

# BrightFocus<sup>®</sup>

## Chats

Understanding Dry AMD and Geographic Atrophy

September 28, 2022

1:00 PM EDT

Transcript of Teleconference with Dr. David Liao, Retina-Vitreous Associates in Los Angeles, California

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

**MS. DIANA CAMPBELL:** Hello, and welcome to this month's BrightFocus Chat about macular degeneration. My name is Diana Campbell and, for more than a decade now, I've had the privilege of working with you all who are impacted by macular degeneration. The topic of today's Chat is "Understanding Dry AMD [or Age-Related Macular Degeneration] and Geographic Atrophy," which we'll likely refer to as GA [geographic atrophy] as we go forward. We're going to spend about half an hour learning about dry AMD, GA, and potential treatments on the horizon, and we're excited today because this topic is especially timely as the FDA is currently reviewing the first-ever treatment for geographic atrophy.

This Chat is brought to you today by BrightFocus Foundation. We fund some of the top scientists in the world who are working to find better treatments, and ultimately cures, for macular degeneration, glaucoma, and Alzheimer's disease. And we do events like today's Chat to get

the latest news from science as quickly as possible to families that are impacted by these diseases. You can find much more information on our website, [www.BrightFocus.org](http://www.BrightFocus.org).

We are delighted to bring back today's guest, Dr. David Liao, who is a retina specialist at Retina-Vitreous Associates [Medical Group] in Los Angeles, California. In addition to seeing patients at his practice, Dr. Liao has been involved in a number of research studies involving retinal diseases, such as macular degeneration, diabetic retinopathy, and retinal vein occlusions. He has authored and co-authored a number of publications and abstracts related to those clinical conditions as well as basic science research. Now, with all of that said, Dr. Liao, thanks for joining us today.

**DR. DAVID LIAO:** Hi, thanks for having me back. And, yeah, as you mentioned, I'm a retina specialist out in Los Angeles, California, and I think this is an exciting time for folks with dry AMD and geographic atrophy because there are a lot of new potential treatments on the horizon. And all of these medications have gone through clinical trials, and they're just making their way, hopefully, to FDA approval sometime in the near future.

**MS. DIANA CAMPBELL:** I think that's really exciting for everybody on the call today. Let's start with the basics. What is dry AMD, and how does it affect our vision? And after that, what exactly is geographic atrophy, and how do the two relate to each other?

**DR. DAVID LIAO:** Sure. So, I'm sure many of the folks out there are already familiar with some of this, but dry AMD—or age-related macular degeneration—is the early form of the disease, and what the doctor will see when he or she looks inside the eye is these fatty deposits known as drusen. Initially, there's really minimal effect on vision, and over time the drusen can slowly enlarge and there may be some mild blurring or distortion. There is a more advanced type of dry AMD, and that's geographic atrophy, and this is where those parts of the central retina—the macula—become thin, and this can lead to some blind spots off to the side; difficulty reading, for instance, because of those; needing more light. And slowly, as time progresses, these thin spots can expand, and if they affect the very central part of the vision, then vision decreases substantially, but this does

take quite some time to happen.

**MS. DIANA CAMPBELL:** I know people often mention they have wet AMD and dry AMD. As dry AMD gets worse and advances, is there a way of knowing whether it will wind up as geographic atrophy or wet AMD, or what's that relationship?

**DR. DAVID LIAO:** Sure. Yeah, so a lot of people feel that wet and dry AMD are mutually exclusive. Actually, they can both exist in the same patient, in the same eye ... in one eye or the other. So, wet AMD—as opposed to dry AMD—is where you get bleeding or swelling in the retina, and that is due to new blood vessels that have grown up into the retina, and they're leaky, and many people receive injections—like Avastin®, EYLEA®, Lucentis®, a number of other medications—to treat that. All AMD starts off as dry AMD, so when you have wet AMD, you just have wet AMD on top of the dry AMD. So, the dry AMD doesn't go away, you just have both. Doctors usually just call it wet AMD because that is what we've been treating these days with the injections. It's very difficult to predict who will progress from just the early stages to get dry geographic atrophy or the wet AMD. We know there are certain risk factors, and by doing the eye exam, you can kind of put these risk factors together and give your patient an estimate—a rough estimate—to say, for example, there's a 20 percent chance of developing wet AMD over the next 5 years or what have you, based on the severity of the disease. And we know there are other risk factors, like smoking, that can adversely affect, or vitamin use that can positively affect risk for these types of things, but the best way is just to see your eye doctor and get routine check-ups.

**MS. DIANA CAMPBELL:** Absolutely. So, you mentioned the percentage for dry AMD becoming wet AMD. Is there a similar percentage of people who have early dry AMD who will progress to geographic atrophy?

