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# Improving Adherence and Persistence With Durable Anti-VEGF Therapies for nAMD

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**Dr. Do:**
Hello and welcome to our Case Consult, Improving Adherence and Persistence with Durable Anti-VEGF Therapies for Neovascular Age-related Macular Degeneration. I'm Dr. Diana Do, Vice Chair for Clinical Affairs and Professor of Ophthalmology at the Byers Eye Institute at Stanford University School of Medicine. Joining me tonight is my friend and colleague, Dr. Peter Kaiser, Professor of Ophthalmology, the Cheney Family endowed Chair in Ophthalmology at the Cole Eye Institute at the Cleveland Clinic. Peter, welcome.

**Dr. Kaiser:**
Thank you, Diana. Pleasure to be here.

**Dr. Do:**
Tonight, I want to discuss an important clinical case with you and get your feedback, Peter, on how to manage very interesting and challenging cases with neovascular age-related macular degeneration. Today's case should illustrate the burden of treatment that many patients have with our current anti-VEGF therapies.

In addition, we'll talk about strategies to reduce the burden of frequent visits and then how to incorporate new therapies that were recently FDA approved. And finally, we'll just talk about how do we define treatment success.

Let's start off with this case that I saw in the clinic. This is a 72-year-old gentleman who was referred for a second opinion regarding blurry vision due to wet age-related macular degeneration. He was complaining of blurred, decreased vision in the right eye. He was treated by a prior retina specialist for his active wet AMD. Of note, in his fellow left eye, that eye has poor vision due to a scar from advanced wet macular degeneration.

Peter, in your clinic you must also see many patients who present with different levels of vision. What do you think about patients who have one good seeing eye and the other eye already lost to macular degeneration? Do you treat them differently?

**Dr. Kaiser:**
You know, I think that's a very good question, one we see all the time. An obviously, the patient knows exactly what will happen to their right eye, their good eye, in the, you know, either absence of treatment or if we're not aggressive enough. And so, because of that, knowing the outcome in the fellow eye, I do treat these patients a little differently. If you have a backup eye, so to speak, you can be a little bit more cavalier, but in this case, we're going to be very aggressive. We're going to want to switch quickly medications if one is not working, because we have several available to us. And I tell these patients, you know, even when you're doing well, I'm probably going

to continue to treat you because I want to avoid some of the complications down the road that could happen if we were to stop treatment.

**Dr. Do:**
I agree. Those are great insights with this monocular patient. We really want to optimize the vision in the good right eye.

We would look back at his history, he has received prior anti-VEGF therapy, both with off-label bevacizumab, and then more recently with aflibercept 2 milligrams. His last injection at the outside Retina Clinic was 2 months ago.

If a patient who's had prior treatment comes to your clinic, do you also employ a different strategy because this is not a treatment naive patient?

**Dr. Kaiser:**
You know this is a sort of, second opinion that we all see in our practice almost on a daily basis and it's important for people to understand that off-label bevacizumab is the treatment of choice for many, many retina specialists to start therapy. In addition, there are many insurance companies that will ask us to start with bevacizumab, and then if the patients not doing well or not responding in a way we expect, we're allowed to switch the medication. In this case, the previous physician started the patient on aflibercept, which would be a very reasonable switch.

And so, when I get a patient like this in my clinic, ideally, I ask them, you know, do you have a previous OCT scan? Did your previous doctor bring it? Did you happen to take a picture of it? Because I really want to know, was their last anti-VEGF injection 2 months ago because they're doing very well and so they extended the interval, or is the patient coming to me with similar appearance as they had previously 2 months prior?

**Dr. Do:**
Great, very good practical advice. The relevant medical history shows that he has a history of hypertension and hypercholesterolemia. He's taking medicines for those systemic conditions. And important social history reveals that this patient does not drive, and he relies on his daughter, who is working to take him to visits.

This patient has demonstrated expressed to me that there is a burden of coming to the clinic, especially because it takes not only his time, but the time of his working-age adult daughter to bring him here, so he feels a little guilty about that as well.

You live in Cleveland and have a lot of patients traveling long distances to come see you as well. Is there anything that you tell them about these medicines in order to help their compliance, given it's so challenging to come back so frequently for anti-VEGF therapy?

**Dr. Kaiser:**
Yeah, I think this is one of the common situations, and what I really like to do is to have the caregiver, the daughter, the friend who's driving the patient in listen to what I have to say and really impress upon them the importance of continuing the treatment and if necessary, more aggressively, especially in a monocular patient. But we're going to do our absolute best to minimize the number of treatments that we give the patient to, of course, be cognizant of the fact that they may have to take a day off from work. I have some patients that have to literally drive from another state, pick up their parent, bring them to Cleveland, bring them back, and then drive home. This is a, truly, a one-day visit, a full day for them. So, you know, I think it's important that they understand why we're doing the treatment so frequently and so, I really like to have the patient and the caregiver in the room so that they can understand that.

