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Retina Clinic: Current Treatment Options in DME

Announcer:
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Dr. Eichenbaum:
New, more durable treatments are available for patients with diabetic macular edema [DME]. In the past, we've had an armamentarium of treatments with similar durability. Now we have more choices, and we can decide what's best for each patient in clinic.

This is CME on ReachMD, and I'm Dr. David Eichenbaum.

Dr. Barakat:
And I'm Dr. Mark Barakat.

Dr. Eichenbaum:
It's an exciting time for retina, because our choices are increasing, our armamentarium is improving, and we have more commercially available options now with biologics than we ever have had before in our space. There are even more treatment modalities on the horizon, and the pipeline is rich; it is broad; the scope of it is immense.

As we get started, Mark, can you please tell us how you're using the new commercially available modalities to help your patients with diabetic macular edema?

Dr. Barakat:
That's a great question. Well, you know, when we talk about the new modalities, first we have to look back at the old modalities. They work great, don't get me wrong, but the question is what are the burdens? What are the hurdles with the old modalities? And those are basically treatment frequency. There is an issue in terms of the patients coming in, so it's economic or otherwise, well established, certainly in a diabetic population more so than anything else.

And the question is, are we treating these patients sufficiently to get the optimal results that we know we can achieve with these treatments? And so really, it boils down to can we lengthen the interval without losing the efficacy in terms of drying power or in terms of visual acuity? So it's really exciting to have some of these newer options available that promise to do just that.

And the real question then becomes, how do you select certain patients, and when do you make that switch? And that is certainly something that I look forward to discussing with you today.

Dr. Eichenbaum:
I agree, Mark. Our patients need more durable treatment options. Our patients need more access; our patients need more choice for the drug. Our patients need to be able to maintain the results that we see in our randomized controlled trials without succumbing to

treatment burden, which results in real-world outcomes that just don't match what we have in randomized clinical trials. We're hopeful that new agents will allow that to become a reality.

If we look at YOSEMITE and RHINE 2-year data, we're encouraged. This is the first data set ever to look at either treatment-naïve or well washed-out diabetics and treat them with a biologic in a fashion that allows, in the personalized treatment interval arm or what we call the variable treatment arm in the FDA-approved label, to flex and extend over time, starting right after loading with 4 injections in the very first year. If we look at that data through 2 years, almost two-thirds of the patients achieved dosing every 16 weeks, and their visual outcomes match that of patients treated with either faricimab every 8 weeks or aflibercept every 8 weeks. That's dramatic. That's a halving of the treatment burden, and about 80% of the patients achieve parity to the q8-week fixed interval dosing with q12-week or longer dosing. That's the first time we have seen that.

What's especially important in the randomized controlled data, as well as in the real world, over 100,000 commercial faricimab doses given as of today, we have not seen cases of retinal vasculitis or occlusive retinitis related to the use of this drug. That's remarkable.

However, it's not the only durable agent that we now have available for diabetic eye disease. We also have brolucizumab, which was just approved for the treatment of diabetic macular edema.

Mark, you have experience with this data. What can you tell us about the KITE and KESTREL data set?

Dr. Barakat:
Great point. So brolucizumab is yet another option in terms of lengthening the treatment interval for diabetic macular edema patients. From the KITE and KESTREL trials, two phase 3 trials with a loading phase and then ended up extending the interval for patients to 8 and 12 weeks. And in year 2 within KITE, actually extended it to 16 weeks. And it showed us at the year 2 results that somewhere between 33% to 48% of these patients actually went longer and without losing anything in terms of visual acuity compared to the aflibercept control arm or anatomic results, which were both robust and sustained throughout. So that's very encouraging.

And I know we're not talking about KINGFISHER here per se, but that's also an interesting trial because that was monthly brolucizumab versus monthly aflibercept and actually showed anatomic superior gains in the brolucizumab arm compared to aflibercept arm. So there's even a possibility that perhaps we're getting a little bit more bang for our buck with brolucizumab. Now, however, any conversation that includes brolucizumab must also deal with intraocular inflammation and vasculitis. And those rates were, of course, also seen within this data set.

Now, somewhat encouraging was lower rates than seen in the AMD [age-related macular degeneration] population. We're not quite sure why that is. But it still was there somewhere between 2% and 4% in terms of inflammation, approaching 1% in terms of vasculitis, and somewhere in the range between 0.5 and 1.6 or something percent in terms of occlusive issues. So that is a real-world concern, which of course may limit the applicability of brolucizumab in the real world.

For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Mark Barakat, and here with me today is Dr. David Eichenbaum. Together, we're discussing new treatment options for diabetic macular edema and how to best transition them into your clinic.

Now, the question really becomes, David, as you have these options available, how do you apply this? And how do you choose the patient in which to make this transition?

Dr. Eichenbaum:
Well, Mark, you and I are probably earlier adopters of new agents. That's for a variety of reasons. One of which is that we're involved in the clinical trials and we've seen patients go through treatment with these agents pre-commercially, even though we don't know what their treatment assignment is, versus active control with standard of care agents. We know patients are getting these agents and we know patients do well in the trials, so we're likely to reach for them when they become available in our commercial population as well.

Like a lot of docs who do decide to use agents, I do think that you and I probably use new agents in treatment-experienced patients the most, patients who would never be in the clinical trials. Clinical trials are treatment-naïve or well washed-out patients for diabetes. But in my practice, I think 85% or 90% of my faricimab use is in patients who are midstream in their treatment who've been receiving other treatments.

