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Chats

Treatment Options for Geographic Atrophy

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Transcript of Teleconference with Veeral S. Sheth, MD, MBA, FASRS, FACS, Partner and Director of Clinical Trials, University Retina

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

MS. DIANA CAMPBELL: Hello. My name is Diana Campbell, and I am pleased to be here with you today for today's Macular Degeneration Chat, "Treatment Options for Geographic Atrophy." This Chat is brought to you today by BrightFocus Foundation. Macular Degeneration Research is one of our programs here at BrightFocus. We fund exceptional scientific research worldwide to defeat Alzheimer's disease, macular degeneration, and glaucoma, and we provide expert information on these heartbreaking diseases. You can find much more information on our website, www.BrightFocus.org. Now, I'm pleased to introduce today's guest, Dr. Veeral Sheth, who will discuss geographic atrophy, an advanced and severe form of dry age-related macular degeneration, and the landscape of treatments that are currently available. Dr. Sheth is a native Chicagoan who specializes in diseases of the retina and vitreous. He is a Clinical Assistant Professor at The University of Illinois Chicago, as well as a Partner at University Retina and Macula Associates. 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 clinical trials and has research interests in macular degeneration, diabetic retinopathy, and vein occlusion, as well as surgical pathology. He is involved in clinical trials to develop new drugs, delivery devices, and gene therapy. Dr. Sheth, thanks so much for joining us today.

DR. VEERAL SHETH: Diana, thank you for the kind introduction. A pleasure to be here today.

MS. DIANA CAMPBELL: I know this is a really hot topic; we've already been getting lots of questions on this, so we'll go ahead and start the discussion off by actually defining geographic atrophy—or, as we will likely call it and abbreviate it during the call, GA. For many people, it's a term they were not as familiar with until you started hearing a lot more about it over the past year or so as treatments have become available, even though statistics say that more than a million people in the U.S. alone currently have GA. Could you start by sharing with us: What is geographic atrophy, and how does it differ from or how is it related to dry macular degeneration?

DR. VEERAL SHETH: Yeah. Great place to start. So, you brought up the point that a million—and probably more than a million—Americans have this disease, but until recently, it wasn't something that we talked a lot about, and I think part of that is because we didn't have any treatments for it, and so, a lot of times we would see patients that have this type of macular degeneration, and frustratingly, we weren't able to offer them anything. And so, I think part of why we're starting to talk about it more, we're starting to hear about it, we're seeing commercials on television, is because, finally, as of earlier this year, we have treatment options for patients. So, let's talk a little bit about it. Geographic atrophy is a form of dry macular degeneration, and I think it's probably important to really define what dry macular degeneration is. So, what is the macula? The macula is the central part of the retina. What is the retina? The retina is the back layer of the eye; it's almost like the film in the camera. It's the part of the eye that processes your vision. And so, the macula, being the central part of that, is responsible for your central vision. And so, any degeneration that happens in that area is going to cause a degeneration in

your central vision. That's the vision that we use to read or look at faces or watch television with, or when we're on our devices, that's the part of the retina that's processing that information. And so, any degeneration in that area is going to affect all of those activities that we just talked about.

The dry component—why do we say “dry macular” versus “wet macular”? Well, for the longest time—for about 20 years—we've really focused in on wet macular, and when we say “wet,” we say wet because there's fluid leaking into the retina. That fluid could be blood, it could be components of blood, leaking into the retina causing vision loss. Why have we talked about that for 20 years? Because we've had great therapies, treatments, for those types of macular degeneration cases. But “dry” means that there's a degeneration that doesn't have fluid involved; there's no bleeding. And then let's talk about dry macular for a second. Dry comes in a lot of different flavors, as well. There are more mild forms of it, there's intermediate and more advanced forms, and the most advanced form of dry macular degeneration is called geographic atrophy. “Atrophy” means thinning or loss of that retinal tissue. In other words, in that central part of your retina, you're actually starting to see a loss of that tissue. And when you lose nerve tissue, when you lose retina, it's not working, and so you get central vision loss, blind spots in your vision, distortion in your vision, all of those things as a result of what we call geographic atrophy.

