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## VOLUME 1 — ISSUE 4: TRANSCRIPT

# Featured Cases: Retinal Vein Occlusion (RVO)

Our Guest Author is Dr. Peter Campochiaro, the Eccles Professor of Ophthalmology and Neurosciences at the Wilmer Eye Institute at The Johns Hopkins University in Baltimore, Maryland.

After completing this activity, the participant will demonstrate the ability to:

- Describe the potential benefits and risks of intraocular anti-VEGF drugs in treating retinal vein occlusions;
- Explain the potential benefits and risks of intraocular steroids in treating retinal vein occlusions; and
- Determine patient characteristics that favor one treatment modality over another.

This discussion, offered as a downloadable audio file and companion transcript, covers the important issues related to *Retinal Vein Occlusion* in the format of case-study scenarios for the clinical practice. This program is a follow up to the Volume 1, Issue 3 *eOphthalmology Review* newsletter — [Retinal Vein Occlusion](#).

### Unlabeled/Unapproved Uses

The author has indicated that this presentation will include references to unlabeled or unapproved uses of bevacizumab and triamcinolone.

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### Faculty Disclosure

Dr. Campochiaro has indicated that he has served on advisory boards for Genentech, Pfizer, and Regeneron. He has served as a consultant for BMS, Genentech, GSK, Lpath Incorporated, Pfizer, and Regeneron. Dr. Campochiaro has received grants and research support from Alcon, Alimera Sciences, Genentech, Genzyme, GSK, and Molecular Partners.

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**DR. NEIL BRESSLER:** Welcome to this *eOphthalmology Review* podcast. *eOphthalmology Review* is presented by the Johns Hopkins University School of Medicine. This program is supported by an educational grant from Genentech, Incorporated.

Today's program is a companion piece to our Volume 1, Issue 3, *eOphthalmology Review* newsletter on *Retinal Vein Occlusion*. Our guest for that issue is Dr. Peter Campochiaro from Johns Hopkins University. This activity has been developed for ophthalmologists and retina specialists, and there are no fees or prerequisites for participating in this activity. The accreditation and credit designation statements can be found at the end of this podcast, and for additional information about accreditation, Hopkins policies, and expiration dates, and to take the posttest to receive credit on line, please go to our website newsletter archive, [www.eophthalmologyreview.org](http://www.eophthalmologyreview.org), and click on the issue 4 podcast link.

Learning objectives are that after completing this activity, participants will demonstrate the ability to:

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- Determine patient characteristics that favor one treatment modality over another.

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I'm **DR. NEIL BRESSLER**, the course director of *eOphthalmology Review*, and on the line we have with us Dr. Peter Campochiaro, the Eccles Professor of Ophthalmology and Neuroscience at the Wilmer Eye Institute at the Johns Hopkins University in Baltimore Maryland.

Dr. Campochiaro has indicated that he has served on advisory boards for Genentech, Pfizer, and Regeneron. He has also served as a consultant for Bristol-Myers Squibb, Genentech, GlaxoSmithKline, Lpath Incorporated, Pfizer, and Regeneron. And he has received grants and research support from Alcon, Alimera Sciences, Genentech, Genzyme, GlaxoSmithKline, and Molecular Partners.

The presentation today will include off-label discussions of bevacizumab and triamcinolone.

Dr. Campochiaro, welcome to this *eOphthalmology Review* podcast.

**DR. PETER CAMPOCHIARO:** Thanks, Neil, it's a pleasure to participate.

**DR. BRESSLER:** So now, let's see how we can take the information that was in Volume 1, Issue 3, specifically where we discussed various treatments including ranibizumab in the BRAVO and CRUISE trials, and intraocular corticosteroids in the SCORE study and the GENEVA study. In this way we can see how that information might apply to a particular case. So Dr. Campochiaro, perhaps you could tell us about our initial case.

**DR. CAMPOCHIARO:** A 60-year-old gentleman had had good vision in his right eye until two weeks ago, when he experienced severe loss of vision. His examination showed a vision of 20/200 with numerous intraretinal hemorrhages and cotton wool patches throughout the retina and severe edema.

