Macular Chats

Taking Charge of Your Geographic Atrophy
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Transcript of Teleconference with Dr. Veeral Sheth, Director of Clinical Research, University Retina and Macula Associates

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Please note: This Chat has been edited for clarity and brevity.

MS. KACI BAEZ: Hello, and welcome. My name is Kaci Baez, and on behalf of BrightFocus Foundation, I'm excited to be your host for today's Macular Chat, "Taking Charge of Your Geographic Atrophy." Our Macular Chats are a monthly program designed to provide people living with macular degeneration and the family and friends who support them with information straight from the experts. BrightFocus Foundation's Macular Degeneration Research program has supported nearly $53 million in scientific grants exploring the root causes and potential prevention, treatment, and cures for macular degeneration and is currently investing in 49 active research projects across the globe. I'm excited to introduce today's returning guest speaker, Dr. Veeral Sheth. Dr. Sheth is a native Chicagoan who specializes in diseases of the retina and vitreous. He also is a clinical assistant professor at the University of Illinois at Chicago. He is director of clinical trials at one of the busiest clinical trial sites in the country. He has been Principal Investigator for over 60 trials and has

research interests in macular degeneration, diabetic retinopathy, vein occlusion, as well as surgical pathology. He is involved in clinical trials developing new drugs, delivery devices, and gene therapy. Dr. Sheth, thanks so much for joining us today.

DR. VEERAL SHETH: Thank you so much, Kaci, for that wonderful introduction. I'm excited and honored to be back on the program and looking forward to the discussion ahead.

MS. KACI BAEZ: Wonderful. So, today's topic is geographic atrophy, which we have talked about before with you and on other Macular Chats. But as a quick refresher, and for those who are not familiar, could you start off by explaining what GA is?

DR. VEERAL SHETH: Yeah, so great question. It's a great place to start. I think before we dive into what GA is, let's take a step back and just talk about the retina in general, because what we're talking about ultimately is taking place in the back of the eye where the retina sits. So, the retina is a thin nerve lining that lines the back wall of the eye. And if you think of the eye like a camera, you've got a lens in the front, which ... we're all familiar with what cataracts are. Cataracts are the lens in your eye becoming cloudy over time, and that's in the front of the eye. Well, in the back of the eye, you've got this nerve tissue called the retina. And that retina is really like the film in the camera, so it processes your vision, ultimately, before it all gets sent down the optic nerve to your brain. So, arguably the most important part of the eye, just like the film is the most important part of the camera. Now, when we dig deeper here, so if we look at the centermost point of that retina, that area is called the macula. The macula is where your central vision comes from. So, that vision that we use to look at people's faces or read your book or use your tablet, all that stuff that comes from your central vision is processed in the retina in the macula. And so, why do we care about something that degenerates the macula? It's because it causes degeneration in your central vision—again, the most important part of your vision.

So with that in mind and with that context, what is geographic atrophy? Geographic atrophy is an advanced form of macular degeneration. So, everything we're talking about really impacts the central vision, and in

particular, geographic atrophy is a form of dry macular degeneration that really starts to inhibit your ability to see with that central vision. Now, I said something kind of interesting there, which is dry macular degeneration. So then, the question comes up a lot in my office, "Well, what's the difference between dry and wet?" or, "Dr. Sheth, do I have dry form or wet form of macular degeneration?" So, I think that's worth a separate side conversation for a minute here. Wet macular degeneration again, it happens in the same part of the eye, which is that macular, the central retina. We call it wet because there's often bleeding or fluid building up in the retina, and that can lead to central vision loss. And so, we have talked a lot about wet macular degeneration over the last 20 years because we've had really great treatments for wet macular degeneration, but we haven't had great treatments for dry macular degeneration—in particular, geographic atrophy—until last year. So, that's why I think it's become a much more hot topic of discussion, because it's something that we actually have treatments for today, so that's why we're talking about it. And ultimately, atrophy means thinning or loss of nerve tissue. And so, what we talked about with geographic atrophy is this progressive loss of retinal or macular nerve tissue, which causes progressive loss of central vision. Sorry, that was a long-winded answer to your question, but I wanted to make sure we had a good background there.