MS. DIANA CAMPBELL: Thank you for that really good description. I love hearing it described as the film in a camera and the visual that that gives us to really understand what's happening, so thank you for putting that into really understandable lay terms. As far as progression goes, how quickly does intermediate dry AMD progress to advanced dry AMD or geographic atrophy? And to follow up with that, if someone has received a diagnosis of dry macular degeneration or AMD, how often and when should they be following up with their doctor to discuss potential progression to GA or identification diagnosis of geographic atrophy?

DR. VEERAL SHETH: Okay, great questions. There are a couple parts. I'll answer your first part. Your question was really progression, and how quickly does intermediate dry macular progress to the more advanced forms, in particular geographic atrophy? And I think it's an important

point to just take a step back and say, look, it is a spectrum. We do see macular start off as mild macular; these are cases where we see a few little findings in the retina, and at that point, we're potentially informing our patients about it. And as it progresses, you see more changes to that macula, which are more concerning because as it advances, it becomes more likely over time that it can progress to something like geographic atrophy or wet macular degeneration, right—those are the two ends of the spectrum. To your question about how quickly does it change from intermediate dry AMD to more advanced dry AMD, there's no real cut-and-dry answer to that. There's a lot of variables here.

So, what are things that might cause the macular degeneration in a patient's case to progress more quickly? So, genetics, right—we know that there's a big genetic component to macular degeneration; if you've got a strong family history of it, there's a chance that your macular degeneration may progress more quickly, so it's really important, one to know what that family history is, and certainly relay that information to whoever's taking care of you and doing your eye exams. Things like environmental factors that sometimes we do have control over, I'll give you one: smoking. Smoking really causes an accelerated progression in your macular degeneration, and so if you've got two patients that present with the same disease, the person that's smoking is going to likely progress more quickly than the person that's not smoking. So, that's an important driver in how quickly or how slow that disease can move. Things like diet, right, we kind of take these things for granted sometimes, but one of the reasons your doctor may recommend certain vitamins is because we know that certain antioxidants—like vitamin E, zinc, copper—those things can slow down damage that's occurring in the macula. Look, just a green, healthy vegetable every now and then can help slow things down. So, we know that diet affects that, as well. And then age, right? The older you are—this is called AMD, age-related macular degeneration—so, the older you are, the more quickly it can progress. And so, those are just different variables that can all factor together to cause faster or slower progression in this disease.

Your second part of your question was: If someone now is diagnosed with dry AMD, when should they follow up to their doctor—their eye care

provider? And the answer to that is: It depends, right, and it depends on a lot of those things we just talked about. What is their risk? Do they have a strong family history? Are they a smoker? And how advanced is their disease? And so, a lot of that math is going to be done by the person taking care of your eyes. If they think you're at low risk and you've got fairly mild disease, they may say, "Come back in 6 months or a year." But if you've got more advanced disease, and you certainly have more risk factors, then they may say, "Well, look, maybe come back in 3 months or come back in 6 months." So, I think a lot of it depends on a lot of those factors we discussed, but it is absolutely something that you're going to want to discuss with your eye care provider.

MS. DIANA CAMPBELL: Thank you. Let's switch over to when they've already received a GA diagnosis. Does progression tend to happen at a faster pace once geographic atrophy has set in? And we have listeners asking: How much does a GA diagnosis increase the probability or possibility of going blind? Let's start there, and then I have a couple other questions from the audience.

DR. VEERAL SHETH: Yeah, great questions. As I mentioned, geographic atrophy is one of the most advanced forms of macular degeneration, so certainly, because of that, the risk of losing vision ... and the word "blindness" is a little tricky because patients will ask about this all the time, "Am I going to go blind?" And with macular degeneration, if your only problem with the eyes is macular degeneration, you're not going to go blind in the sense that you wake up and all of the sudden the world is dark on you. But it does affect the center-most part of your vision—arguably the most important part of your vision because, again, that's where your fine focus comes from, but your peripheral vision is not affected by it. And I say that because people can function perfectly well if they have geographic atrophy in one eye and the other eye is not experiencing that; they can have a full field of vision and good central vision. So, that's just something to keep in mind. But if your question is, "How quickly is it going to speed up once you get that diagnosis?" I kind of default back to the answer to the last question, which is: There's so many variables here, including genetics, including are you a smoker or not, including some of those environmental and age-related things that we talked about, and

