Macular Chats

Saving Sight: How Long-Term Treatment Helps Slow Geographic Atrophy
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Transcript of Teleconference with Sara Fard, MD, Board-certified ophthalmologist and Vitreoretinal surgeon at Illinois Retina Associates

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

DR. JIMMY LIU: Hello, and welcome. My name is Dr. Jimmy Liu, and I'm the new Director of Vision Science Programs at BrightFocus Foundation. I'm pleased to be your host today for today's Macular Chat, "Saving Sight: How Long-Term Treatment Helps Slow Geographic Atrophy." Macular Chats are a monthly program¾supported in part by sponsorships from Apellis, Genentech, and Regeneron¾designed to provide people living with macular degeneration and the family and friends who support them with information straight from the experts.

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BrightFocus Foundation's Macular Degeneration Research Program has supported over $56 million in scientific grants exploring the root causes and potential prevention, treatment, and cure of macular degeneration, and is currently investing in 44 active projects across the globe.

Now, I would like to introduce today's guest speaker. Dr. Sara Fard is a board-certified ophthalmologist specializing in vitreoretinal surgery. Born in Iran and raised in Toronto, Canada, Dr. Fard's academic and personal journey reflects a lifelong commitment to excellence, compassion, and service. She completed her undergraduate studies at the University of Toronto and earned her medical degree from the University of Maryland School of Medicine. It was during medical school that she discovered her passion for ophthalmology, drawn to the profound impact of restoring vision and the precision required for ocular microsurgery. Known for her calm demeanor, attention to detail, and genuine empathy, Dr. Fard combines her deep clinical knowledge with a patient-centered approach. Her specific passions in retina include diabetic retinopathy and our topic today, age-related macular degeneration, in both their treatment and prevention. Thank you for joining us today, Dr. Fard.

DR. SARA FARD: Thank you, Jimmy. Thank you for that wonderful introduction, and it's a pleasure to be joining you today.

DR. JIMMY LIU: Of course, and it's so great for you to be on this call and a pleasure to speak with you today too. So, let's jump right into the questions. So, the first question that I have is: For those that are unfamiliar, can you explain what geographic atrophy is and how it fits within the spectrum of age-related macular degeneration?

DR. SARA FARD: Yes, absolutely, and thank you to all our participants for joining us today. So, geographic atrophy—sometimes I'll just say GA—is the advanced stage of nonexudative, or dry, age-related macular degeneration and consists of localized and well-demarcated loss of outer retinal layers and its underlying layers that may expand over time. Geographic atrophy is the final stage of dry age-related macular degeneration.

DR. JIMMY LIU: Perfect. When you diagnose geographic atrophy, or GA,

what signs should individuals look out for?

DR. SARA FARD: Geographic atrophy is diagnosed via clinical examination that shows atrophy or a loss of cellular layers in the retina. We can confirm it in the clinic with imaging of the retina. Individuals should look out for blind spots in their vision, which will usually be near their central vision, as well as difficulty seeing at night and with reading.

DR. JIMMY LIU: Nice, so just to recap, the retina, which are the important cells that help translate what you see into information your brain can understand from your eye, start to die, or atrophy, when someone has geographic atrophy, which affects your ability to see centrally. And the only way to confirm if you have geographic atrophy is through retinal imaging through your health care provider.

DR. SARA FARD: Exactly. Thank you, Jimmy, for clarifying and simplifying. Exactly, it's with retinal imaging, as well as with a retinal exam in which your ophthalmologist basically puts on a headset and takes a look at your retina with a lens.

DR. JIMMY LIU: Perfect. And so, another question that I have is: GA was long considered untreatable, so what breakthroughs led to the development of current therapies?

DR. SARA FARD: Great question. Basically, research into its pathology and genetics have found that geographic atrophy involves dysregulation of a certain pathway in the immune system. This pathway is called the complement pathway. Therefore, we've had targeted drugs that have developed that inhibit molecules in this pathway. There's C3 molecules and C5 molecules, all part of the immune system. These drugs were tested in Phase 3 clinical trials and approved by the FDA in 2023.