**DR. BRESSLER:** I think one of the first things that comes to mind is, how do you even explain to this patient what happened to his vision and why it's so decreased

**DR. CAMPOCHIARO:** What I generally do is make an analogy to the plugging of a sink, that he's had an occlusion in the main venous outflow channel of the eye, which results in a backup of fluid. That results in some hemorrhages and some edema, but also some increase in the tissue pressure within the retina. As a result, the flow of blood into the eye is also compromised so that some areas of the retina are lacking in oxygen. And because of that lack of oxygen, the retina produces an increased amount of vascular endothelial growth factor, or VEGF. Although the occlusion itself is the precipitating event, this production of VEGF also contributes to a lot of the problems. It causes more edema and more hemorrhages, and it really adds to the problems.

Right now we don't have a good way to get rid of the occlusion itself, but we do have treatments that help us deal with the VEGF.

**DR. BRESSLER:** What kind of treatments do you explain to him might be possible for this swelling or edema that has been associated with his vision loss?

**DR. CAMPOCHIARO:** I explain that there are now some good drugs that bind specifically to VEGF. One is ranibizumab, which is an antibody fragment, and the other is bevacizumab, which is a full-length antibody. And then there are also intraocular steroids, which don't bind directly to VEGF, but they decrease somewhat the production of VEGF in the retina. So those are three possible alternatives in treatment.

**DR. BRESSLER:** And typically, what would you recommend in this particular case as far as an initial treatment approach for the patient? What would you tell him you might initiate for treatment?

**DR. CAMPOCHIARO:** I explain to the patient that the intraocular steroids have some additional complications above and beyond those of the anti-VEGF drugs. They can cause progression of cataract and can also cause increase in intraocular pressure and glaucoma, and they carry a small risk of endophthalmitis, whereas the anti-VEGF drugs have only that small risk of endophthalmitis. So in general, I recommend anti-VEGF drugs initially.

**DR. BRESSLER:** Now, as we understood from the newsletter, the trials had attempted using six monthly injections initially when treating this macular edema. Do you typically recommend to the patient that they likely will be undergoing these six monthly injections, or do you recommend that perhaps you evaluate the eye and treat as needed over those first six months?

**DR. CAMPOCHIARO:** Generally, I will use six injections. I try to explain to them that this is a problem in which the occlusion trips things off, but the production of VEGF really participates. And once the VEGF levels are high, it can exacerbate the disease to increase the edema but also increase capillary nonperfusion.

The trials have shown that all patients with vein occlusions, either branch or central retinal vein occlusions, have this increase in capillary nonperfusion over time. But if you block the VEGF, the nonperfusion is reduced. So for that reason and for the reason that patients can have a better longer-term outcome with early aggressive treatment with anti-VEGF treatments, I tend to recommend this period of six months of treatment.

**DR. BRESSLER:** Also in the newsletter we saw from the CRUISE study that after month six, there was a slight decline in the vision and there was perhaps some recovery thereafter. What do you think was going on there, and how should that affect perhaps our planning of how to manage these patients in the second six months?

**DR. CAMPOCHIARO:** That's a very interesting observation, and it suggests that even after getting injections every month for six months, these patients have ongoing production of VEGF. As soon as the injections are withdrawn, a significant number of patients have recurrence of the edema. And as a result, the FDA, when they evaluated these data, suggested that perhaps this means that the patients were withdrawn to PRN treatment a little bit too soon. One of the questions they wanted answered in a postmarketing study is, would patients be better off if they had a longer period of monthly treatment and didn't go to PRN treatment at six months?

**DR. BRESSLER:** So tell me, how might this be tested to figure out if perhaps not just six monthly injections, but perhaps a greater number of monthly injections should be considered, how is that planned to be tested?

**DR. CAMPOCHIARO:** It is being tested in the SHORE trial, in which patients with vein occlusion, either branch or central retinal vein occlusions, receive seven injections of 0.5 mg of ranibizumab between baseline and month six, and then at month six it is determined whether they're randomized, based on whether they meet retreatment criteria.

If they don't meet retreatment criteria, they just continue to receive monthly injections. But once they don't meet retreatment criteria, they are randomized either to receive monthly injections or to go to PRN.

**DR. BRESSLER:** I see, so in that way we may find out when they are randomly assigned to continued monthly injections, if that gives us any better results, or if, in fact, just going back to PRN after month six maybe gives you the same result. I think that will be very important.

Now let's take this patient for now, because many of us have been using an anti-VEGF therapy for over six months. Let's say this patient had some improvement, perhaps as good as 20/50, which is a substantial improvement, but after six injections a lot of fluid

still remains in the macula. What do you do at this point when you have treated six times, perhaps the vision is improved, but maybe there is, we'll say, 430 microns of central subfield thickening?