**Dr. Do:**
Let's look at the image that we obtained at our clinic, and he did not have access to his prior images. So, on today's examination the affected right eye was 20/80. The left eye, which has the macular scar is 20/300. The intraocular pressures are normal. OCT was obtained. It shows presence of subretinal fluid as well as an elevated pigment epithelial attachment, which I suspect is a fibrovascular PED.

At this time, Peter, do you think there is utility to additional imaging modalities, such as forcing angiography? Do you think it's necessary in this case?

**Dr. Kaiser:**
No, in this case, no. This is a very typical Type 1 choroidal neovascular membrane. If I had any question, or I was concerned that this may be some sort of masquerade, I would have a very low threshold for doing a fluorescein angiogram. If this was, say, an Asian patient or a pigmented patient, and I was concerned about PCV, I would have a low threshold to get an ICG. In my practice, really, an OCT and an OCT angiogram are all that I would need to decide about treatment in a wet AMD patient.

**Dr. Do:**

I agree. I think we're using fluorescein angiography a little bit more selectively, especially because in the past there was a shortage, actually, of the fluorescein dye. And OCT really is essential in making the diagnosis and monitoring the patient.

So, this patient obviously still has active wet AMD. What would you recommend at this time? There are some options that we could consider, using aflibercept 2 milligrams, which he had received about 2 months ago, but now shortening the interval, let's say 4 weeks for his next visit. Or we can use aflibercept 2 milligrams and maybe go 6 weeks. Or would you switch right now to the new FDA approved aflibercept 8 milligrams? And would you consider monthly doses before then extending the treatment interval? Or, we also have FDA approved faricimab, which is also an effective and safe treatment option. What do you think is reasonable in this case, Peter?

**Dr. Kaiser:**
Well, the interesting thing, Diana, is all of these are really reasonable, right? So, for me, you know, they're 2 months out, they have obvious fluid, this doesn't say that aflibercept 2 milligrams has actually failed, unless we have previous scans to look at to see, indeed, the fluid is either the same or worse. So, a very reasonable option would be to lower the treatment interval, because we know that two months is too long, to either 4 or 6 weeks to see how the patient did. But it's also just as reasonable to say we should switch this patient to either faricimab or high-dose aflibercept at 8 milligrams.

And in terms of loading dose, I usually don't load at that point, but in this case, we don't really know what the patient's previous, how – you know, basically they were being treated previously. I probably would start with a month or 6-week dosing for any of the other two, also, just to see how the patient did.

**Dr. Do:**
We have to take into account all these factors in addition to patient's prior history, you know, what the limitations of their transportation are, you know, if they have any comorbidities that might affect their outcomes.

So, in this patient, I decided to continue with aflibercept 2 milligrams, which he had received about 2 months ago, but I decided to shorten the interval. So, I told him, let's treat you with the aflibercept 2 milligrams, but see you in 4 to 6 weeks to see the response, and let's take a look.

So, we gave him the medicine, aflibercept 2 milligrams. This is 6 weeks after that treatment. The vision still remains 20/80 and there still is fluid. It's shifted a little bit, but there still is subretinal fluid.

Peter, what do you think we should recommend at this time point?

**Dr. Kaiser:**
So, you know, this is interesting, right? The patient's doing – is relatively stable on the OCT, stable on visual acuity, but again, this is a monocular patient. We need to be more aggressive. The aflibercept absolutely should have lasted 6 weeks. So now we know we need to consider something different, and if something different would be either to switch to patient to faricimab or to high-dose aflibercept.

**Dr. Do:**
Good. So, I think I was thinking along the lines of what you suggested, that there still is disease activity with the 6-week interval and let's consider something else. And it's very reasonable, as you said, to look at these new FDA approved therapies, aflibercept 8 milligrams, which has four times the molar dose compared to aflibercept 2 milligrams. Or even switching to faricimab, which inhibits both VEGF-A and angiopoietin-2.

Let's look at what I did. This is the patient. Received 8 milligrams. Six weeks later, he comes back. The vision has improved by one eye to 20/70 and we can see that that sub retinal fluid has resolved, and the height of the pigment epithelial attachment appears to be a little bit lower.

Do you think this is a reasonable image of success in this patient?

**Dr. Kaiser:**
You know, certainly this is a great outcome. The fluid is definitively better. You notice that the pigment epithelial attachment is actually, also slightly better. So, this patient's doing well. So, they've definitively responded at a similar interval, and the big question you're going to need to wrestle with now is do I keep them at this interval, or do I extend already at this stage?

**Dr. Do:**
Yes, I think we could do either. We can give another injection at 6 weeks and see how they do or maybe some people would now think, with the 8 milligrams of aflibercept, that might provide longer durability. But I think this is an excellent case that shows, with our new anti-VEGF therapies there is another option for patients that might be more beneficial and have more durability to decrease the treatment burden.

Thank you, Peter, for joining me with this case and providing your careful insights.

**Dr. Kaiser:**
Thank you for having me, Diana.

**Announcer:**
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