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The Struggle Is Real

Announcer:

Welcome to CE on ReachMD. This activity is provided by Evolve Medical Education and is part of our MinuteCE curriculum.

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Dr. Talcott:

This is CE on ReachMD and I'm Dr. Katherine Talcott. Here with me today is Dr. Roger Goldberg. Let's dive right in with the discussion.

Dr. Goldberg, tell us what are some of the key limitations of today's treatments for exudative retinal problems that prevent our patients from achieving optimal visual outcomes.

Dr. Goldberg:

Yeah, so, Kat, great to be here. Thanks for having me. And I think we all recognize that there's still, even though we've got great agents to treat wet AMD and DME, there's still a tremendous need for new and better agents. And when you survey the American Society of Retina Specialists and ask what are the greatest unmet needs, it really comes down to better durability because a lot of the agents we have, they work, but they require relatively frequent dosing. The first 2 agents, ranibizumab and bevacizumab, used off-label. Those were really monthly or sometimes monthly visits with what was called PRN dosing, so you had to see them every month. Aflibercept 2 mg, that came out and that offered monthly or every-other-month dosing. And that was kind of a big improvement. And then it started with brolucizumab, which we don't use much now due to safety issues. But brolucizumab, faricimab, and 8-mg aflibercept are kind of now the newer-generation agents, where we really offered patients extended dosing every 3 or even 4 months.

But it turns out that, first of all, in the real world, patients aren't able to extend the interval as long as what we see in the clinical trials, where you're still seeing the patient every month; you can rescue them. In the real world, we don't tend to see the patient every month, even if we're extending them out every 3 or 4 months.

And part of the reason we don't do that is we want to limit not just the injection burden, but we also want to limit the office visit burden because it's a lot for our patients and staff to come in, and so most of us use what's called a treat-and-extend algorithm where we're trying to maintain a dry retina.

And we know from lots of studies, even from those great clinical trial settings that started with CATT and IVAN, and then HAWK and HARRIER, and even in the faricimab studies, that when you have fluid fluctuations, when you're letting fluid reaccumulate and then dry up the retina, and reaccumulate and dry up the retina, you end up with worse vision at 1 or 2 years into treatment. So we try to avoid those zig-zagging in the CST and in the fluid of the retina because we know that leads to worse outcomes over time.

And I'll just add, kind of in the long term, probably related to chronic undertreatment, we give back a lot of the vision that we gain, particularly in wet AMD. I think the SEVEN-UP study, which is the long-term extension out to 7 years of the original ranibizumab ANCHOR and MARINA studies. And by, basically, years 4 and 5, patients were back to their baseline vision, so the 10 letters that they'd

gained, they'd given all back. And then by year 7, they'd actually lost about 2 to 3 lines of vision. So in the long term, patients aren't doing as well as the clinical trial data indicates they should.

Dr. Talcott:

Yeah, I think those are really good points. And I think we're even seeing that in some of the extension studies for the second-generation agents. While those patients are initially able to get great gains, they're starting to lose some of those visual acuity gains when we follow them over time. I agree with you. I think, as you mentioned, we have really good tools in our toolbox now to be able to treat these retinal diseases, but they really require patients to come in frequently. There can be problems if they get lost to follow-up, if they have other medical problems for which they have to miss visits.

And then I think in the clinical studies too, sometimes, especially in the second-generation studies, sometimes I think patients were tolerated to have more fluid than we would necessarily feel comfortable with in clinic. So I agree with you that, although we have great tools in our toolbox, I think that there's still an unmet need for drying and durability. And there can be potential room for improvement for future therapies.

Dr. Goldberg:

Yeah, and even these newer agents like 8-mg aflibercept and faricimab, there's still pulsatile dosing where you give a huge bolus and then it slowly wears off. So you're seeing this huge spike and then diminution of effect, and you're trying to figure out, well, when do I need to give another huge spike again? So it's not exactly that first-order kinetics or smooth control that we think is best for our patients.

Dr. Talcott:

Yeah, I think those are really good points.

Well, this has been a great conversation, but our time is up. Thank you so much for listening.

Announcer:

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