MS. KACI BAEZ: Thank you so much. It's super helpful. There's so many terms related to macular degeneration. I think that having a deep understanding of the introductory level is extremely helpful. And so, our next question is, "After a doctor diagnoses an individual with geographic atrophy, what happens next? How quickly does geographic atrophy progress, and is the progression rate the same for everyone?"

DR. VEERAL SHETH: Okay, good questions. Let's start with the first part of your question, which is, "So, a doctor diagnoses a patient with geographic atrophy. What happens next?" It depends. There's not a blanket kind of one-size-fits-all answer to this, but what I'll tell you is really based on my experience and what happens in my office. I think the next important step after I've diagnosed a patient with GA is to really explain that diagnosis to the patient, because it's not something that is,

again, well known by everybody. So, kind of the conversation I just had about the background and what the retina and macula are and what the differences between wet and dry are, that's how I start that conversation because I think it's really, really important for a patient to understand if they have this problem, what is the problem? Because then that sets up the next part of the conversation, which is, "Hey, what are my options?" So, we talked about geographic atrophy. We talked about what that disease really means and how it can impact that patient, in particular, in their life. I'll ask a lot of questions. So, are you bothered by this", and "what are the things that are potentially impacted in your life?" Because I want to get to know how much of this disease is bothering a patient and how much it's really impacting their ability to remain independent. That's always the key for me as I want my patients seeing as well as possible and maintaining that independence as much as possible. And then, based on that conversation, we start talking potentially about the options. The options, including monitoring and observing, which we've done forever and ever, or talk about certain treatment options that are available. Again, these treatment options just became available early 2023, so we haven't had them for that long, and so we now are starting to talk about those with patients. And so, that's how the beginning of that conversation goes.

The next part of your question was, "How quickly does geographic atrophy progress?" And, again, there's no one-size-fits-all answer to this. I think it's a lot like any medical problem. I think different patients are going to be impacted differently. So, for some patients, we do see that the GA tends to spread more quickly. It's hard to tell when a patient is coming in for the first time though, because you've just got a single snapshot in time on that patient, so it's hard for me to tell that patient, "Look, it may progress quickly or it may not." I do tell them, though, what the odds are. And the odds are that, in general, about two-thirds of patients that are diagnosed with GA will lose the ability to drive within 2 years. So, we've seen that with clinical trial data that 67 percent of patients that are diagnosed with GA lose that ability to drive less than 2 years. And so, I have that conversation because I want to put things in perspective. Now, that particular patient, they may progress more quickly; they may progress slower. A lot of that depends on if I have some idea of their track record. Do I have a picture or scan from their retina from 3 months ago

or 6 months ago that I can compare it to? And if I do, then maybe I can give them a more precise answer to that question of how quickly will it progress. And so, I think I've answered your question. I think the last part was, "Is the rate the same for everyone?" And I think the answer is no. It's like anything else with the human body, everybody's a little bit different.

MS. KACI BAEZ: That's a great point. And it's always a good reminder that everyone is different, and it's just good to work with your doctor on what's right for you. And so, our listeners today had a lot of questions related to the GA treatment options. And we got one question related to how do the current treatment options for geographic atrophy work, but also wanting to know how does the complement pathway system work, and specifically, the difference between complement C3 and C5. So, understanding that that's the foundation for the treatment options, I wondered if you could briefly explain how this works.

DR. VEERAL SHETH: Yeah, good. This is a very technical question, which is, "What is the complement pathway?" So, before we answer that, the question is really, why are we even bringing up complement pathway? So, many, many years ago, we did some research and found that one of the associations between patients that had really progressive atrophy or patients that had this tendency to form geographic atrophy, we saw that they had an overactive inflammatory system. In other words, a certain pathway in the eye—in particular, this pathway called the complement pathway, which leads to inflammation—was just overactive. And so, because of that, that became a target for research and development over the next two decades. And so, what we've seen now with these new treatments is that they target exactly that pathway. They target the complement pathway. And so, what that means is what we're trying to do is slow down that pathway that causes inflammation. So, it's not necessarily considered an anti-inflammatory, like a steroid, for example, but it does address that pathway, and it really lowers the activity of that pathway, in other words, which then lowers the activity of the inflammation in the eye, which then slows down the disease. And so, you talked about C3 and C5. So, if you look at this pathway, there's lots of steps along the way in this pathway. It's like this giant puzzle that fits together. Well, C3 and C5 are two pieces of that puzzle, and if we inhibit

