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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Optimizing Anti-VEGF Sequencing: Strategies to Reduce Burden and Personalize Care

Announcer:
You're listening to *Eye on Ocular Health* on ReachMD, and this episode is sponsored by Regeneron. Here's your host, Dr. Brian McDonough.

Dr. McDonough:
This is *Eye on Ocular Health* on ReachMD, and I'm Dr. Brian McDonough. Joining me today to examine treatment sequencing strategies and optimization approaches across the anti-VEGF therapeutic class is Dr. Mitchell Goff. He is a retinal and vitreous diseases, macular degeneration, and diabetic retinopathy specialist at the Eye Institute in Salt Lake City, Utah. He is also with Rocky Mountain Retina Consultants. Dr. Goff, welcome to the program.

Dr. Goff:
Thanks, Dr. McDonough. I'm happy to be here.

Dr. McDonough:
Let's start with the big picture, Dr. Goff. How has the mindset around anti-VEGF therapy evolved from a one-size-fits-all model to a more dynamic approach?

Dr. Goff:
So in the early days of anti-VEGF therapy, we had only a couple of agents available to us, and the treatment paradigm at the time was essentially monthly treatment or very frequent treatment. It was a paradigm shift, of course, for these diseases. Prior to this, vision outcomes were just not the same as they are with these current therapies, but it was a big treatment burden. And then over the years, as we did more clinical trials and gained experience with these agents, we've tailored the approach, and now there are more long-duration agents, and the treatment paradigm has shifted to extending the interval between the treatments and personalizing the regimen for each patient. Really, every eyeball has a different regimen. And it's an exciting thing. It's become a lot easier for patients in that regard.

Another way the landscape has changed over the last couple of decades is just our choice of drugs. We had a limited number of options for many years, but over the last few years, it feels like it has exploded. We've got a number of new options on the table, which is a really good benefit for patients.

Dr. McDonough:
And when you're considering first-line anti-VEGF agents like aflibercept or ranibizumab, what clinical factors typically inform your initial selection?

Dr. Goff:
As you know, there are a number of anti-VEGF agents available to us now. There are what we term the "second-generation agents" available to us, which, generally speaking, may have a longer duration of action. So we do have choices to make initially.

Number one, when I'm thinking about this, I have the guiding principle that I want to control their underlying disease, and I want to do that with the fewest number of injections into the eye. We have to remember that these are invasive procedures and they do carry some risk, so if I can control their disease with fewer shots, I think that's of paramount importance. So I try to be very data-driven or evidence-based, whatever term you want to use. And so the clinical trials for these second-generation agents are very convincing in that they

provide the same vision outcomes as the other agents, and they do so with fewer injections on average. Additionally, the safety profile is identical with these newer agents. So I tend to use the second-generation anti-VEGF agents primarily because they're equally effective, they seem to last longer for most patients, and the safety profile is the same.

Number two, though, the other issue that's always present is market access things. We do have to deal with various insurance coverage or lack thereof and the issues that come with that. A lot of times, patients are covered, but they still have a copayment, and they can be substantial for some of these drugs. So we do have to tailor the treatment choice depending on market access issues at times.

Dr. McDonough:
Now, once you've started treatment, Dr. Goff, what markers prompt you to start thinking about switching therapies?

Dr. Goff:
That's a good question. There's a lot of talk out there about biomarkers based on optical coherence tomography, or OCT. This is a scan that looks at the macula, and it is one way that we gauge disease activity. And I think these are interesting. But to me, they are not as relevant for switching agents. They give us some good information about how patients will respond to these agents, which is nice to know. But I don't think it's that relevant, honestly, when I'm thinking about switching agents. Like I said, I will try to use the most effective and long-lasting treatment when I can initially, and then I will consider changing that if there's persistent disease activity with associated vision loss.

And to me, the most significant sign of persistent disease activity is persistent intraretinal fluid with associated vision loss. So if I've treated someone with Agent X and three to six months have passed and they still have persistent intraretinal fluid and associated vision loss, I think it's time to start thinking about switching agents.

Dr. McDonough:
And as a follow-up to that, do lesion subtype or baseline anatomical features, like polypoidal lesions or RAP, play a role in your sequencing strategy?

Dr. Goff:
Just to a very limited extent is what I would say. I know that some lesion types are thought to respond less to these therapies; a RAP lesion or a polypoidal choroidal vasculopathy lesion may respond differently. But I still abide by my guiding principle, which is the most long-lasting, effective, and safe drug. So I will use these second-generation anti-VEGF agents for virtually all lesion subtypes.