DR. JIMMY LIU: Perfect. Can you walk us through those approved treatments, which are named Syfovre® and Izervay™, and how they work to slow the progression of GA?

DR. SARA FARD: Sure. Syfovre, that's the brand name. Its generic name is pegcetacoplan, and Izervay, which has a brand name of Izervay and a

generic name of avacincaptad pegol, just so you guys are all aware. So, like I said, they're both basically complement inhibitors, meaning that they inhibit molecules in the inflammatory pathway, the complement pathway. So, Syfovre is a C3 inhibitor, so it blocks all downstream complement activation. Izervay is a C5 inhibitor, so it blocks formation of C5a and C5b and this membrane attack complex. Both these approved treatments slow the progression of geographic atrophy, or death of the retinal cells, like you discussed, but they do not restore lost tissue. So in summary, that was very complicated, but basically both of these drugs just inhibit molecules in the inflammatory pathway.

DR. JIMMY LIU: Perfect, thanks. And so, as an additional question that might sound a little silly, but if Syfovre and Izervay target different pathways that help slow geographic atrophy, is it possible to use both drugs simultaneously to slow down GA?

DR. SARA FARD: Thank you, Jimmy. That is a great question, as well, and it's something that many people wonder, but currently, using Syfovre and Izervay together is not recommended because there's no clinical studies of combination therapy. The pivotal trials that we have, which are OAKS and DERBY for Syfovre and the GATHER1 and GATHER2 for Izervay, these pivotal trials have tested each drug alone, but they did not study the simultaneous inhibition of C3 and C5. And so, actually, in fact, there could be some safety issues when we target both of these molecules in the same inflammatory pathway. With simultaneous use of both of these drugs, there's going be a deeper blockade of this complement inflammatory pathway in the body, and that might not necessarily be better and actually can lower your immune system and inflammatory response so much so that it can be dangerous. So currently, it's best just to pick one agent, monitor carefully, and treat consistently to slow geographic atrophy growth. Switching drugs, however, from one to another could be considered if you have a safety issue with one drug or there's logistic preferences, such as insurance coverage or frequency of dosing, but simultaneous dual therapy is not evidence-based at this time.

DR. JIMMY LIU: Perfect, thank you so much for that explanation. And then continuing on, what should people expect during treatment, how

often are injections needed, and what is the procedure like for both of these drugs?

DR. SARA FARD: Okay, in terms of what people should expect during treatment, the Syfovre intravitreal injections occur every month or every 2 months, and then Izervay injections occur every month. The FDA had this prior 12-month duration limit that it removed for Izervay in February 2025, but there have been some studies that have explored every-other-month injections for Izervay, as well, but the current U.S. label for Izervay is monthly, whereas, again, Syfovre is every month or every 2 months.

The procedure for an intravitreal injection is topical anesthetic done by your ophthalmologist. Then we put some betadine to basically clear the bacteria. We do the quick injection of your eyes at a specific location that we mark, and then we quickly check your vision and your eye pressure and then go over some return precautions for you.

DR. JIMMY LIU: Great, that's an awesome explanation of the procedures. So, in terms of the two drugs itself, there is some long-term data that has been recently revealed about the effectiveness of these treatments in preserving vision and retinal structure. Could you describe a little bit about those studies?

DR. SARA FARD: Absolutely. So basically, in terms of the long-term data about the effectiveness of these treatments, for Syfovre, there's a trial called the OAKS trial, and that showed that Syfovre slowed the geographic atrophy at 12 months. And then, there's the OAKS and DERBY trials that have showed that Syfovre slowed geographic atrophy growth at 24 months. And then, there's a third one, an open-label GALE study that showed an increasing effect with continued treatment into years 3 and 4 with emerging functional benefits. And I'll explain what that means more simply.