**DR. CAMPOCHIARO:** What I try to do, Neil, is to determine whether there's been any progress in terms of improvement over time in the edema and the vision. If there has been some evidence of improvement over time, I tend to recommend continuing the course.

Sometimes it's difficult to determine, because patients may come back every month and the thickness is roughly about the same, but their vision may be improving slightly. And sometimes it's useful to bring a patient back a little bit more quickly, perhaps at one week, and determine whether they're getting that reduction in edema that we normally see early on after VEGF antagonist. And it's just not lasting a complete month.

**DR. BRESSLER:** What if they came back a week later and it was only a little better? In this case I'm discussing with persistent edema, it went from 430 we'll say to 400. I wouldn't expect it would necessarily get that much better over the next few weeks. Do you just presume this person has reached a point of stability and you're done? Would you consider any other treatments? How might you approach that?

**DR. CAMPOCHIARO:** I would at least have a discussion with the patients about the intraocular steroids. And note that in some cases they can be helpful, even when VEGF antagonists have had limited effect.

**DR. BRESSLER:** I think that was very helpful, and now we'll go on to another case. So thank you again, and I think we'll go on to case involving a branch retinal vein occlusion.

**DR. CAMPOCHIARO:** Okay, Neil. This is a case of a 65-year-old female who had good vision in her left eye until one month ago when she became aware of reduced vision. She was diagnosed with a branch vein occlusion and told that her vision was 20/80. She had severe intraretinal hemorrhage and was told that it would be best to wait until the hemorrhage clears before considering any treatment.

She comes in to see her physician for a second opinion. Her best corrected visual acuity was 20/70 and there was severe hemorrhage and edema in the macula.

**DR. BRESSLER:** As I understand it, this patient is reported to you as a branch vein occlusion with some macular edema, and it's recent. What do you recommend for these patients: do you recommend an initial observation period, do you recommend initiating some treatment, and if so, what treatment?

**DR. CAMPOCHIARO:** First of all, I explain to them again sort of the background of what causes this problem that it's an occlusion, but this time on a smaller blood vessel and that with a branch vein occlusion.

Then I mention that, just as in central vein occlusion, once this occlusion occurs, it causes reduced flow of blood into the eye and as a result, increased production of VEGF. And I mention that good treatments are available for it that can have a substantial benefit right from the outset. So I generally recommend treatment right away.

**DR. BRESSLER:** Previously we had the option of considering laser for branch vein occlusions with macular edema, yet I notice many of our colleagues now consider initiating with an anti-VEGF drug. Which do you recommend to this patient if she wanted treatment and did not want to wait to see if there was spontaneous improvement? Would you recommend laser, would you recommend an anti-VEGF treatment, or something else?

**DR. CAMPOCHIARO:** One thing you have to consider is how much intraretinal hemorrhage is there. Because if there is a lot of intraretinal hemorrhage, laser is not safe because it can cause some damage to the inner portions of the retina.

The anti-VEGF treatments cause the hemorrhage to resolve more quickly, and they also cause a very rapid improvement in edema, whereas lasers have a relatively slow effect. So generally I'll recommend starting off with an anti-VEGF treatment.

**DR. BRESSLER:** In the companion piece, the eOphthalmology Newsletter, we also discuss the possibility of using intraocular corticosteroids for macular edema from a branch retinal vein occlusion.

Why might you choose to start with an anti-VEGF drug over an intraocular corticosteroid?

**DR. CAMPOCHIARO:** The intraocular corticosteroids have additional side effects of causing progression of cataract and also potentially causing increased intraocular pressure and glaucoma. So if a patient is pseudophakic or if there are other extenuating circumstances that make the steroid treatment potentially safer that becomes more of a consideration. But in a phakic patient, generally I'm going to lean toward the anti-VEGF treatment.

**DR. BRESSLER:** So let's presume that this patient started on an anti-VEGF regimen and got an injection of ranibizumab, and a month later the visual acuity improved somewhat from 20/70 all the way up to 20/40 and there was substantial improvement in edema, but there was still some edema present. She gets two additional treatments, so now she's had three monthly injections of ranibizumab, and when she comes back the visual acuity is 20/25, and there is no residual edema in the eye. Would you continue anti-VEGF injections or would you observe at this point?

