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New Perspectives on Managing DR: Applying the Latest Strategies Into Clinical Practice

Announcer:
Welcome to CME on ReachMD. This activity is part of a special series titled “The Mission Continues: Saving Sight Through Early Referral, Diagnosis and Treatment for DR/DME” and is provided in partnership with the National Eye Institute of the National Institutes of Health, of the U.S. Department of Health and Human Services, along with Prova Education. It’s supported by an independent educational grant from Regeneron Pharmaceuticals. To view this activity or others in the series, please visit EyeHealthAcademy.org/SaveSight

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Dr. Sridhar:
New data have come out that add to our understanding of the management of diabetic retinopathy. What are those data, and what impact will they have on our general ophthalmology colleagues?

This is CME on ReachMD. I’m Dr. Jay Sridhar, and joining me for today’s discussion is Dr. Avni Finn. Avni, welcome.

Dr. Finn:
Thanks. It’s great to be here with you, Jay.

Dr. Sridhar:
Avni, we know that diabetic retinopathy can present in any of the 34 million patients with diabetes in the United States, and the risk increases with a higher hemoglobin A1C and longer duration of this microvascular disease. Avni, what is the risk of blindness in our patients when we first diagnose diabetic retinopathy?

Dr. Finn:
That’s a great question, Jay, and one that we’re still answering. But we can see that the risk of blindness increases with diabetic retinopathy severity. There is a great paper that was recently published, that showed that the risk of sustained blindness increases as we go from moderate to severe to proliferative diabetic retinopathy. We see that those patients with NPDR are over 2 times more likely to develop sustained blindness, and those patients with proliferative diabetic retinopathy are 4 times more likely to develop sustained blindness. And this, for us, underscores a need for early diagnosis of NPDR and close follow-up, and then also talking to our patients about the clinical implications of their disease and any modifiable risk factors.

Dr. Sridhar:
Great point, Avni. The Protocol W and PANORAMA trials looked at anti-VEGF treatment in patients with moderate and severe non-proliferative diabetic retinopathy. Can you remind the listeners a little bit about what the different stages of NPDR look like?

Dr. Finn:
Yes, so grading of retinopathy can be difficult, and in studies, we use the diabetic retinopathy severity scale, but this is complex and often not clinically useful. So in clinic, we’ll often use the 4-2-1 rule to diagnose severe NPDR. We’ve created a short animation here to

help us visualize the progression of NPDR and diagnose it. Let's take a look.

[3D ANIMATION PLAYS]

Announcer:
We know that patients with diabetes are at risk for nonproliferative diabetic retinopathy, or N-P-D-R, which can be broadly classified as mild, moderate, and severe.

Mild NPDR is characterized by the presence of at least one microaneurysm.

The progression to moderate NPDR is signaled by the presence of multiple microaneurysms along with other findings such as dot blot hemorrhages, venous beading, and/or cotton wool spots.

Severe NPDR can be identified using the 4-2-1 rule. The classification applies if the retina has any of the following criteria: hemorrhages in all four quadrants, venous beading in two or more quadrants, or prominent intraretinal microvascular abnormalities, or IRMA, in one quadrant.

These seemingly small distinctions are significant because they influence the use of newer treatment protocols for preventing vision loss.

Dr. Sridhar:
Now that we've seen how NPDR can progress, it's easier to appreciate why it's so important to be able to visualize as much of the retina as possible to make an accurate diagnosis. Avni, you want to share some details on this patient case for us?

Dr. Finn:
Sure. So this was a patient of mine, and she was a very young patient in her mid-30s and had type 1 diabetes for over 20 years. She was actually very well controlled and knew a lot about her disease but came in for the first time noticing new spots in her left eye. We saw her right eye, which was her eye that was completely asymptomatic, might have had some areas of neovascularization. And what this case highlighted for me was the utility of wide-field fluorescein angiogram [FA]. You can see on the wide-field FA here that she really had multiple areas of neovascularization with leakage throughout her retina, and these were really not as apparent on fundus exam as they were on fluorescein angiography. So for my patients with diabetic retinopathy, especially if they've reached the more severe non-proliferative disease and proliferative disease, I really like to get wide-field fluorescein angiography and wide-field imaging on them.

Dr. Sridhar:
Yeah, it's a great point. Wide-field angiography and wide-field imaging, at least for me, has drastically kind of affected how I view these patients. I'm with you. Sometimes even before they get to more severe stages clinically, I'll get wide-field photos and wide-field angiography, because I think we often underestimate the severity of retinopathy, and it's helpful guidance and monitoring, especially with the newer treatment options we have available based on trial data.

Dr. Finn:
For our audience, Jay, I'd also like to point them to a place that they can practice their diagnostic skills in our image-based activity, by going to EyeHealthAcademy.org/SaveSight.

Dr. Sridhar:
For those just tuning in, this is CME on ReachMD. I'm Dr. Jay Sridhar, and today Dr. Avni Finn and I are discussing new evidence around the management of patients with non-proliferative diabetic retinopathy and what that means for our clinical practice.

Avni, we've referenced Protocol W and PANORAMA, where patients with moderate and severe non-proliferative diabetic retinopathy were treated with anti-VEGF injections. Avni, what did the data from these trials show us?