so there's no clear-cut way of answering that question, but what I will say is: There are certain characteristics that your doctor is going to look at with that GA as a retina specialist. We're not just saying, "Do you have GA or not?" When you have GA, we're really looking into, okay, what are the characteristics? Are there multiple spots of GA? How large is the GA? Where exactly is the GA in your retina? Because all of those variables for us can then help guide us to: How quickly do we expect this GA to accelerate or change over time? Again, then allowing us to inform our patients about that. So, again, not to be coy or not to avoid the question, but the answer is really: It depends. But there's a lot of variables at play, including what your eye doctor is seeing in the eye and how they're defining it.

MS. DIANA CAMPBELL: Absolutely. I'm going to go to a couple audience questions. One is related to the environmental factors we were discussing, and the question is specifically: Does screen time—you know, focused time on computers and/or phones or other screens—does that contribute at all to progression?

DR. VEERAL SHETH: Yeah, it's such a timely question, because I think what we learned—especially as retina specialists—what we learned during the pandemic is a lot of people are on their screens a lot more, right, whether it's because you're working from home, whether it's because we've just seen an explosion in these devices that we have around us, whether it's tablets or phones or whatever it is, and we're on them all the time now. And so, we're constantly asking the question of: Hey, is that hurting us in a way that this is going to impact things like macular degeneration? Or things like nearsightedness? And the answer is: We think so, but it's such a new thing for us, right, we haven't had these devices for 50, 60 years; really it's been 5–10 years where we've seen the increased use of these devices. So, because of that, because things like macular degeneration are a slow-moving kind of disease, they're something that you don't see in 30- and 40-year olds; you tend to see them in 60-, 70-, 80-year olds. We don't have great answers to that yet; I think we will at some point, especially once we've had more time with these devices, and as people that have been using the devices at earlier ages get a little older and we see the impact on that, we'll have better answers. But what

I would tell you is what I tell my patients, which is: Look, everything in moderation. I think anything where you're going overboard or doing just excess amounts of things like this where you're on the screen for 8, 10, 12 hours a day, which we see pretty commonly for people that are on the computer for work and things like that, I tell people, "Look, you've got to take breaks, you've got to give your eyes a rest." I think the question of wearing glasses that help kind of filter out blue light, putting on screen guards that help filter out some of the light—I think these are all good ideas, just common sense ideas. We don't have the best evidence yet; I think one day we will, but I think these are kind of common-sense things that we can do. One, not just to reduce eye strain, but eventually to reduce some of these harmful effects of these screens that are in front of us.

MS. DIANA CAMPBELL: I like that practical advice. I know for me, being on the computer all day and then back and forth on my phone, I definitely feel like my vision is blurrier and my eyes are tired by the end of the day, so that's something I can observe, but I imagine there are other processes that are likely going on beyond that.

DR. VEERAL SHETH: Yeah, and listen, to that point, we're also getting introduced to these screens much earlier, right. I mean, you talked about your son. Well, kids are on these devices quite a bit now, and we still are just learning about the impact. So, I think, again, that's just blanket advice about moderation.

MS. DIANA CAMPBELL: Absolutely. Okay, we've got another question, from Ralph, who is asking about home monitoring: What changes in particular that one notices as they do the Amsler grid should they immediately call their retina specialist about? And are there other signs that people should be looking for at home, kind of looking out for as a signal that their vision might be worsening?