For Izervay, there was a GATHER2 trial that showed ongoing slowing of progression of geographic atrophy through 2 years with an increased treatment effect versus 1 year, with consistent safety results. So, in fact, for Izervay, based on the results of this study, the FDA removed the duration cap for the U.S. label in February 2025 so that the label is now

unrestricted for duration.

But basically, there's specific trials for Syfovre and Izervay, and they've shown that when you treat these patients for longer, versus the controls, which is just a sham injection, there's even more slowing of progression of the geographic atrophy.

DR. JIMMY LIU: That's incredible. Thank you so much for summarizing the long-term data for both of those drug treatments. And so, the next question that I have, Dr. Fard, is: Why is sustained treatment important in managing geographic atrophy, even if patients don't notice any immediate changes in their vision?

DR. SARA FARD: So, the geographic atrophy in age-related macular degeneration, Jimmy, grows steadily, and the long-term data shows an increased effect with continued long-term injections. So, the goal is to delay retinal tissue loss, but it may take 1 to 2 years or more to see a big effect compared to the controls.

DR. JIMMY LIU: Lovely. And then, how does ongoing therapy help protect retinal tissue and support daily visual function over time?

DR. SARA FARD: The ongoing therapy will help protect the retinal tissue and daily functioning as the treatments will hopefully lead to slower lesion expansion, thereby preserving more functional retinal tissue for a longer time. In studies, Syfovre has shown a slower loss of central light sensitivity and fewer new blind spots. And pooled Izervay analyses have suggested lower rates of categorical vision loss, both compared to controls, suggesting slower rates of progressive vision loss in treated eyes than controls.

DR. JIMMY LIU: Awesome. That's a great explanation. And are there any measurable differences in outcomes between patients who begin treatment early versus those who wait?

DR. SARA FARD: That's a great question as well, Jimmy. But retrospective and follow-up analyses have shown that earlier and continuous therapy preserves more retinal tissue than a delayed start and that treatment

effect often strengthens after the first year for both Syfovre and Izervay. Also, it can be important to note that more retinal tissue may be saved if the patient starts their injections when the lesions are smaller and the fovea is not involved, which are typical of earlier stages of disease.

DR. JIMMY LIU: Perfect. So again, it is really important to make sure that you go to your health care provider to check your eyes to make sure that you do not have any developing signs of AMD or geographic atrophy, and that these specific treatments, if they're done early, can really help preserve vision.

DR. SARA FARD: Exactly.

DR. JIMMY LIU: Thank you. And so, the next question that I have that I think is really important for people on the call is: How do you address concerns about the side effects or treatment burden with these specific drugs?

DR. SARA FARD: Okay, thank you, Jimmy. And to go back on your last point, it's exactly what you said, that this age-related macular degeneration process is slowly progressing, and if you start before these lesions affect the center and cause that scar tissue or lead to that death of cells in the center of your vision, then you can preserve more of those cells for a longer period and use that useful vision. But in terms of side effects or treatment burden, basically, common side effects of injections of Syfovre and Izervay, similar to any injections, are the subconjunctival hemorrhage, which is just basically the bruise of the white part of your eye; floaters; transient eye pressure increases; and mild discomfort.

But with these injections in particular, there is a concern about increased rates of conversion from dry to wet age-related macular degeneration. With label-reported data at 2 years being for Syfovre, about 12 percent conversion to wet AMD with every-month and 7 percent for every 2-month injections compared to 3 percent in controls. And for Izervay, the conversion to wet age-related macular degeneration has been about 7 percent 1 year and 11.6 percent at 2 years with monthly injections, compared to 9 percent in controls. So if you do have that conversion to the wet age-related macular degeneration, your injections will stop being

Syfovre and Izervay and will be anti-VEGF injections, which are currently the standard of care.

There are other rare but serious side effects, as well, such as a post-injection infection that can happen with any injection. But the Syfovre label also includes a very rare—0.01 percent per injection—of this infection, so it is very rare to have these infections after an injection. But there are serious warnings of retinal vasculitis, which were often occlusive and all followed the first injection within 2 to 3 weeks of injection with the Syfovre. So to reduce the risk of injection, the ophthalmologist will proceed with a sterile technique and close follow-up and warn the patient about return precautions, especially in the first 2 to 3 weeks after an injection. And then to decrease treatment burden, which means like coming frequently for these injections, patients can discuss these injections every 2 months instead of monthly.