those pieces—in other words, if we take them out of the puzzle—it can help slow down this this pathway or this process of inflammation. And so, these are two things that have been targeted. And the two treatments that we have today, while they're very similar in that they work on this complement pathway and slowing down that pathway, they are slightly different in that one of the treatments that was approved targets C3, so it helps eliminate that from the pathway, and the other uses C5 and inhibits the pathway that way. And so, while there's some similarities to the treatments, those are the basic differences. But at the end of the day, all of it is aimed at slowing down that inflammatory process, which causes disease progression or geographic atrophy worsening, in other words.

MS. KACI BAEZ: Thank you. That is so helpful. And so, in addition to the two FDA-approved injections for GA, we've got some listener-submitted questions related to the AREDS2 vitamins. Specifically, "Are the AREDS2 vitamins still recommended for GA?" And also: "My ophthalmologist told me that the vitamins are just as effective as the injections in slowing down the progression of GA. Is that true? And if so, why should we get the injections?"

DR. VEERAL SHETH: Yeah. So, I think that in terms of the vitamins, we have to understand why we tell people to use the AREDS2 vitamins. The reason we use vitamins is that those vitamins are effective in slowing down macular degeneration in early stages. In other words, what we're trying to do is reduce the likelihood of someone that has, let's say, moderate or intermediate dry macular degeneration. We want to slow down or reduce the likelihood that they progress to a more advanced form of macular degeneration; that could be either wet macular degeneration or GA. And so, by starting these vitamins, we reduce the likelihood that they progress to that more advanced form. But once you have the more advanced form—and that's either wet macular degeneration or geographic atrophy—then we start talking to patients about the treatments designed to address those specific issues. And so, it's like anything else in medicine. Well, I'll give this example of a patient that's at risk for diabetes. If that patient doesn't have diabetes but is at risk, we tell them, "Look, you've got to watch your diet. You've got to exercise. You've got to do all those things to make sure it's less likely you develop

diabetes." But once that patient develops diabetes, then oftentimes we're starting to talk about treatments for diabetes—insulin and metformin and all the other hosts of medications—because now they've developed that more advanced issue, which is the diabetes itself. So, it's very similar in the eye. When you have the more mild forms of macular, we say, "Use the vitamins. That will slow down the likelihood that it's going to become more advanced." But when it becomes more advanced, we start talking about the treatment options that exist for those. I think that answers your question. Did I did I touch on everything there?

MS. KACI BAEZ: Yeah, I think that's really helpful. And I think it goes back to just everyone is different as well, and the stages of the disease are different also. So, there's different considerations when you think about the treatment options. That's really helpful. We do have some questions about side effects for the treatments and for the injections. Some side effects are concerning to some of our listeners, and one listener says, "I'd like to know whether it is worth having the new injection because it only stops the progression by a small percent." Could you address some of the hesitations around the side effects that have been brought up by our listeners?

DR. VEERAL SHETH: Yeah. So, there's two important points that you bring up there, which is the hesitation to start treatment because it only stops the progression by a small percent, and then the other side of it, so not just how well do the treatments work, but the other side of it is, what are the downsides? What do I have to be worried about? What are the side effects? What could go wrong? These are two really, really important points, and I talk to every single patient of mine, especially those that are considering starting treatment, because at the end of the day, I want to make sure the patients understand what the medicines do and what they don't do. So, let's talk about that for a second. So, what do the medications that we have do at this time? So, we have these medications that we have to remember, we have to use them as intravitreal injections. What that means is we have to do injections of these medicines every month or 2 months into the eye. So, we numb the eye up, and we administer that treatment once a month or once every 2 months into the eye, and that's how we get the effect of the drug. And

so, that's how we do it. So, that's important because when we talk about side effects, one type of side effect is from the procedure itself. So, if I do an injection, it doesn't matter what we inject, but there's always a risk of infection. The rates are very low, but there's always a risk of infection. And an infection inside the eye can be very, very dangerous. And so, we counsel our patients on that. We take every precaution possible to lower that risk. And for the most part, the risk is very, very low, and patients do very well, but it is something you absolutely have to talk to patients about. And as a patient, you have to know it's a possibility before engaging in the treatment.