**DR. CAMPOCHIARO:** My tendency is to continue the anti-VEGF treatments, for the reasons that I mentioned before: there are problems with the high levels of VEGF causing additional complications, so I would like to keep a very good suppression early on.

With a patient who is doing as well as that, if she wants to hold off on injection, I don't feel so strongly that I insist on it. But all things being equal, I would prefer to treat aggressively initially and do the full six months of treatment.

**DR. BRESSLER:** So this patient had six monthly injections, and not only did the edema not come back, the visual acuity continued to improve and now was 20/20 and there was still no edema six months after all of these injections. What would you do at this point, would you observe?

**DR. CAMPOCHIARO:** Yes, at this point I would observe and recommend that the patient still continue pretty frequent follow-up because I want to see if there's recurrent edema.

**DR. BRESSLER:** Let's say the patient came back a month later. It's not uncommon for us to see the edema come back. Would you then just resume the

anti-VEGF drug? Would you consider laser treatment? Something else?

**DR. CAMPOCHIARO:** I would discuss with the patient that she could continue with the anti-VEGF treatment because we know that it's had a good response. We also know that after six treatments the edema has come back, and we don't know how long she is going to require injections to get to a period where she can go without injections and still be edema-free.

I note that grid laser can help get her to the point where she no longer needs injection a little faster. So I bring up that discussion again and just let the patient decide whether she would like to continue with the PRN treatments of anti-VEGF, or go to grid laser and then also with PRN anti-VEGF.

**DR. BRESSLER:** Of course, we now have excellent information on what happens for the first six months, so at least it helps guide us, and as you said, we don't know whether we should be adding more treatment, should it be laser, should it be anti-VEGF. So I think we will benefit from seeing whether other treatments or regimens are beneficial in the future.

Now I understand some other studies are trying to figure out whether just putting in a scatter of laser to the areas of nonperfusion might also reduce the need for additional retreatments. Do you want to tell me a little about that investigation?

**DR. CAMPOCHIARO:** Yes, in the RELATE trial, we're looking at whether treatment of scatter photocoagulation to areas of nonperfusion can get patients to a state where they no longer need injections more quickly. We know that those areas of poor perfusion produce increased VEGF, and therefore it's important to know whether laser treatment can decrease the VEGF levels and therefore decrease the need for injections.

In that trial, patients are getting treatment with anti-VEGF for six months and then they're randomized to get either laser plus PRN anti-VEGF or just PRN anti-VEGF.

**DR. BRESSLER:** We have certainly come a long way with treating this, yet it's clear we still have a lot to learn about it. I look forward to the information that will come out of that study and some other studies in the future.

We'll return in a moment with Dr. Peter Campochiaro from Johns Hopkins University as we discuss cases of retinal vein occlusion.

**DR. BRESSLER:** Hello, I'm Dr. Neil Bressler, I'm the James P. Gills Professor of Ophthalmology, Chief of the Retina Division at the Wilmer Eye Institute at the Johns Hopkins University and course director for eOphthalmology Review.

eOphthalmology Review is a CME-certified program presented by The Johns Hopkins University School of Medicine. eOphthalmology Review has two parts: a newsletter delivered by email and podcasts like the one you are currently listening to. Each presents current, concise, peer-reviewed literature reviews and commentary in areas of importance to ophthalmologists, retina specialists, and retina fellows.

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**DR. BRESSLER:** Welcome back to this eOphthalmology Review podcast. I'm Neil Bressler, Course Director of the program, and our topic is retinal vein occlusion. Our guest is Dr. Peter Campochiaro, the Eccles Professor of Ophthalmology and Neuroscience at the Wilmer Eye Institute at The Johns Hopkins University.

We've been looking at how some of the new information Dr. Campochiaro discussed in the newsletter issue can be applied in the office in patients who have retinal vein occlusion and macular edema. I think we have time for one more case, so Dr. Campochiaro, why don't you give us yet another challenging case to discuss.

**DR. CAMPOCHIARO:** Okay, Neil, this is a case of a 58-year-old gentleman with glaucoma who had progressive visual field loss despite maximal medical therapy in his right eye. He had a trabeculectomy, and postoperatively he had a functioning bleb, an intraocular pressure of 8, and visual acuity of 20/30 in his right eye. He did well for about a year but then had sudden decrease in vision to 20/200, and a central vein occlusion was found in his right eye. His foveal thickness was 550 microns.