DR. VEERAL SHETH: Yeah, great question. Home monitoring is really important. We talk to all of our macular degeneration patients about this. So, you talked about the Amsler grid; so, hopefully, everyone on the call knows what that is, and if not, it's a little grid that has a series of boxes of lines, and the key is you test each eye independently—so,

cover one eye and take a look at reading distance at that grid—and if you have no macular degeneration, all those lines, theoretically, should be straight. Now, if you have some degree of macular degeneration, even just intermediate dry macular degeneration, you may have a little bit of distortion—so, some of those lines may not be straight, they may be a little wavy. And if that's your normal baseline, that's your normal baseline because some degree of that is expected if you've got some degree of macular degeneration. Now, the key is—and your question is, "When do you notify your doctor?"—is when you start to notice changes from your baseline. So, if you start to say, "Look, the lines are looking wavier to me," that's a good reason to call your doctor. If you say, "Look, I'm starting to see real blur in that Amsler grid," that's a reason, or, "Hey, I'm seeing a dark spot in that grid"—any of those things are kind of triggers for you to say, "Look, I'm going to call my doctor." And your doctor's going to listen to you, they're going to say, "Look, I expect that because of what you have," or, "Hey, that sounds different, why don't you come on in and let's take a look?" So, I think it's worth making the phone call and then letting them decide what the right next step is for them.

MS. DIANA CAMPBELL: Great. Another quick question from a listener: Does having GA in one eye increase the likelihood that they'll have GA in the other eye, whether or not they already have dry AMD in that eye?

DR. VEERAL SHETH: Yeah, it's a great question. One thing that I can tell people is that the general thing is that if something's happened in one eye, it's more likely to happen in the other eye. That goes for macular degeneration, that goes for cataracts, that goes for really any problem. And it's no different for GA. So, GA, yes. If you've got it in one eye, you are at a higher risk of developing it in the other eye. And that, again, goes for dry AMD, wet AMD, GA, all of it. And I think it's important because your doctor's going to know that, and they're going to be looking for that every time. People that are listening that go to see their doctors for GA or wet macular degeneration know that, generally speaking, their specialists are really not only looking at the eye they're treating, but also looking at the other eye specifically for this reason.

MS. DIANA CAMPBELL: Absolutely. I know a lot of times in the Chats,

people like yourself will say, “Not only is every person different, but every eye is different, really are treated as two different potentials”. We’ve got plenty of people on the call today with both wet AMD in one eye and dry AMD in the other, so that’s good to know.

DR. VEERAL SHETH: Absolutely.

MS. DIANA CAMPBELL: We’ll ask one last quick question about dry AMD, and then we’ll shift over to the treatments that have become available this year. So, the question is: There are many people who are currently on AREDS2 vitamins because they have been identified as having dry AMD. Listeners are asking, “Are AREDS effective at all once the dry AMD has progressed to geographic atrophy?”

DR. VEERAL SHETH: Yeah, it’s an important topic because it is one of the things that we’ve told people about, told patients about, for decades, and so really, what is the purpose of AREDS vitamins? The purpose of AREDS vitamins—and now we’re talking about AREDS2 formulation of these vitamins—is to reduce the likelihood of that dry macular degeneration progressing to the wet macular degeneration. So, whether they have GA or intermediate dry macular degeneration, I recommend these vitamins to my patients because I do think it lowers the risk of them developing the wet type of macular degeneration, and so I think it’s important, and I think it’s a great question to ask, and certainly it’s a good question for patients to ask their eye care providers about because at some stages of macular, we may not even recommend the vitamins, and so I think it’s a really important thing to discuss with your provider.

MS. DIANA CAMPBELL: Absolutely. And then, of course, going back to the different scenarios that might be occurring in one eye or the other, so it could be helpful for one, I suppose. Okay. Let’s kind of shift over to the exciting news of the year. It’s been a really busy year in ophthalmology, but especially related to the first-ever treatments for geographic atrophy. In February and then in August, we saw the first two drugs approved for treating geographic atrophy. Could you give us an overview of the treatments that are now available?

DR. VEERAL SHETH: Certainly. In the intro, I know you mentioned that

we do a lot of clinical trial work. So, we've been doing clinical trial work in geographic atrophy for many, many years, and so we've had this kind of pent-up excitement about potentially being able to treat patients that have geographic atrophy for many years, and that all kind of exploded earlier this year, like you said, when we had our first treatment approved, which was called Syfovre®, and then, subsequently, about a month ago, a second treatment called Izervay™, and so this has really changed everything in our field. This reminds me of 20 years ago, when we had our first treatments for wet macular degeneration approved, where before that we had no real good way of stabilizing people's vision, and at that time, 20 years ago, it was a game changer. So, I feel that happening again in our field, and it's incredibly encouraging because we have now, for the first time, like you said, something to offer patients.