**DR. DAVID LIAO:** Sure, yeah. So, the standard statistic for wet AMD, for example, is about 10 percent of people with macular degeneration are going to get wet macular degeneration, and then it will account for almost 90 percent of the folks who have severe vision loss. The amount of people with advanced geographic atrophy is somewhat similar, so

it may be about 10 percent, but keep in mind that these are just kind of whole average as people age, for example, the incidence of dry AMD or geographic atrophy will increase just as the amount of wet macular degeneration will increase as well.

**MS. DIANA CAMPBELL:** Right. Here's a somewhat similar question, but this actually deals with both. It's from a listener. Statistically, if you're diagnosed with AMD—so either one—how likely are you to go blind? Is there a percentage or other way to assess that or get a sense for risk?

**DR. DAVID LIAO:** This is a very common question that people ask. The first thing I tell patients is that with AMD, despite the severity of it, most people don't go blind to the extent that they lose all vision—that they don't see anything, for example. So, even in severe cases, central vision is lost, but peripheral vision is still there, so you can still maintain mobility, you can still get around your home, and so forth. Now, the outlook before we had these injections—for example, for wet AMD—wasn't great. I mean, people would progress to central vision loss. But nowadays, with the anti-VEGF injections that we talked about, it's very uncommon that you are going to have severe vision loss in both eyes because of the wet AMD. Now, dry AMD—and we're going to talk about that later in the talk—can also produce vision loss, but hopefully, with some of these medicines, that will change as well because there'll be treatments to slow the progression down.

**MS. DIANA CAMPBELL:** Absolutely. No, that's great. And what a huge milestone for those that do have the advanced form of dry AMD or geographic atrophy. The revolution with the wet AMD treatments was so huge, and I think this is equally exciting for all of us. So, let's see. Let's dig a little bit deeper. This question has been coming up a lot. We've got, actually, a number of people who have mentioned that they didn't know that they actually had geographic atrophy until they asked their doctor. So, my question is: What constitutes a diagnosis, and how does a doctor assess whether it's still dry AMD or whether it's progressed on to GA?

**DR. DAVID LIAO:** Right. So, first, of course, we do the eye exam. There are other diagnostic tools in the offices, like OCT. There are special photos that we take of the eye, especially what we call fundus autofluorescence,

and these are very good at showing up the thin areas in the retina and the underlying layer, the RPE. And so if you have any of those findings, then you may have geographic atrophy. And basically, what your doctor or retina specialist will do is take photos—serial photos over time—and you can look at the progression. And again, fortunately, the progression is very slow, but over the years what we usually see is we'll see that the thin areas expand and then coalesce, and then very late in the disease, then, it may affect the central vision, and then the patients usually notice a decrease in their central acuity.

**MS. DIANA CAMPBELL:** Okay. Great. Thanks for clearing that up. So, as I just said, these are really hopeful times for people with geographic atrophy with the first-ever treatment under review and so many others close behind. Let's talk about that first. What does the one that's currently under FDA review ... can you talk a little about that, the method of delivery, how it treats the eye ... how the medicine treats the eye?

**DR. DAVID LIAO:** Sure, yes. So, for a long time there ... well, since up until now there hasn't been any treatment to slow down geographic atrophy, and so there's been intense research into what's the cause of geographic atrophy. And we think that in dry macular degeneration, there's an ongoing low level of inflammation inside the eye located particularly at the drusen, and the inflammation is part of what we call a complement cascade that is a normal part of our immune system, but it seems to be overactive in that area. And so, all of these medications, for example, pegcetacoplan, targets the complement cascade. They kind of tamp down the level of inflammation, and thereby, they slow the expansion of these thin spots. So, this particular medication, pegcetacoplan—it's made by Apellis Pharmaceuticals—is an inhibitor of the complement cascade, and it's administered either once a month or every other month in the office, and it's an eye injection, just like people get for their wet macular degeneration with Lucentis® or Eylea®. We basically numb the eye, clean the eye, and do the injection on the sclera—the white part of the eye—and folks go home. There may be some irritation afterwards, but that usually fades. Then, they'll come back, and we'll monitor the progression of the dry ... geographic atrophy, and hopefully, at least in the clinical trials, we see a slowing of expansion. So, it doesn't reverse the loss, but it really

inhibits the progression—the expansion and coalescence—of these thin areas so that people keep more of their vision for longer periods of time.

**MS. DIANA CAMPBELL:** Great. So, to kind of recap what you said because I know people will ask: This drug is going to slow progression, slow the expansion of the thin spots that are developing, but they're not going to regain vision that they've already lost, right?