So, that's the procedural side effect, so now then you have to talk about, what is the side effect of the actual medications themselves? So, the medications, like any medication, can have potential side effects. And we know this because of the clinical trials that were run with these treatments. And so, one of the side effects that we worry about is a slightly higher risk of conversion to wet macular degeneration. We saw this slight tendency for patients that were getting the treatment with these newer medications to develop wet macular degeneration. We know that patients with macular degeneration, in general, and particular, patients with geographic atrophy are already at a slightly higher risk of developing wet AMD, but we saw slight increases in that tendency. The good news is that the rates overall were pretty low, and the good news is also we have really, really great treatments for wet macular degeneration should that problem arise, whether you're on these treatments or not. And then, the other risk of treatment and then the medication, in general, like any medication we inject into the eye, we worry about inflammation. And so, we have to take that very seriously as well. Thankfully, the rates are pretty low in terms of how many patients develop this type of an issue. But again, if a patient has really good vision, we have to think about these things, because if you are one of those rare cases, it could impact your vision. And so, this is why we've got to talk about all these things ahead of time. I want to make sure I counsel my patients on this and really give them a good understanding of it.

The other thing that you mentioned really relates to the small percent of difference that these medicines make, and I think that's an important

topic to discuss. What is the purpose of treating patients with these medications? The way I talk to my patients about it is I say, "Geographic atrophy is a progressive disease, and even with the treatments we have today, the geographic atrophy, even if you get treatment, is going to progress. But what these treatments do is they help slow down the progression of that GA." And so, GA is kind of like a runaway train. We already talked about how quickly it can progress. It's like this runaway train, and what the treatments do is they help slow down that train, but they can't stop the train. So, nothing we have today currently available to us and FDA approved can stop that disease progression. And so, if patients are really going to get involved with treatment, they have to know that, look, even if we start treatment, things may get worse, but the likelihood with these treatments is that it'll slow down the progression. And if we fast forward a year, 2 years from now, the likelihood is that if we didn't treat the patient, then 2 years from now, they're probably going to be worse off from a vision standpoint and from how much atrophy they have compared to if they would have started treatment. So, that's really the conversation I have because it's important because 6 months into treatment, a year into treatment, patients will tell me, "Dr. Sheth, I'm still, you know, I feel like I'm still getting a little worse." And I tell them, "Look, the odds are you probably are getting a little worse, and then we can see on your scans, it is getting worse." But what I can tell them is the likelihood is we've slowed down the disease and that we've changed the course of that disease for their benefit.

MS. KACI BAEZ: That's really helpful. So, when thinking about the treatments, and there are two FDA-approved treatments, could you briefly explain what those are and if someone would be a better candidate for one treatment compared to the other, and also if a person should start one of those treatments at a certain time during their disease progression?

DR. VEERAL SHETH: Okay. Yeah, great question. So, the first part of your question was what are the two treatments that are available? So, there's two medications, and it's good to discuss because I think there's a lot of TV commercials now on these, so I think it's good that we're bringing this up. So one is a medication called Syfovre®. Syfovre was the first one that was approved back in February of last year. That is a C3 inhibitor, so

I'm glad we had that complement discussion and C3 and C5, because this is where it all ties in. So, it's a C3 complement inhibitor. And then the other medication is IzervayTM, which was approved last summer and is a C5 complement inhibitor. And what I'll tell you is there has never been a clinical trial that's compared the two against each other, so I can't tell you here is one medication that's better than the other. I think some physicians have preferences to use one over the other. In our clinic, we do have patients that are on both; in other words, we've used both in our in our offices. And so, those are the things that we kind of look at. We really educate the patient. When we talked about side effects, we talked a little bit about inflammation in the eye. The rates of inflammation are slightly higher with the Syfovre. So, it's something I counsel the patients on. They're slightly lower, in terms of inflammation, with the Izervay, and so sometimes that helps patients make a make a decision on which medication they want to start.