DR. JIMMY LIU: Great, that's an awesome explanation about the different side effects of these two different treatments, which, again, Syfovre, which is spelled S-Y-F-O-V-R-E, and then Izervay, which is I-Z-E-R-V-A-Y. And as a follow-up question, Dr. Fard, for those who experience mild discomfort in their eye from these injections, how long does that usually last if that happens?

DR. SARA FARD: Mild discomfort in their eyes, I guess it would depend on what is the cause, but typically, patients might have a little bit of soreness after the injection, a little bit of irritation because of the betadine, which is the antiseptic. That will last just that day and resolve by the next day in almost all cases. You can use some artificial tears the next day to help you, as well. But if you are having any serious side effects, that being, you know, worsening vision, flashes, floaters, red eye, lots of pain that persists beyond a day, you need to see your ophthalmologist. But that typical soreness usually only lasts 1 day.

DR. JIMMY LIU: Perfect, thank you so much for that explanation. What advice do you have to give to patients who are hesitant to start this treatment because they feel their vision is still okay? And I know we've talked a little bit before about the earlier, the better, but just maybe as a re-emphasis.

DR. SARA FARD: Absolutely, thank you. Geographic atrophy does often spare the fovea—and the fovea is the center of the macula and the center of the retina, which allows for central vision. Early on, the geographic atrophy spares the fovea, but once the atrophy or the death of these cells reaches the central fixation, then vision loss is irreversible because it's like loss of cells, and we can't regenerate the cells. So, the goal of these injections is to delay the progression of the disease process, to allow more time for the functional vision, that central vision, for hobbies that you have, like taking care of your children or grandchildren and for driving.

DR. JIMMY LIU: Perfect, yeah. So just like what Dr. Fard said, it's really important to go see your eye doctor to make sure that you're not developing signs of AMD so you're able to do those hobbies you enjoy doing or seeing your family and loved ones. Another question that I have, Dr. Fard: Are there any other or any promising therapies or technologies on the horizon that could further improve outcomes for geographic atrophy patients?

DR. SARA FARD: Okay, so thank you for asking that. There are new routes and targets, including subcutaneous complement inhibition, which is called the Sienna trial, and oral candidates as well instead of injections, which is named the JADE trial. Both of these trials are available actually at my practice, Illinois Retina Associates, but they both do require to follow up onsite monthly.

The Sienna trial, which is the subcutaneous complement inhibition, is a Phase 3 trial. Patients must have noncentral geographic atrophy that your ophthalmologist can diagnose with an exam and imaging. And the treatment includes subcutaneous injections of these different targeting agents versus a control. These are therapeutic agents that also target complement inhibition. So basically, it's sort of like an injection in your skin that is going to target the same pathway, but it's not an injection in your eye.

And then, we have the JADE trial, as well, which is a Phase 2 trial. It has an oral target. And it's an oral agent that you take by mouth. It's a phospholipid modulator, and it works by reducing inflammation by antagonizing or basically blocking certain receptors on immune cells

and eye tissue. And this allows for decreased inflammation and preserved vascular function in the vessels of your retina. So, those are two of the trials that we have ongoing at Illinois Retina Associates that you guys can ask about, but there are also other emerging cell and gene therapies like RPE cell therapies, as well.

DR. JIMMY LIU: Wow, that's incredible, Dr. Fard, that instead of getting monthly or 2-month injections, that you can take something that's either oral or subcutaneous (through the skin) in order to help with someone's geographic atrophy. That's really cool.

DR. SARA FARD: Absolutely.

DR. JIMMY LIU: Yeah. And then, how do you see the standard of care for geographic atrophy evolving in the next few years?

