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### Persistent Fluid in Wet Age-related Macular Degeneration: Understanding the Disease Pathophysiology

#### Dr. Kitchens:

Persistent fluid can lead to worsening outcomes for patients with wet age-related macular degeneration, or Wet AMD for short. So which of our patients are at higher risk? And how can we individualize treatment for these patients to optimize outcomes? These and other questions are what's to come on today's program.

This is ReachMD, and I am Dr. John Kitchens.

Joining me to discuss management strategies for persistent fluid and patients with Wet AMD are Dr. Lloyd Clark, who's a retina specialist at the Palmetto Retina Center in South Carolina. And Dr. Szilard Kiss, a retina specialist at Weill Cornell Medical College in New York City. Dr. Clark and Dr. Kiss, welcome to both of you.

#### Dr. Clark:

Thank you, John.

#### Dr. Kiss:

Thank you, John. Pleasure to be here.

#### Dr. Kitchens:

You're welcome. Before we focus on persistent fluid, let's first touch on Wet AMD and its unpredictable course. Lloyd, how do you tailor therapy to each patient with Wet AMD?

#### Dr. Clark:

Well, John, first thanks so much for having me. You know, for me, tailoring therapy is all about individualized treatment, trying to get the retina dry first with monthly injections. So I generally start with monthly therapy, in order to get the retina as dry as possible.

You know, approximately 20% of eyes or so maybe 15 to 20%, maintain four-week interval treatment. These are our most difficult to treat patients and they're the ones that stay on monthly therapy, and perhaps are well controlled or still have persistent fluid. A second group of patients are those that can be extended somewhere between 4 weeks and 12 weeks of interval dosing.

In my clinical practice, that's maybe about 40% of patients. Those are the most difficult patients in many ways to manage because you're for me, I'm constantly changing their dosing interval, trying to extend their dosing as much as possible, but keep their disease state in good control. And then finally, the third group of patients that are comfortably extended to 12-week therapy, that's about 40 to 45% of eyes. We've seen that in clinical practice, we've seen that in numerous clinical trials as well. So the good news is, is close to half of our patients can be extended out to quarterly therapy without disease activity.

So, you know, for me, the key here is keeping the retina dry. I tend to equate drying with durability. A patient -the drugs not working along time if they require frequent dosing to keep the drug to keep the disease under control. So a good drying agent is a durable agent in my practice.

#### Dr. Kitchens:

Well, that's a great background on Wet AMD. And with that in mind, let's zero in on that first group of patients you talked about, the patients that require frequent treatment, or those with persistent fluid. Szilard, how do you classify or define persistent fluid?

#### Dr. Kiss:

John, thank you again for having me. Um, great question. You know, when I think about early persistent fluid, I think about persistent fluid maybe after one or two injections. When I think about late persistent fluid, I think about continued activity with fluid to maybe six or seven or eight injections. This affects my treatment paradigm in terms of how I individualize the follow-up and the number of injections. When I first see a patient, and I look at the compartment that the fluid is found in, I tend to think of it in two ways, the intraretinal fluid that is seen, as well as the subretinal fluid. When we give one or two anti-VEGF injections, we see how that fluid responds. If there's early response, but not complete, I continue with the same interval. As we continue with the injections, we are looking to see if they're drying. What is drying mean for me? Drying means decreasing the intraretinal fluid, as well as the subretinal fluid. You know, does it matter if patients are dry? I think it does. I think in the long term, and I think it matters mostly if the intraretinal fluid is drying up. When I think about, you know, fluid recurrence or persistent fluid after one year of injections, I want to make sure that I've got the right diagnosis. There are some things that may mimic macular degeneration. I want to make sure that the patient doesn't fall into that category.

But if I'm confident that we do have wet macular degeneration, then I stay the course. When several studies have shown that in those patients who have persistent fluid, continuing the frequent four-week or one-month injection interval leads to better outcomes. And so you know, continuing with the course, and reassuring the patient that what we're doing is the right thing is what I do in both those situations.

**Dr. Kitchens:**

And Szilard, are there any characteristics that can kind of give us an idea of which patients might be more likely to have that persistent fluid or just require a more aggressive dosing interval of anti-VEGF therapy?

**Dr. Kiss:**

Great question, John. And I think that the use of OCT has led us to sophistication in macular degeneration that we haven't had before. We used to classify all patients under wet macular degeneration. And now we're beginning to see as we individualize therapy, that the place of the fluid may be important. And those patients who present with significant intraretinal fluid, those are the harder to treat patients. Those are the patients that are not likely to extend out.

That is opposed to patients who had activity from macular degeneration, but may just have a small sliver of subretinal fluid. In those patients, they may be easier to dry up, or we may not necessarily need to dry them completely. I think those characteristics persists throughout the treatment paradigm.

Many of our patients now have been with us for 5, 7, 10 years, and I look for the same things. Is there a recurrence of intraretinal fluid? Is there a recurrence of subretinal fluid? If we have recurrence of intraretinal fluid, once again, we become more aggressive in the treatment paradigm with more frequent injection intervals.

**Dr. Kitchens:**

Lloyd, coming back to you, do you think that a patient's response to treatment can become more variable over time? Or do they stay pretty consistent once you determine, kind of in that middle group, 'Hey, you're an 8-week, a 10-week sort of person, are they going to stay consistent to that? Uh, or is it really variable?

**Dr. Clark:**

Well, I think it can be both. My experience is that the patients that stay relatively consistent are the ones that can go out to 12 weeks. So again, 40 to 45, close to 50% of eyes. And if you keep these eyes under good control, a 12-week therapy, my experience is that those patients are - are safe to manage at extended intervals in general.

The difficult group of patients are the other 50% that fall somewhere between monthly therapy and 12 weeks. I think in that - in that case, sort of all bets are off, some of those patients can become quite consistent at 8, 6, 10-week intervals. But in general, I think about patients that are less than 12-week therapy as being susceptible to variability. And I think those are patients you have to be very careful with.

**Dr. Kitchens:**

Well, those are some really fantastic insights and understandings around the management of patients with persistent fluid, customization of therapy for patients with wet age-related macular degeneration. I want to thank my guests, Dr. Szilard Kiss, and Dr. Lloyd Clark, for coming on today. And, um, it was great to speak with both of you.

**Dr. Kiss:**

Thank you so much, John. It was a pleasure to be here.

**Dr. Clark:**

Thanks, John, what a treat.

### References:

1. Kaiser PK, Wykoff CC, Singh RP, et al. Retinal fluid and thickness as measures of disease activity in neovascular age-related macular degeneration. *Retina*. 2021;41(8):1579-1586.
2. Jaffe GJ, Kaiser PK, Thompson D, et al. Differential response to anti-VEGF regimens in age-related macular degeneration patients with early persistent fluid. *Ophthalmology*. 2016;123(9):1856-1864.  
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