**DR. DAVID LIAO:** Exactly. I think it's important for folks to understand that just because with the wet macular degeneration medications, it reverses some of the swelling to an extent, and people get the improvement in vision. This is really like a slowing down, and I think of it this way. If, for example, it was going to take you 5 years to lose vision or get really impaired vision, and if that is delayed by a couple of years, then that gives you really a couple of 2 or 3 years of extra vision; so, that's a significant thing, and that's how I would look at it.

**MS. DIANA CAMPBELL:** Oh yeah, absolutely. And then, the other question that I know we'll get—if I look at my screen, I'm probably already getting it. If you're already in treatment for wet AMD and you're having whichever—Lucentis® or Eylea®—injections every 4 to 8 weeks or so, what happens now with an injection for dry AMD? Can you get injections for both, and what does that look like?

**DR. DAVID LIAO:** Sure. So, when the FDA approves something, they'll approve it for a specific use. So, they'll approve this most likely ... hopefully, we'll see that sometime in November of this year that they'll approve it for the use with dry AMD. And folks, as we mentioned, can have wet macular degeneration and dry AMD at the same time, so it will be up to the doctors. They can use it quote-unquote "off-label" to treat the dry AMD that people have with wet AMD. The clinical trials weren't designed specifically to look at that type of population, but it will be used, and I think it's ... people have had, for example, in the clinical trials, they developed wet macular degeneration during the trial, and they've had treatment for both ongoing in the trials. So, I think as we get more and more data and results from the trial, we'll see how folks respond to the medication if they have both dry and wet AMD at the same time.

**MS. DIANA CAMPBELL:** Right. Well, that's encouraging that the folks from the trial were able to use those once they developed wet AMD. I think that will give a little bit of hope. Most people or many people that we work with have both—one in one eye and one in the other, or even both in one eye as you mentioned earlier. So, that's great. Let's see, I had another question from a listener. "My current doctor is an optometrist and has been regularly checking my AMD—dry—for 3 or 4 years. Is this care adequate, or should I be seeing an ophthalmologist?" And she says she's 81 and still sees reasonably well, and the current care seems adequate, but at what point should she consider changing?

**DR. DAVID LIAO:** Right. So, I think if you have a good doctor and you have a good relationship—be it the physician or ophthalmologist or optometrist—I think I would just continue that relationship. Now, with these new treatments available, I think we'll have to get the word out, especially as retina specialists, to make everybody aware just because folks might not know there's a treatment for dry AMD and in the past, they've just been saying, "Well, come back in 6 months," "Come back in a year." But now it may be worthwhile just to have the conversation after your next appointment and say, "Maybe, we'll have, like, a one-time consultation with a retina specialist, see what's out there, if these things are applicable to me." And that will give you peace of mind that you know that you've kind of asked all the questions that you need to.

**MS. DIANA CAMPBELL:** That's great advice. I also think another easy way people could tell how they're being tracked is whether or not they're getting those pictures you mentioned taken—getting imaging and other pictures. So, if their optometrist isn't doing that, it sounds like they might want to do that consult and then perhaps change. Okay. Go ahead.

**DR. DAVID LIAO:** Oh, yeah. No, no, yeah, I think it's all the doctor–patient relationship, and I think just being comfortable with your physician is a very important thing.

**MS. DIANA CAMPBELL:** I couldn't agree more, and we hear from a lot of folks that do have a really good working relationship and they can ask the questions they have and others whose doctors don't have as much time to talk with them, and they're left with questions. I think you're right,

absolutely. With any doctor you're seeing that relationship is so important. Okay, so we are going to transition now to ... well, we had some exciting news with the Apellis review, but let's also briefly review other potential treatments that are coming along in clinical trials that look promising. And as we go, are they similar or different to ... how are they similar or different to the Apellis drug? I know we've got some gene therapies, potential oral treatments, regeneration, vitamin A. What's the list, and what should people be looking for?

**DR. DAVID LIAO:** Yes. There's been intense interest in how to treat this disease. So, one of the other treatments that's coming out is from a company called Iveric Bio; the name of the drug is Zimura, and it's similar in function. It works a little bit differently along the complement cascade, and they're finishing up their clinical trials, so I would expect that they would be hoping to get approval from the FDA also shortly, maybe sometime in the next year or so. But it's also done by injections in the clinic, just like we talked about. There are also other ways of tamping down the complement cascade that people are looking at. One of them is danicopan—that's a medication from Alexion Pharmaceuticals—and so that is an oral inhibitor, so that may ... if it turns out to work well, that may be easier than getting shots. There are also folks that are looking at gene therapy. There's a company that's called Gyroscope. They have an engineered vector that is implanted in the eye surgically, and what it does is it makes the eye quote-unquote "make its own medicine" to tamp down the complement cascade activity. And so, that may have advantages in that the medicine is continuously made for a long period of time, so perhaps you don't have to get so many injections after the initial surgery. There are other medications out there looking at, like, inhibition of the vitamin A cycle inside the eye to try to decrease toxic by products. All of these would certainly be good at preventing progression. I know a lot of folks out there want treatment if their disease is already advanced, and that's probably where stem cells would come in. There's been several trials where folks have surgically implanted stem cells underneath the retina. They make a small hole in the retina during surgery, and they implant the stem cells in there. And people have seen that the stem cells have been able to survive in the eye, not necessarily improve vision on the whole scale. These trials were mainly looking at safety. There are other



trials, for example, where people have grown a stem cell patch, and that's implanted surgically underneath the retina with a special instrument. And so, a lot of these things are coming out. The stem cells are quite a bit farther away from becoming a reality—they're more in the safety phases now—but, hopefully, in the next, you know, 5–10 years, some of those will get closer to being able to help patients in the clinic.

**MS. DIANA CAMPBELL:** Well, we will definitely have to keep you on the speaker circuit so you can help explain to each of these to us as they come. There are so many exciting different targets. It's just so much information, and I know we'll get questions on it, so we will absolutely be doing follow-ups on this.

**DR. DAVID LIAO:** Of course. Hopefully, we'll have some good news.

**MS. DIANA CAMPBELL:** Absolutely, yeah. And that's a good point. As BrightFocus, and I'm sure you as well and all the retina specialists will share, after the decision is made in November, with all of our audiences what the results were and what they can look for next. So, everybody should know that they will hear from us in November about that. Let's see. With these ... we talked about this, but I'll ask it more specifically: With these treatments in mind, how important is it to get that specific diagnosis? So if you've been told you have moderate dry AMD and you're not sure if you've progressed, in order to get treatment, will they require or do you know if they'll require the specific GA diagnosis, or what's the importance of getting that exact diagnosis going forward?

**DR. DAVID LIAO:** Right. Yeah, so when the FDA approves it, it will be for that specific GA diagnosis, and I think, again, it is important just because we haven't had any treatments and folks may not have noticed a quick change in their vision, that they haven't been to their doctor for awhile, and they haven't had a conversation about these things for awhile. So, it's good just to maintain your regular checkups and make yourself aware of what may be applicable to your disease because if this is something that you'd be interested in, getting treated earlier will compound the beneficial effects, so you'll be getting a drug for longer, and it will be able to slow the geographic atrophy for a longer period of time.

**MS. DIANA CAMPBELL:** That's great. And I know there are about a million people—is what I've heard—in the U.S. with geographic atrophy. Do you think it's underdiagnosed, though? Do you think there are more people that we need to get messages out to, maybe just check in a little earlier than they might have on their progression?

**DR. DAVID LIAO:** Right. I definitely think it's underdiagnosed. It's not something that has been a big topic just because, really, there were no treatments available.

**MS. DIANA CAMPBELL:** Right.

**DR. DAVID LIAO:** So, even if you did diagnose this, there wouldn't be a whole lot that you could offer. So, I think that a lot more people will get diagnosed, and hopefully, a lot more people get treatment out of it.

**MS. DIANA CAMPBELL:** Okay. We'll make sure to remind people of that as well, and I think that's so important. And I'd like to add for the listeners, all of the treatments on the horizon that we're talking about here have been made possible with clinical trial volunteers and other types of studies that go into the approval process. I just want to mention, as I have before, if you do have dry AMD and you're interested in participating in an interview various companies are doing interviews to learn about your life with AMD. So, if you're interested in hearing more about that, please call or email me at BrightFocus to get more information.

Let me ask you a couple of questions that have come in from the listeners, and then we'll kind of close up soon. Okay. What is the speed of geographic atrophy, and how can we tell if it's progressing?

**DR. DAVID LIAO:** Right. So, the speed of geographic atrophy is very slow. Basically, you start out with these small, thin patches in the retina or in the macula, and then they slowly expand over time. So, the estimated size of these growths is about 1.78 square millimeters per year, so that's very small, although the eye is a small space. And so, you don't usually notice a lot of central vision loss, but you may notice other things like a decrease in light sensitivity. It causes these little blind spots, so you may have trouble reading. For example, the next word may disappear until you move your

eye in a certain direction. And so, that may progress very slowly over time—like years, 5, 10 years or so—but when that thinning reaches the central area, that’s when folks notice more of a decrease in the central area. So, we’re really to slow this progression. So, again, maybe if it’s not ... if it’s 5–10 years, it may be 7, 12, 13 years, and that’s a valuable thing I tell people all the time.

**MS. DIANA CAMPBELL:** Right, absolutely.

**DR. DAVID LIAO:** Yeah, yes.

**MS. DIANA CAMPBELL:** