of steroids involves interaction with several different receptors with different affinities and different actions, which is more complex than than the action of ranibizumab or bevacizumab, which have only one action, binding of VEGF. It may be that sustained delivery of low doses of steroids is better than bolus injections.

Dr. Ho: I agree that these are important considerations. Although we have access to more data in the past year on RVO than we have ever had, it is still early. Over time, we will continue to refine our treatment protocols for our patients with RVO as the data and our clinical experience evolve. ■

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Applying New Data to Refine the Management of Retinal Venous Occlusion

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CME QUESTIONS

1. What are the risks associated with applying laser photocoagulation in retinal venous occlusion when hemorrhaging is present?
a. nerve fiber damage
b. photoreceptor damage
c. corneal damage
d. none of the above

2. The 6-month results of the BRAVO trial demonstrated:
a. 72% of patients in the ranibizumab groups gained 15 or more letters
b. more than 50% of patients in the ranibizumab groups gained 15 or more letters
c. only 20% of patients in the ranibizumab groups gained 15 letters
d. 45% of patients in the sham group gained 15 letters.

3. The SCORE-BRVO trial showed no difference in the efficacy seen between laser and steroids in year 1.
a. True
b. False

4. Data from the 6-month trial for the sustained-delivery dexamethasone device showed:
a. A robust steroid effect up to 6 months for most patients
b. 29% of patients with the implant gained 3 lines of vision at 2 months
c. complications rates with the implant are low
d. all of the above
e. a and b

5. In SCORE-CRVO, the recommendation based on the study results was that:
a. the standard of care for CRVO should be adjusted to allow treatment with steroids
b. laser should continue to be the standard of care
c. the standard of care, which is observation, should be changed
d. a and b
e. a and c

6. Levels of VEGF in BRVO and CRVO are:
a. lower than in AMD
b. higher than in AMD
c. similar to AMD
d. none of above

7. In CRUISE, ___ % to ___% of patients in the ranibizumab groups were three-line gainers, compared with only 16.9% of patients in the sham injection group.
a. 35 and 40
b. 40 and 42
c. 46 and 47
d. 50 and 53

8. Hayreh et al showed that all CRVO have some relative amount of ischemia.
a. True
b. False

8. Did you find this activity to have commercial bias?
a. Yes
b. No

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