And then, the second part of your question was, "When do you start treatment?" So, there's no right or wrong answer to this. I think that some of the thought process is, if you're going to slow the disease down, you're probably better off doing so as early as possible. So, let's say, for example, geographic atrophy is starting to cause a blind spot in your vision. And let's say it's not right in the middle; it's off to the side a little bit. And let's say that the natural progression of that is that blind spot's going to get bigger and bigger over time and that, eventually, it's going to spread across the central part of your vision, making things like reading and seeing your family members' faces much harder. And so, the theory there is, "Well, why don't we get to that issue earlier so we can slow down the progression of that blind spot and maximize that vision over the long term and, ultimately, delay the progression of that macular starting to impact that central vision as much as possible?" And so, that's the way I look at it, and that's the conversation I have with my patients is that, "Look, these are the treatments that are available. Here's why you may or may not want to start the treatment. And here's the logic on starting sooner rather than later." You take the other side of that, and you say, "If a patient's already lost a lot of central vision, is it worth starting that treatment?" It depends, but it's not going to bring back that central vision. We talked about what these treatments do. What they don't do is bring back vision. They don't

improve that vision loss. They really just slow things down. And so, that's important for patients to understand, because a lot of us think once you've lost that central vision, you're late in the process. It's not that you can't treat or shouldn't treat because you can still slow down the size of that blind spot and the progression in that blind spot, but what I would love to do for all my patients is prevent them from having that central blind spot in the first place.

MS. KACI BAEZ: That's an excellent point because some of our listeners do want to know if this will reverse the vision loss, and it's an excellent point that the treatments are not going to reverse, but rather just slow the progression. And one listener submitted a question: "Does the injection for GA in one eye affect the other eye?"

DR. VEERAL SHETH: Oh, it's a great question. The answer is we don't think so, and here's why. We have lots of data and clinical trials where we inject one eye and we also watch what happens in the other eye. This is in wet macular degeneration trials, which we've done for decades. This is also in GA trials, which we've done for a long time. And what happens when we inject it into the eye? So, the question is really, "Why do we inject the treatment into the eye?" That sounds horrible. Why don't we just give people pills or IV medications or something that's not touching the eye? And the answer to that is when we give something like, for example, by mouth, to treat the eye, the reality is not enough of that medicine gets into the area where it needs to get, which is the back of the eye. And so, the most effective way to give those treatments is right directly to the eye. Now, when we do that, we can give tiny, tiny amounts, because we're getting it right where it needs to go. If you look at how much is being injected into the eye, it's very much droplets of medication that go into the eye. It's a small amount. But in that, and the point of me saying that, is we get a good concentration right where it needs to go, and we don't really have a lot of medication going elsewhere, including the other eye, so the impact or the effect is not really seen on the other eye. And that's why we do it that way because the other side of it is a lot of the folks that get these medications also have other medical issues. They may have high blood pressure or cardiac issues, so they're on other medications. And so, when we give it to the eye and it stays in the eye, it's less likely to impact

the rest of their body or interact with the other treatments they may be getting.

MS. KACI BAEZ: Thank you for that information. It's so helpful. And in relation to what you're saying, we have a question here from a listener: "I understand that GA is an advanced form of dry macular, but what confuses me is it possible that you can have GA and wet macular at the same time?"

DR. VEERAL SHETH: The easy answer to that is yes. So, the way I think about macular degeneration is it's a pathway. So everyone with macular—I would say most people—start with mild macular degeneration. Some people have heard of the term drusen. And so, you get little blips on those OCT scans or those retinal scans that you may have seen if you're familiar with the disease, and then that progresses. That that mild AMD progresses to intermediate—these are all still dry. Intermediate then can progress to advanced. Now, here's where things split usually. So, either you can have wet AMD or you can have GA or you can have both. And it's not that both start at the same time necessarily. You can have a wet AMD patient that then develops GA; you can have a GA patient that then develops wet AMD. So, it is entirely possible that a patient has both in one eye.

MS. KACI BAEZ: Thank you for that explanation. We do have a lot of questions related to these injection treatments, and another one is, "If GA has invaded the fovea, are the benefits of the injection treatments reduced?"