So, what does that mean? What are these treatments really aimed at doing? So, before this, we talked about geographic atrophy and how the atrophy, or the thinning in the retina, can gradually spread over time, and what that means is, the vision loss associated with those areas that are becoming atrophic, or thin, starts to expand. In other words, if you've got a blind spot from atrophy, the blind spot gets bigger over time. Well, these drugs, what they do is, they don't reverse the blind spot—in other words, they don't put retinal tissue back in—but what they do is they slow down the further damage that's going to happen in that eye.

In other words, if you're on a trajectory of that atrophy getting worse and worse and worse over time, these drugs are going to slow down that trajectory. They won't stop it, so they won't kind of halt it in its tracks, but if you think about atrophy like a runaway train, this can really help slow that train down. So, we're excited because what we know that means for our patients is that, if I have a patient that's starting to lose vision from atrophy and I start them on one of these treatments, I know that a year later or 2 years later or 3 years later, that these patients are going to be better off because I took them off that runaway train and I put them on a slower train. So, that vision loss, we've really started to slow it down in a meaningful way. We talk to patients all the time that are kind of on the verge of losing some of that central vision, and let's say they're 20/40 today, but I know that that macular degeneration's going to get worse,

and within a year or two, they may be 20/60 or 20/70. We're talking about the difference between being able to drive and run your own errands to now, potentially, losing your license. And so, if we can slow that process down and delay that as much as possible, that, to me, is going to have a meaningful impact on that patient's life.

MS. DIANA CAMPBELL: I love how you articulated that. And I know it's been a bit of a decision for folks, and we'll talk about this in a moment, but weighing side effects with doing something that you know is good for you, but you're not seeing necessarily the immediate benefit. So, we'll continue to talk about that in a moment. I know both of these drugs target different areas or components of the complement pathway; could you kind of go over how they work in the eye and then the differences between the two in terms of approach? And then, I guess, touch on whether ... contrast and compare—are the treatment regimens the same? In particular, is it the same intervals in between injections? So, both how the drug works and then how the two treatments differ and are the same.

DR. VEERAL SHETH: Yeah. Okay. Good question. So, you mentioned "complement" at the very beginning of that question, and I think it's important to kind of talk about what that is just briefly. So, complement is a process in our bodies—everywhere in our bodies, but in particular in the eye—responsible for potentially something like inflammation. And we know historically that the complement factor or this kind of hyperactivity of this complement in the eye may be associated with worsening geographic atrophy. We know that from gene studies and things like that in the past, and for longer than a decade, we've known that there's an association there. And so, the thought was: Okay, well, if we can slow that complement activity down in the eye—in other words, kind of tune that inflammatory pathway down a bit—can we then slow down the damage being done in the eye? And so, that was kind of the theory behind why we are targeting that approach for this type of disease. And so, what we've seen with these two treatments is they both indeed really looked at slowing down that process. They do this in slightly different ways, but what we've seen is, by doing that, we've seen, clinically, we've been able to slow the disease down. And so, it's important to understand, okay, well, what are we doing? Essentially, what we're doing is kind of

turning the inflammation down in those deep layers of the retina, which are responsible for the geographic atrophy progression. And so, if we turn those down, we can slow down the damage being done. Okay. So, then your next part of the question was: How are these similar? So I kind of ... that's how they're similar. The other similar approach is they're both given in the same way—they're both intravitreal injections. So, we have to numb the eye up and then give the injection so that the medicine goes directly into the eye. And that's for people on the call, they probably are aware of these types of treatments; we've been doing this for wet macular degeneration for 20 years, for things like diabetic retinopathy and retinal vein occlusions for a long, long time. And so, the type of procedure is not new by any means; it's just the treatment itself is new—both of these treatments. And then how often are they given? They're both approved to be given monthly; the Syfovre can be given every month to every 2 months, so you can go every other month with the treatment and still have a good, efficacious effect. The Izervay, we right now currently have it approved for every month treatment, and by giving these treatments, you can really see a meaningful slow-down in the disease. And then they can be given for quite a long period of time in order to kind of continue that slow-down of the disease. I think I answered most ...was there another part of that question there? I might've missed it.