DR. SARA FARD: So, thank you, Jimmy. This is obviously a hot topic for many ophthalmologists and researchers and patients, but over the next few years, there will likely be earlier detection of geographic atrophy with our retinal imaging, and there's also going be likely more individualized dosing regimens with more long-term data with improved safety profiles of the current therapies available. So, the studies that I talked about are following patients up to 3 to 4 years with Syfovre, but maybe at that time, we'll have longer-term data, we'll know more about safety, we can maybe individualize things more on the specific patients, have more agents available, maybe even have the oral or the subcutaneous skin injections that we talked about with all of those agents.

DR. JIMMY LIU: That's awesome, yeah. That's great that there is an evolving standard of care for geographic atrophy for patients out there that patients can look forward to. So, I think we have time for some additional listener questions if that is okay with you, Dr. Fard.

DR. SARA FARD: Absolutely.

DR. JIMMY LIU: One of the questions that we received from one of the listeners was ... and this may go on a little bit about talking about retinal scans: How do I know my treatment is working? What can you see in

those retinal scans that tells us that my treatment is working?

DR. SARA FARD: Jimmy, that's a great question. At this time geographic atrophy, related to age-related macular degeneration, in itself is slowly progressive, but it does progress in patients. And these drugs slow the progression of the geographic atrophy like we talked about, right? So, there's no way in an individual to say this drug is definitely working or not. However, in our trials, we've seen that compared to controls, not getting these Syfovre and Izervay injections, the rate of progression of the death of the retinal tissue is faster than those getting treated, especially with longer duration of therapy. So, in an individual, a patient getting these injections, we will be able to see that with time, maybe a year, 2 years with these injections every month or every 2 months that the age-related macular degeneration is slowly progressing, very slowly. But we can't say this drug is the reason or ... there's no way in an individual right now to say this drug is definitely working. All that we can see is that this eye is very slowly progressing in its age-related macular degeneration and this may be likely due to the drug, given the studies that we have based on these drugs.

DR. JIMMY LIU: Yeah, great. Thanks so much for that explanation, Dr. Fard.

DR. SARA FARD: You're welcome.

DR. JIMMY LIU: Yeah, another question that we had was we talked about those two different pathways that lead to geographic atrophy. And so, one listener asked, "How do you know if C3 or C5 complement pathway is my issue? Could we be treating C3 when I'm actually impacted by C5 complement pathway?"

DR. SARA FARD: So basically, the causes of age-related macular degeneration and geographic atrophy are very complicated and multifactorial, right? And what that means is that basically somebody who has age-related macular degeneration, like the dry stage, has it because of many things, right? There's some genetics. There's some inflammation, that's the complement pathway in the eye. There's like some smoking, healthy diet—maybe that's all related to the inflammation. But basically,

the complement pathway has different targets, like C3 and C5. And in an individual, basically, the studies have shown both C3 and C5 are involved in the immune process and the age-related macular degeneration. These drugs are targeting the C3 or the C5, but in an individual, both the C3 and the C5 are involved in age-related macular degeneration and it's just the drugs are targeting different points in the same pathway, leading to the same results.

DR. JIMMY LIU: Perfect, thank you so much for that explanation. We have two more listener questions. So, one question that we had was: Can you have wet AMD and geographic atrophy in the same eye at the same time? And if so, which is more important to treat?

DR. SARA FARD: That's actually such a great question. So, geographic atrophy means death of cell layers, right? We can see it clinically when we look at your eyes. We can see it on imaging and confirm it with imaging. It gives us a better look with something called OCT and also fundus autofluorescence. You can have geographic atrophy with the wet age-related macular degeneration because geographic atrophy in itself just means death of certain layers in your retina and so forth. However, if you have the geographic atrophy without any signs of the wet age-related macular degeneration, so without any swelling of your retina, without any bleeding of your retina, that is just called advanced dry age-related macular degeneration, and you're a candidate for the Syfovre and the Izervay.