DR. VEERAL SHETH: Yeah, it's a great question. So, once it's hit the center of the vision, the question is, "What is the purpose of treating that? Why would we initiate or continue treatment?" And it's interesting. What we have to think about with geographic atrophy is what the patient's symptoms are. If a patient notices, "Okay, look, I've lost my central vision, but I can still see around that." And many patients will tell you that they can see around that central vision loss, and it's enough for them to be able to navigate, be able to walk from one place to the to the other, be able to go to the grocery store and get that gallon of milk. And so, just because you've lost that exact center point of your vision doesn't mean now all of a sudden the rest of your vision isn't useful. It's very useful. And so, in that

scenario, if you've lost that center point; the area of atrophy is still going to grow, potentially; and that means that the blind spot in the center could potentially continue to grow, meaning that valuable retina—that valuable real estate that's helping you process that vision—is going to start to be lost as well. And so, in those cases, I talk to patients about it. I say, "Look, I'm not going to all of a sudden get you back to 20/20, but I hope to slow this down so that all these things that you're doing today, you can continue to do today."

MS. KACI BAEZ: Absolutely. And I think a lot of people are just looking to improve their quality of life. But with these new treatments, comes a lot of questions. And so, some of the questions we have are related to the lifespan of the treatment, such as, "Once you decide to start treatment, how often do you need to get treatment? And are there any guidelines around treatment?" For example, if someone is 95 years old, they want to know—one listener wants to know—is that too late for them to start treatment?

DR. VEERAL SHETH: Yeah, a lot of points you're bringing up. I think we got to definitely attack those one by one. So, the first part of your question is, it's kind of like, you know, how long do we or can we treat this? The other way patients ask me that question is, "Doc, once we've started, is this going to be a treatment that I have to get forever or have to do forever?" And the way I answer that is that there's never a "have to." It's always your choice as a patient to say, "I want to continue a treatment," or "I don't want to." But it's important to understand why you would maybe want to continue treatment. We have good data from years of treating patients with these treatments that we're talking about. And what we see, in general, is that, one, these treatments start working right away. In other words, if you were going to progress quickly with your GA, we start to slow down that progression almost immediately. What we also see is the longer you're on the treatment—in other words, the more you stick with it—the greater that difference between the untreated and treated patient. In other words, we continue to change your trajectory and slow the disease down compared to a patient that wasn't getting the treatment. In other words, that benefit grows over time. We never stop it, but the slowdown continues as you continue treatment. And so, my advice to

patients is, you can stop whatever you want, but the benefits of those treatments continue to build on themselves over time. And so, I think that's important for patients to understand.

The other point that that I would make in that question of like, "Do I need to keep using this forever and ever?" is I always tell patients, "Look, it depends on what the next generation of treatments gives us." We may have a treatment that works twice as good or we may have a treatment that works twice as long so you need less injections. And so, there's a lot of great research and development being done. And I say that not because I tell people, "Hey, you should wait for the treatment 2.0," but I tell them, "Look, if and when those newer treatments come to us, it's better for us to start some of these treatments that we have today so that you're not digging yourself out of a bigger hole when those newer treatments come around." And so, I talk about it in that long view for patients, because it is a chronic disease, and it's something we've got to manage over time.

The other question you had was ... you gave me the example of a patient that's 95 years old; when is it too late? And I would tell you the age is less important to me than what that patient's goals are. I have 95-year-old patients that are driving, they're sewing, they're reading, they're very active. And in those patients, we have the discussion of, "Do you want to start treatment or not." And I have patients that elect to treat. My oldest patient that's being treated is 103 years old, and I'm convinced she's going to live to 130. So, she wants to be able to see for the next 30 years. And I think that's reasonable. All jokes aside, I think that's an important thing to consider, which is, "Are you active, how important is your vision in terms of your goals and your independence?" Now, the flip side of that is, "Are you are you able to come in for the visits?" So, you asked about how often these treatments are given, and these treatments are given roughly every 1 to 2 months. And that's a lot of visits. You have to be able to come in every month or two, and because you're getting injections, you may need someone to be able to drive you. You may need a family member or a caretaker to come with you. And so, that is an important consideration as well, and it's something that we take very seriously before we initiate treatment for a patient because we really want them to understand that sometimes it's not just the patient committing to the treatment, it's

everybody else committing to the treatment.