MS. DIANA CAMPBELL: No, I think you've got it. Thank you. We have a question from the audience. We had the opportunity to talk a little bit more in depth about Syfovre after the February approval. We've got a listener asking for the most recent data—or, as they said, statistics—for Izervay in terms of a percentage of slowing down progression. Can you talk a little bit about what that data looks like?

DR. VEERAL SHETH: Yeah. So, there were a couple, for the Izervay in particular, there's a couple of studies done. They were called the GATHER1 and GATHER2 studies. And these were the studies that helped get the FDA approval. And what they demonstrated in those studies is somewhere between a 17 and 34 percent reduction in the growth of these geographic atrophy lesions. So, we're talking somewhere between 17 and 34 percent slowdown of these lesions. And so, I tell people that because, and I not only tell them that, I show them the pictures of their atrophy when they're

in my clinic, because I think when you see this and when you see this on the screen in front of you, you can really appreciate, "Well, yeah, if I slow this down and I can prevent this from really kind of growing in the central retina, we can have a meaningful effect on vision."

MS. DIANA CAMPBELL: Absolutely. Let's see. I'm scanning through a couple different questions we have here; I'll go with the next one, being: How do doctors evaluate which to use in patients? And is it possible, we have a lot of people wondering: If they've started with one, are they able to then move to the other? I know with wet AMD in particular, doctors tend to try one, and if they're not pleased with the results, they switch. Is that the case for these two drugs, as well?

DR. VEERAL SHETH: Yeah. It's a great question. And so, the first part was: How do you pick between these two treatments? And what I'll tell you, Diana, is that these are both really new treatments, right? And when we have two new treatments like this, we're really kind of using them both and getting a feel for what's happening in the real world because both have really good clinical trial data, meaningful and good slow-down in those clinical trials. What we want to see now kind of that next stage of adoption, is, okay, let's get it in our hands, let's use it, let's see how patients do with it, and we're just in the early innings of that, right? We just had one approved in February and one last month, and so if we have this conversation a year or two from now, the answer might be different, but we're so early in the process that I think there's no real... at least in my personal practice, we're using both treatments. So, the next part was: Can you switch? And that's a tougher question to answer because neither of these clinical trials looked at that, right? So, we don't have any clinical trial data that had a patient on one of these treatments that then switched to another treatment. So, there's no real great way of me answering that question. Do I think that in the real world we will be doing that, where we'll have a patient on one and, for whatever reason, we may switch them to another treatment? Absolutely. I think it happens all the time in wet macular degeneration, so I do foresee that happening, as well, with geographic atrophy treatments. And so, again, once we have more time with these therapies in the real world, I think the answer is yep, we're going to do that, and my instinct is that you can do that without really too

much concern.

MS. DIANA CAMPBELL: Yeah, a really good point about how new these treatments are. You know, I feel like we've been waiting for these for a long time and looking forward to seeing how it works in the real world. But absolutely, I realize we're not even a year in on either, at this point, so we'll make sure to continue to follow up on that as time goes on and revisit that discussion next year. Before I get into side effects and balancing those, which we have a lot of questions about that, are these treatments advised or available for those who already have wet AMD? What does that treatment plan look like?

DR. VEERAL SHETH: Yeah. A really good question, and again, one of the things that I can tell you is that we didn't really study, in a broad way, patients that had wet macular that now were starting on treatment for geographic atrophy. But what I will tell you is, in our clinical practice, since these drugs have been approved, we are indeed treating patients that way. So, in other words, if I have a patient that I'm treating for wet macular degeneration and they have geographic atrophy, I have started some of those patients on the treatment for the geographic atrophy, in particular because I think that that is driving some of their vision loss or that could soon to be driving some of their vision loss. I want to get ahead of that atrophy in those cases. And so, we are seeing that, but again, not broadly studied in these clinical trials, so can't give you real good data on it yet. I think I answered that question. Any other questions on that?