Dr. Finn:
Sure, Jay. So these trials showed us that early treatment of moderate to severe NPDR can reduce risk of vision-threatening complications. So starting with Protocol W, this was a prospective study that enrolled eyes that had moderate to severe NPDR without diabetic macular edema. And the study was designed to evaluate whether giving these eyes intravitreal aflibercept could prevent proliferative diabetic retinopathy and also center-involving DME in these eyes with advanced retinopathy. The primary outcome that they looked at was the development of DME and vision loss, and we saw that preventive aflibercept did reduce the incidence of center-involving DME 3-fold in these patients, and PDR 2-fold in these patients. And then PANORAMA, which was a phase 3, double-blind trial that assigned patients to either getting aflibercept every 16 weeks or every 8 weeks or getting sham injections, showed us that those patients with severe NPDR without DME that were treated with aflibercept were able to achieve a 2-step or greater improvement in their DRSS score

And those patients treated with more frequent injections had a greater benefit than those treated less frequently. We saw that these patients also had a decreased risk of PDR and complications like neovascularization and DME that can be vision-threatening.

So, Jay, based on these data, how do you manage your patients with moderate to severe NPDR?

Dr. Sridhar:
That's the million-dollar question, after a wonderful summary. You know, it's so interesting, because these are patients, traditionally, where we did not intervene. If they did not have macular edema, they're generally asymptomatic at these stages, we were told, you know, counsel patient on blood sugar and blood pressure control – which is still important today – and observe and watch these patients closely. You know, the big thing I took from this trial data, when I talk to these patients, is I initiate the conversation about anti-VEGF therapy options earlier. I think that I don't necessarily start all these patients on treatment, but I look at the sham group, and I use that data to inform the patients, I use the imaging findings to inform the patients, and we begin that discussion. And I watch these patients very closely. I'm more likely to repeat ultra-widefield imaging or angiography more often in these patients, and if we start to see signs of progression, then we start to talk about recommending injection therapy with anti-VEGF.

And this is a case that kind of shows us what can happen in these patients. This is a 35-year-old man with type 2 diabetes for 8 years. Unfortunately, like a lot of our patients, he does not know his A1c, and he is asymptomatic. He comes in just for routine follow-up. He is 20/20 in both eyes. At the time he was seen, you know, he had evidence of non-proliferative diabetic retinopathy on his photography and examination, but was told at that point, hey, we're going to watch you closely; come back in 4 months. Unfortunately, as it happens in many of our diabetics, there is a real gap in follow-up and a loss to follow-up, and the patient didn't come back for another 4 years. And you can see in the fundus photography at 4 years later, this is now a patient with proliferative diabetic retinopathy with high-risk characteristics, with neovascularization, with subhyaloid hemorrhage, and this patient has migrated to a different category of risk for blindness.

So based on a case like this, Avni, in the context of the data you presented, how do you kind of interpret how to put this all together for your patients?

Dr. Finn:
Yeah, Jay, that's an excellent question. You know, for me, this data really provides a starting point to have a conversation with my patients. Previously with patients like this, I would normally have counseled them on clinical factors, on improving their blood glucose, on improving their blood pressure. And although I still very much do that, because, as we know, diabetic retinopathy is an indicator of systemic disease. This gives me a starting point to have a discussion about potentially starting treatment on these patients earlier, because, as we know, starting treatment on these patients earlier, through these trials, has shown us that we can potentially prevent vision-threatening complications.

Dr. Sridhar:
Yeah, those are wonderful points, and I think, again, I really look at the sham group and how they did in those 2 trials, PANORAMA and Protocol W. And you put it in the context of the real world, where patients often have difficulty with adherence to appointments. If you have patients who can adhere to appointments and you can get them in, well, the data from Protocol W suggests that the visual outcomes can be the same, but that's a clinical trial population. A lot of our patients we saw, with the pandemic and other stressors in life, it's hard to keep coming in for visits to monitor. And so, yes, you do need frequent injections for the injections to work – they work better than less frequent injections, but that ability to modify the disease course is really, really exceptional and such a boon in a field that traditionally did not have options for altering the disease course of these patients.

So, Avni, as we wrap up today, what would you want our listeners to take home as the big messages from this session?

Dr. Finn:
I think the big messages are we're still learning a lot about how to alter and treat patients at earlier courses of disease, and so patients that we might not have otherwise thought about treating with moderate non-proliferative disease, we want to see earlier because we can perhaps offer treatment options to them. And the other thing that is really important is, I think, that ultra-widefield imaging, especially with fluorescein angiogram, can be really helpful in these cases to identify disease earlier, identify areas of nonperfusion, and diagnose disease in patients earlier.

Dr. Sridhar:
Fantastic points. And I would just reinforce that we're in such an exciting time in our field, with our diagnostic tools advancing, like ultra-widefield imaging, with therapeutic options that we now know work based on our trial data. It's just important to get these patients referred appropriately, get them in, get them evaluated, and monitor them closely, even if you aren't going to start treatment early. And then in the patient who does show signs of progression, we will often start treatment now.

So, Avni, thank you so much for your time today and for your wonderful insights into the clinical implications of PANORAMA and Protocol W. It's always a pleasure to talk to you.

Dr. Finn:
Thanks, Jay. It was great to be here with you and talk as well.

Announcer:
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