MS. KACI BAEZ: That's an excellent point, and I think those are all considerations that people should have when they speak to their provider. And so, do you have any advice on how individuals can be more involved and proactive in their treatment decision and even making the decision to get treatment, and what considerations and questions should they ask their provider?

DR. VEERAL SHETH: Great question. I think, and what I tell my patients, and really how we empower them, is ask a lot of questions. We're in a time point where we do have new treatments, which means that not every doctor is using them. I think any time something is brand new, you don't see 100 percent adoption within the community of treating physicians. But what you do see right now is a slow growth of people starting to use these treatments because they understand the value of these treatments. And I think a lot of it, like anything new, I think there's doctors that want to see how these treatments are working. They want to learn from other doctors that are using them. And so, I think you're starting to see this growth. But part of what drives that are patients asking about these treatments. If a patient asks a doctor who is maybe not as familiar or comfortable using these treatments, asks them about the treatments and says, "Hey, I'm interested in it," I think that starts to get people thinking and starts to get doctors thinking about these treatments and how they can benefit their patients. So, I think that's an important point. You know, one question that always comes up is, "Should a patient get a second opinion if they want a treatment like this but are not being offered the treatment?" Because I've heard that conversation quite a bit as well. And the answer is, I think it depends. I have no problem with second opinions. I encourage my patients if there's any questions or doubts or concerns to look for second opinions because, ultimately, you are the owner of your health. You are the ones that are the most engaged in understanding of what's happening to your own body, head to toe. And I think that ownership is important, and I think that you looking for answers and asking those questions is perfectly in line with what you should be doing and ought to be doing. And so, I encourage my patients, and if they really are motivated to get a treatment or at least to seek information, to find

the resource that's going to give you that information you need. And that could be a second opinion, it could be a website, it could be a handout. However, it could be a broadcast like this. And so, I think it's important for patients to really know the facts and make educated decisions.

MS. KACI BAEZ: I think that's a great point. There's so much information out there as well, and BrightFocus is pleased to offer an abundant amount of information on AMD and GA. Looking at some more listener-submitted questions, some of them are related to what's in the pipeline. And you mentioned a pill earlier about the treatment of GA, and that's actually a question we have. And we have a listener who wants to know if there is a pill in the pipeline for the treatment of GA and also maybe what you see as the most promising breakthrough in the near future for the treatment of GA.

DR. VEERAL SHETH: Yeah, good questions. So, let's talk about different routes of treatment. In other words, what else are we looking at besides intravitreal injections or eye injections. And this goes back to what you were talking about earlier, which is we are involved in a lot of clinical trials. And so, I can tell you that we are looking at new treatments. One, for example, is a monthly subcutaneous injection, so you can think of it almost like you would give yourself insulin, but you would instead give a medication once a month that is also a complement inhibitor, a C5 inhibitor, that can slow down the growth. And there's pluses and minuses to that. Some people would much rather do that than get an eye injection, and the benefit of that is, potentially, with that single injection once a month, it can treat both eyes, because it's going all over the place. The downside of some of these systemic treatments are what we talked about—there's potentially interactions with the other treatments you're on—and so, that's something to consider. They have worked on oral medications. So far, the results are not so great with those, and so we're still working on the magic pill for that. There's also gene therapy, which I think is an interesting area. And so, what gene therapy is, is injecting, in a one-time fashion, injecting something into the eye that helps the eye create its own medication, its own therapeutic, which is almost sci-fi working, like look at it. But we're starting to see good results on that. These are all still in early stages. We still have a long way to go

in terms of running the clinical trials and then evaluating the data and then seeing if the FDA ultimately approves that. But it's an important conversation because patients will ask me, "Well, when is that treatment going to come out," because we talked about some of the things in the pipeline, but just because they're in the pipeline doesn't mean that we're on the verge of seeing those available for the mass market there. So, I think, we're still years away from a lot of those treatments—I would say at least 2 or 3 years away—but the work is being done, and there's a lot of great research being done in way of getting better treatments. So, I said it before. We're at 1.0. These injections that we have today that are available are GA treatment 1.0. Ultimately, there will be a 2.0 and 3.0 and, hopefully ultimately, a cure for all of these things. But that's where we are relative to the research being done.