MS. DIANA CAMPBELL: Related to that, I'm going to kind of shift over into balancing the conversation about potential side effects and balancing those with the benefit of delaying the progression. And so, on that same topic of wet AMD, I do have folks who are wondering what percentage, or what's the risk of developing wet AMD after having an injection of either Syfovre or Izervay?

DR. VEERAL SHETH: Yeah, it's an important question, and it's something that I talk to all my patients about because risks with any treatment in general are really important to discuss with your provider. So, the way I break it down, there's kind of two buckets of risk. One bucket is just the risk of an injection procedure, right, so that could be any

medication you're injecting are going to have a common set of risks. The most important for me is infection. Right, anytime you're putting something from outside of the eye into the eye, there's a risk that there's contamination or something like that. Now, thankfully, I think the risk is very low, and we do certain things from a technique standpoint to keep that risk as low as possible, but absolutely something to talk about, and it's something that I tell my patients about all the time.

Then, there's the risk of the actual drug itself, that's the second bucket, and what we've seen with both of these treatments is that there's potentially a slightly higher risk of developing the wet macular degeneration in the eye that you're treating for geographic atrophy—in other words, an eye that just has geographic atrophy, no wet macular degeneration, if you start treating with Syfovre or Izervay, there's a chance—slightly higher chance—that you develop the wet macular degeneration in that eye. And it's a very important topic, again, to discuss because it's something that I talk to my patients about, it's something that has certainly made some patients think twice about treatment because they don't necessarily want to then start having treatment for wet macular degeneration. But some patients—especially patients where their geographic atrophy is really starting to risk central vision loss and really approaching the central part of their vision—they will say, "Well, doc, I know you have a treatment for wet macular degeneration; I know the risk is there, but I'm willing to take that on because if I can maintain this level of vision, I'm going to do everything I can to do that." And so, it's really about talking through these risks with the patient and then really as a group deciding what's right for that individual.

MS. DIANA CAMPBELL: Sure thing. I'm going to clarify—we have someone asking whether the treatments repair lost vision, and I just wanted to clarify that these are really designed to slow down progression, and they're not going to cause people to regain their vision that's already been lost. And I really like what you said earlier about showing your patients the pictures to be able to see the progression and what it might mean and, really, the example you gave of driving or not driving and losing independence, obviously, I think are important things as part of this conversation. We have two other side effect questions that I'll just kind

of do quickly. Does GA itself or GA treatment increase the risk of retinal detachment? And the second one is: Does GA or GA treatment increase the risk of a failed interocular lens following cataract surgery? They're both a little bit different, but these are of the interest to the audience.

DR. VEERAL SHETH: Okay, good. So, just quick, blanket comment: The GA itself does not increase any of those risks, so the geographic atrophy or having a diagnosis of geographic atrophy does not increase your risk of a retinal detachment or any lens cataract issue. The injection procedure—again, independent of what disease you have, it could be GA, it could be wet macular, it could be diabetic retinopathy—but the injection procedure itself does carry a slight risk of having a detached retina. We talked about the infection risk. The cataract risk is very minimal. Are there cases where it affects the lens in the eye? It can, but very rare. And so, it's one of those things, again, these are things that we do counsel our patients on, especially things like retinal detachment, but again, risk is very low and not necessarily associated with the fact that it's GA or a treatment for GA, but really because of the procedure itself because of how we're giving the treatments.

MS. DIANA CAMPBELL: Sure thing, that makes perfect sense. As we start to wrap up, I know that I've had many discussions with folks weighing the potential benefit with how much progression they think they might halt versus side effects. What are there two or three questions that you would suggest that would kind of guide the conversation with our listeners as they are talking with their doctor throughout this decision-making process?