Now, I'll make mention of a couple of specific factors, though. Sometimes people are concerned about large pigment epithelial detachments, which are often associated with neovascular AMD. And there is a notion that some of the more potent agents may increase the risk of retinal pigment epithelial rupture and lead to vision loss. I've looked very carefully myself at the data regarding this, and I don't think that that's an issue, personally. Retinal pigment epithelial rips happen at a small rate regardless of treatment choice or regardless of treatment. The natural course of pigment epithelial detachments have rips that occur on occasion. So I don't think that's a huge issue for me, but I know that is an issue for some people when they're thinking about their first-line agent.

The other point I'll make is glaucoma. This has been looked at in all the pivotal trials—the elevation of intraocular pressure with the use of these drugs. And for many people, glaucoma is a concern because some of the second-generation agents are a higher volume of medicine, so when we put them into the eye, the pressure is higher. It's transient, and it's generally not an issue. But unfortunately, the pivotal trials only go a couple of years most of the time, so we don't have as much long-term data about the effect of these repeated intraocular pressure spikes. And so for patients with advanced glaucoma, I do give this some thought, and that may sway me to use an agent that may have a lower volume.

Dr. McDonough:
For those just tuning in, you're listening *to Eye on Ocular Health* on ReachMD. I'm Dr. Brian McDonough, and I'm speaking with Dr. Mitchell Goff about how we can optimize our sequencing strategies for anti-VEGF therapy.

So, Dr. Goff, earlier we talked about switching agents, but if we look beyond that, what other strategies can help reduce injection burden without compromising disease control?

Dr. Goff:
So that's a great question. I think that with the second-generation agents and the pivotal trials examining them, particularly aflibercept 8 mg, there were some retreatment criteria in those trials, and they were a little different than what we were accustomed to in the decade before. Specifically, patients were allowed to continue their current treatment interval and, on occasion, even extend it, even in the presence of intraretinal or subretinal fluid, which we historically have thought of as disease activity. So even if patients had some intraretinal or subretinal fluid—as long as their vision was unaffected—they could maintain a longer treatment interval or even extend

that treatment interval in these clinical trials.

And what we learned from this is the patients did fine with that. So I think it taught us something. It taught us that the presence of fluid by itself, without associated vision loss, did not demand that we shorten the treatment interval. And I think that's a big shift.

And in my experience, I've found that it's a little bit of a roadblock for many people in extending the treatment interval. Whenever they see fluid, there is a notion that the treatment interval should be decreased and that they need more aggressive treatment. But I'm not sure that that's always the case. And in my own experience, I've found that I can successfully extend the treatment interval in patients with a little bit of fluid—provided their vision is stable—and they do fine. So I think having an understanding of that and relying on the data from those clinical trials can help us to extend treatment intervals for many of these patients.

Dr. McDonough:
Well, we've certainly covered a lot today, but before we close, Dr. Goff, can you share some practical takeaways to help your colleagues create smarter, more personalized treatment plans?

Dr. Goff:
I guess number one is, I would just always start with the most effective and longest-lasting drug that you're able to start with. We all have to deal with market access, coverage, payment issues, etc., but just start with the most effective and long-lasting drug. Remember that durability, or how long these drugs last, directly translates to safety for these patients. The big risk that we all worry about is endophthalmitis with these intravitreal injections, and every single injection has a risk of endophthalmitis, even though it's very low. The fewer injections you give, the lower risk you're subjecting these patients to. So I do encourage people to use that as a guiding principle.

The other thing is just a very practical thing: keep in mind that patient preferences and their past experience matters. We've got a lot of new agents on the market over the last few years, and I think many of us have switched. And sometimes patients like that. Sometimes they don't for various reasons. And I would encourage people not to discount the patient's prior experience and their perceptions of how their treatment is going. I myself have patients who do prefer an agent that may not have lasted as long as the one I tried or switched to, and I'll go back to it simply for that reason.

The last point that I always try to make is to scan these patients frequently. You've got to remember that this disease is dynamic. It doesn't always behave as you hope it will, and it changes over time. If a patient is stable with a three-month interval on whatever agent you're using for a couple of years, that doesn't mean they'll continue to be stable at a three-month interval. They may change. So I always scan these patients to look for any evidence of disease activity. I do it at virtually every visit. And I also encourage people to scan the other eye routinely. We've got to remember that this is a disease of both eyes, and the rate of having neovascular AMD or diabetic edema in the fellow eye is very high in these patients, and early treatment likely matters. So I scan both eyes, and I do it at virtually every visit. I think that's important.

Dr. McDonough:
Well, as those final comments bring us to the end of today's program, I want to thank my guest, Dr. Mitchell Goff, for sharing his perspectives on anti-VEGF treatment sequencing and optimization. Dr. Goff, it was great having you on the program.

Dr. Goff:
Thank you very much. It was a pleasure.

Announcer:
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