MS. KACI BAEZ: Oh, thank you for that. It really is amazing. There's new progressions, I think, happening every day, but you're right, it can take years to see that develop. So, it is wonderful to have your insight on that process. A couple more questions left. And I wanted to know what kind of resources do you provide to your patients after their diagnosis to help them understand their diagnosis and to make an informed decision on treatment and I should mention, BrightFocus does have a resource on its website at www.BrightFocus.org/GA, and it's a free publication called Understanding Geographic Atrophy. But we'd love to have your take on what kinds of resources are available for something like this. This is a serious diagnosis and decision for people.

DR. VEERAL SHETH: Yeah, so, there's a couple different types of resources that I give my patients or counsel them on. So, there are handouts or brochures that I give out in clinic that describe GA, but also describe the treatment, including the benefits of the treatment and the risks of the treatment, because I think, just like this conversation we're having, it's very important for patients to understand exactly what those benefits and risks are before they start any kind of treatment. Because, I think, the more educated you are upfront and the more you're basing your decision on that information, the more you'll understand what the process is going to be and stay engaged with it over time. I think that's critically important. So, handouts are one thing, but I also very often refer patients to two

different websites. One is your website, which is BrightFocus Foundation and, in particular, what you mentioned, some of the information on GA. I think it's a great resource. It talks about questions you should ask your doctor. It talks about vitamins and the role of everything that we do and how we manage GA. So, I think that's an important one. The other are resources by the American Society of Retina Specialists, or ASRS. I think they have really great patient information, not just on GA but other retinal issues as well. And so, those are the ones I like because you can find a lot of information on the internet. We all know there's good and there's bad. And so, I think it's really important to focus in on those really high-quality sources of information.

MS. KACI BAEZ: Absolutely. It's so important to use scientifically vetted, trusted information. So, thank you for that. Do you have any final remarks or advice to offer to our listeners today?

DR. VEERAL SHETH: I think the fact that the listeners are here listening is a great step. I think it tells me if people want to know information. They're asking the right questions. They're looking at the right resources to get the information. For me, personally, as someone that has worked on research and development for these treatments for wet macular, for dry macular, for GA, I'm just super excited, because we've been working on treatments for many, many years, and to finally have treatment options available to patients for a disease that we had zero treatments for over 2 years ago, to me, that's exciting, because I think there are a lot of patients in my clinic that have hope today that didn't have hope just a couple years ago. I think it's changing the course of their lives. I think it's improving their independence and the amount of time that they'll have to maintain that central vision and that independence that comes along with that. So, to me, I'm very optimistic. I'm very hopeful, and I think it's important for us to continue to push forward to look for better and better treatments, and I think forums like this are very important for us to ask those questions. Because we want to know what patients need. We don't want to just create treatments without that input. And so, that input really matters, and what matters to patients is going to help drive the next generation of treatments.

MS. KACI BAEZ: Absolutely. Thank you so much. This discussion has been extremely informative, and you shared so much today that I think will help our listeners as they navigate their journey with macular degeneration. So, thank you, again, Dr. Sheth, for sharing so much today about GA and the current treatment options with us. And to our listeners, I sincerely hope you found today's program helpful. Our next Macular Chat will be on Wednesday, November 20, and is titled, "Adapting to Life with Low Vision." So, thank you again so much to everyone for joining us today, and this concludes our Macular Chat.

Useful Resources and Key Terms

To access the resources below, please contact BrightFocus Foundation: (800) 437-2423 or visit us at www.BrightFocus.org. Available resources include—

- Macular Chats Archive
- Research funded by Macular Degeneration Research
- Macular Degeneration Overview
- Treatments for Macular Degeneration
- Macular Degeneration Resources
- Understanding Geographic Atrophy
- Expert Information for Macular Degeneration

Helpful treatment options or resources mentioned during the Chat include—

- IzervayTM
- Syfovre®
- American Society of Retinal Specialists
- C3 complement inhibitor
- C5 complement inhibitor