I have a case that demonstrates this. One of my very first faricimab patients was a fellow who's a bilaterally treated patient; he's received over 50 aflibercept injections in both eyes. Prior to that, he received bevacizumab injections. He didn't do well with corticosteroids. He developed an intraocular pressure into the mid to high 30s with the intravitreal dexamethasone implant. And he received aflibercept almost monthly for over 50 doses and never really dried out and was never happy with his vision. I switched him to faricimab midstream. And you'll see after the first injection, he had a subjective and objective improvement. And I attribute that to the second mechanism of action of faricimab, because aflibercept, as we know, is a reliable, potent, high-affinity, anti-VEGF monotherapy.

And faricimab, of course, is a biospecific therapy. And the first thing that I thought of when I saw this patient get better is how blocking the second pathway, the angiopoietin pathway, with the blockade of Ang-2 may have made this anatomical and functional difference.

How about you? How are you using these agents?

Dr. Barakat:
Now you made a really interesting point. I've never quite thought of the fact that we put naïve patients in these clinical trials all the time – you and I and many others – but yet, when we make that transition, I, much like you, I like to transition the previously treated patients first mainly – for a variety of reasons. But one of them, more recently, if I'm going to be frank, is I've had a little bit of experience with brolucizumab, and you don't really know what the real world will show you until 6 months, perhaps a year have gone by. And so, you know, I'm a little bit cautious in testing the water because, to your point, some of these patients were just not in the trial, and we don't quite know how things might interact. Which is why that I'm actually quite pleased that so far with faricimab, the data has been very clean in terms of safety, not just in the trials, but also outside of the trials in a clinical setting.

So my patient that I have here is someone that perhaps didn't get as many aflibercept treatments. He came to me already previously treated, not the greatest historian, but must have had multiple injections according to him. We started him on bevacizumab for a variety of reasons, not least of which was access, frankly, and then later on, transitioned him to aflibercept. Because I also agree with you, aflibercept is a great agent; it does a great job of drying. And it did a great job in drying this eye. Had about a 4- or 5- or 6-week interval. As you can see, they're

transitioning here. And when I tried to flirt with extending him or weaning him off or backing off a little bit and going to 10 weeks, suddenly it starts flaring up again.

And I don't know about you, David. But sooner or later, I just get sick and tired of injecting these eyes over and over and over and keep pounding away with the same thing. Although frankly, I know the data says that we have to.

So finally, when he comes in and at 11 weeks after aflibercept, which is frankly not as far as I wanted to go, but what he wanted to do. Remember, these patients, they don't have the ability to come in as often as we'd like them to. There was a lot of edema present. I made the switch to faricimab, kept the interval the same, the same 11-week interval, and had a drastically improved result in terms of anatomy.

Now frankly, this is an early result for me in this patient. But it's one of those results that you remember, because, again, I'm a huge fan of aflibercept. It works great. And the fact of the matter is, I came in here with this new agent, faricimab, and at least in this one instance, it actually gave me that wow effect that I was hoping for but wasn't quite sure I would see. So this is actually quite a satisfying outcome for me and certainly for the patient.

So the real question is, there's other treatment modalities as well that we really haven't talked about. And one of them is the port delivery system. And so I wanted to pick your brain a little bit about this, David. It's approved for the treatment of neovascular age-related macular degeneration, and it's also currently being studied in patients with diabetic macular edema as well as diabetic retinopathy. And so, you know, I'm not asking you to predict the future, but I guess I am. What do you think we might expect from the port delivery system for the treatment of patients with DME?

Dr. Eichenbaum:
I have a lot of experience with the port delivery system, with PDS. Our site, between me and the other operating surgeon, put in about 2 dozen of them in the phase 2 and phase 3 trials. And we have a third surgeon now who's putting them in in the phase 4 trial. And we're using them commercially as well; at least 2 of the folks in our group have used them commercially. I'm actually implanting my first second eye PDS tomorrow.

So I have a lot of faith in the platform from our experience. The diabetic data, of course, is not yet published. I wouldn't be surprised if PDS is effective in diabetic macular edema, as it's extraordinarily effective in neovascular macular degeneration. The thing we have to kind of grok or get our heads around is the risk of endophthalmitis related to implant exposure. Like any other device, we're going to have to figure out how to be better surgeons, do the procedure more safely, and preserving the efficacy in the patients who have done well and learn how to monitor these patients and take care of the surgical complications, specifically the risk of infection related to an indwelling device inside an eye.

Dr. Barakat:
You know, I completely agree with you. That is one of my hesitations. It's a great platform, it's shown to be very effective in AMD, and I suspect it will be equally so in DME. However, with the infection rates, you know, it's very similar to what we've learned from our colleagues in glaucoma. It's the, you know, having a tube shunt in the eye does impart some degree of risk of infection down the line.

That doesn't mean we stopped doing tube shunts, we just learn how to minimize that with good surgical practices and how to monitor this. And I suspect this will be the way that PDS will be treated going forward as well.

Dr. Eichenbaum:
This has been a great discussion. As we wrap up here, Mark, what's your one key takeaway for our audience today?

Dr. Barakat:
You know, I think the key message is that diabetic macular edema has a high treatment burden. And that's a burden that some of us, no matter how hard we try, have a hard time meeting with the current available treatment options. The new ones coming out, the new ones available here today, actually, offer us the ability to maintain vision, maintain OCT [optical coherence tomography] dryness, and stretch out the interval, which is, you know, a boon to our audience, it’s really exciting. And I look forward to PDS data as well.

Dr. Eichenbaum:
And I’ll add that it’s all about the patients. We're all about equity. We're all about access. We're all about retina care for everybody. And the new agents as well as new delivery systems within the community can partner to make this dream a reality.

That's all the time that we have today. Thank you, Mark, for joining me. It's been a pleasure, and I look forward to seeing you soon.

Dr. Barakat:
Absolutely a pleasure discussing this with you anytime. Happy to do it, my friend.

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