DR. VEERAL SHETH: Yeah, I think there's always good questions you can ask your doctor, and I'm really basing these off of what my patients ask me and what I consider really good questions for them to ask because the information they get is meaningful. It can help them decide how they're going to follow up, or the importance of follow-up, or how they're going to counsel their family members and instruct them to maybe get their eye exams, right? I think all of those things are important, and so how do you ask that question? You start with, "Do I have macular degeneration?" I think if you're going to an eye doctor—and I think a lot of people start

at primary eye care, whether it's your optometrist or ophthalmologist, not necessarily a retina specialist—so I think it's important to ask those eye care providers basic questions: Do I have macular degeneration? Do I have cataracts? Do I have glaucoma? Those are the three that I think are probably the most important to ask about. And if the answer is no, great. Then it's about, "How often do I follow up?" But if the answer is yes, then it's, "Okay, doctor, what can I do to lower my risk?" It may be taking vitamins, it may be wearing sunglasses while I'm out and about, so, there's a whole host of things that, again, are going to be tailored to that individual and really important to have as a one-on-one conversation. And then that last thing I kind of mentioned is: "Do I need to worry about my family members? Do I need to counsel my family members?" And one of the things that comes up a bit in my office is, I have a patient in for macular degeneration, and they ask about their family, and I ask just some basic questions—especially about smoking, right, and that's one of those things where we can tell them, "Hey, if they haven't been told, let's see if they can cut down the cigarette smoking," because we know that's a huge driver in progression, especially if you've got a family history. So, things like that are important to discuss with your eye care provider.

MS. DIANA CAMPBELL: Outstanding. I could've asked this earlier. We just got a question about secondhand smoke. We understand that smoking cessation and trying to quit smoking if you are a smoker definitely reduces that risk; what about secondhand smoke? Is that something that people should be worried about, or has that been studied?

DR. VEERAL SHETH: Yeah, there's not a lot of great data on it, but I think there's enough data to suggest that yes, I think it does matter, especially if you're in a house where people are smoking quite a bit, I think it does matter. I think, fortunately, just when we're out and about, we're exposed to a lot less secondhand smoke. We don't see it as much, at least in the U.S., at restaurants or when we're just kind of at events, and so that's been good, I think that's had a good effect, a positive effect on people's health and their eyes in particular. But yes, I think if you're in a home where there's people smoking, I think it does increase your risk theoretically.

MS. DIANA CAMPBELL: Okay, that's great to know, thank you for that.

We're running out of time. I sincerely hope that everybody found today's Chat helpful, and we know that participation in research studies is what advances the field in terms of treatments, and this has been a great example of that today. And I just want to say that this is an ongoing topic, and we're thrilled to be able to talk about the fact that there are now treatments for geographic atrophy. And to your point, I think the real-world experience will be ongoing, so we'll bring you back at some point to kind of give an update after some time under our belts. So, Dr. Sheth, before we conclude, are there any final remarks or tips or overarching message that you'd like to share with the audience today before we conclude?

DR. VEERAL SHETH: I think the last bit is just if it hasn't come through yet in my statements, I think this is an incredibly exciting time for us as eye care providers because we're finally able to treat this huge unmet need, and we're really excited about it, and so hopefully, this kind of sparks a conversation not just amongst this group but amongst your friends and families and certainly with your eye care providers. Again, I appreciate the time here and the ability to discuss this with everybody on the call. Thank you very much.

MS. DIANA CAMPBELL: We really appreciate your time. We know how busy you are, both with trials and seeing your patients, as well, so we really want to give you a warm thank you for taking the time today to discuss this with us. And as I mentioned, we'll give you a call back after some time has passed, and we can kind of revisit the topic and see where we are. So, thank you again, and thanks to the audience for tuning in. And with that, this concludes the BrightFocus Macular Chat. Thanks so much for joining today.

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—

- [Amsler grid](#)
- [Apps for People with Low Vision](#)
- [BrightFocus Foundation Live Chats and Chat Archive](#)
- [Clinical Trials: Your Questions Answered](#)
- [Healthy Living and Macular Degeneration: Tips to Protect Your Sight](#)
- [How Low Vision Services Can Help You](#)
- [Macular Degeneration: Essential Facts](#)
- [Research funded by BrightFocus Foundation](#)
- [Safety and the Older Driver](#)
- [The Top Five Questions to Ask Your Eye Doctor](#)
- [Treatments for Age-Related Macular Degeneration](#)
- [Understanding Your Disease: Quick Facts About Age-Related Macular Degeneration \(AMD\)](#)

Other resources mentioned during the Chat include—

- New drugs to treat geographic atrophy: Syfovre and Izervay