Now, on the other hand, if you have the geographic atrophy, which is death of those cell layers, now with swelling of your retina that we can see on imaging with abnormal blood vessels, with bleeding, that's called wet age-related macular degeneration, and at that point, the standard of care is going to be another type of injection called anti-VEGF injections. So, you might've heard of injections like Avastin®, Eylea®, Lucentis®, Vabysmo®. Those would be the ones for the wet.

So in summary, geographic atrophy itself just means death of cell layers. If you have it without any of the swelling and without any of the hemorrhage, it's advanced dry AMD, and you can get Syfovre and Izervay. And if you have it with the swelling and the bleeding, then it's called wet

AMD, and you need the anti-VEGF injections, like Eylea or Avastin. And your ophthalmologist can diagnose that correctly and guide you to the standard of care.

DR. JIMMY LIU: Perfect. Thank you so much for that summary and explanation of that question, Dr. Fard. That was really great. And a final question that we had was a listener wanted to ask: Has corrected vision been demonstrated at all, or just reduced lesions when taking either Izervay or Syfovre?

DR. SARA FARD: That's a great question, too, and something to emphasize, and it's something that we will talk about in our key points. Syfovre and Izervay do not reverse vision loss that has already happened. And that is one of the reasons that Jimmy and I were discussing with our group today, our audience today, that you want to get into an ophthalmologist earlier and possibly get these treatments earlier because these treatments of Syfovre and Izervay, they can't reverse the tissue loss that has already been there. They can only further slow the progression of your age-related macular degeneration. So, they're not going to correct your vision, but they're going to basically slow down the vision loss that you would otherwise be having with the age-related macular degeneration.

DR. JIMMY LIU: Perfect. Thank you so much, Dr. Fard. Yes, and again, just to reiterate, like what Dr. Fard said, it's really important to go see your eye doctor to make sure that you aren't developing any signs of AMD so you can make sure that you can see your loved ones, your family and friends, and do all those hobbies that you enjoy doing. So, great. And so, I just want to thank Dr. Fard. Thank you so much for all the information you shared with us today. Dr. Fard, before we close, do you have any message that you would like to share with patients and families navigating a new geographic atrophy diagnosis?

DR. SARA FARD: Yes, absolutely. And I just want to thank you also for all the questions, Jimmy, and thank you to our listeners for taking the time out of their day, and also reiterate your point of seeing your ophthalmologist as soon as possible and inquiring about these medicines and getting treatment earlier than later to slow your geographic atrophy.

But finally, key points for a new geographic atrophy diagnosis are that, one, advanced dry, age-related macular degeneration is a manageable disease. And although the Syfovre and Izervay injections cannot reverse vision loss, and therefore cannot improve vision, like we were saying, they can lower the risk of large visual acuity losses over time by possibly slowing the progression of disease, which has been shown in studies over a year, 2 years, and then even more effective longer. And that patients and families should continue consistent ophthalmological follow-up to monitor for side effects and adverse events and pay particular attention to their lifestyle. So, that includes the AREDS2 supplements if you have intermediate dry, age-related macular degeneration in the other eye that your ophthalmologist can help diagnose. A healthy diet is also encouraged, with green leafy vegetables and omega-3 fatty acids; avoidance of UV exposure, so always wearing your sunglasses; smoking cessation. And note that treatment can help slow progression rates of age-related macular degeneration.

DR. JIMMY LIU: Awesome. Great final advice, Dr. Fard. Well, thank you again for joining us today. Our next Macular Chat will be on Wednesday, October 29. This concludes today's Macular Chat.

DR. SARA FARD: Thank you, Jimmy.

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
- Expert Advice for Macular Degeneration
- Understanding Geographic Atrophy

Helpful low vision tools or resources mentioned during the Chat include—

- Trials and studies
- OAKS and DERBY studies
- GATHER1 and GATHER2 trials
- JADE trial
- Sienna trial
- GALE trial
- Treatments for geographic atrophy

- Syfovre
- Izervay
- Anti-VEGF treatments for wet age-related macular degeneration:
- Avastin
- Eylea
- Lucentis
- Vabysmo