**DR. BRESSLER:** As is so often the case, retinal vein occlusions sometimes present in very complex patients, often with some very difficult glaucoma history, as in this patient. So this patient has a central retinal vein occlusion, quite poor vision at 20/200, and a very thickened central subfield—what would you recommend for him?

**DR. CAMPOCHIARO:** We don't have good data on the pharmacokinetics of anti-VEGF drugs in eyes that have had successful filtration surgery, but it's my impression that there's a shorter duration of effect. Since the patient has already had filtration surgery, one of the major risk factors for intraocular steroids has been eliminated, so that raises the possibility of a dexamethasone implant as a useful option, because by providing sustained release of a steroid, it can overcome the problems with the drug leaving the eye quickly from filtration surgery.

However, this patient is still phakic and so there is still the problem of progression of cataract. So I think I would recommend to this patient considering an anti-VEGF drug.

**DR. BRESSLER:** Even if the patient was pseudophakic, do you have any concern about using a corticosteroid implant, given his history of glaucoma and a working bleb at this time?

**DR. CAMPOCHIARO:** No, I think this is actually a good situation to consider a steroid implant because the patient really doesn't have a risk of decreasing outflow because the filtration bleb is taking care of that, and actually steroids help in terms of reducing the possibility of scarring. So from the standpoint of glaucoma, this is a good situation for intraocular steroids.

**DR. BRESSLER:** So the patient did have an intraocular injection of ranibizumab and returned

a month later and almost nothing had changed. His visual acuity was still 20/200 and the central subfield was still thickened at about 500 microns. What would you recommend, what would you discuss with the patient?

**DR. CAMPOCHIARO:** I don't think a single injection is an adequate trial for an anti-VEGF agent. So since we've started down that path, I would tend to recommend continuing injections with anti-VEGF. But I would go through the discussion again about the risk/benefit ratio of intraocular steroids.

**DR. BRESSLER:** So now the patient went through six monthly injections of ranibizumab and there was some improvement in the visual acuity, up to 20/80, but the central foveal thickness was still about 400 microns. So the person's vision improved from 20/200 to 20/80, thickness improved from 500 to 400, but still quite abnormal. After these six injections, would you change your recommendation, would you continue ranibizumab, or switch to something else?

**DR. CAMPOCHIARO:** I think I would again discuss the potential benefits of a sustained release of steroids in the eye in this situation. But also note that there is still a risk of progression of cataract with that route. I think the patient could still consider continuing anti-VEGF treatments because they have provided some benefit and it's likely that some additional benefit would be provided in the future.

So I would present all of this to the patient and then let him decide which choice he would like.

**DR. BRESSLER:** So this patient did continue the anti-VEGF therapy. He was treated over the next six months, and by month 12, visual acuity remained 20/80, but the thickness had decreased to about 300 to 350 microns depending on the visit. But over this year there has been substantially more nuclear opacity. So how do we handle this, maybe it would be better than 20/80 if we took the cataract out? What would you discuss now in this very complex patient?

**DR. CAMPOCHIARO:** I think in this situation, the thing that really limits you from using the steroid now has been eliminated, because the patient now has cataract and is likely to need cataract surgery to get the best possible vision. And the steroid can actually be of benefit in that situation because

sometimes patients with macular edema get exacerbation after cataract surgery and that might be helped by the steroid.

I think at this point I would recommend an intraocular dexamethasone implant and refer him for cataract surgery.

**DR. BRESSLER:** This is certainly a challenging case, and I appreciate your walking us through that. It's very helpful in planning the management of these cases.

I want to thank Dr. Peter Campochiaro from the Wilmer Eye Institute at Johns Hopkins for participating in this eOphthalmology Review podcast on the management of retinal vein occlusions with macular edema.

**DR. CAMPOCHIARO:** Thank you, Neil. It's been a pleasure participating in this very interesting program.

**DR. BRESSLER:** This podcast is presented in conjunction with the eOphthalmology Review Newsletter, a peer-reviewed, CME-certified literature review emailed monthly to ophthalmologists, including retina specialists. The Johns Hopkins University School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. For physicians, the Johns Hopkins University School of Medicine designates this enduring material for a maximum of 0.5 *AMA, PRA, Category 1 credit(s)*<sup>™</sup>. Physicians should claim only the credit commensurate only with the extent of their participation in this activity. This educational resource is provided without charge, but registration is required.

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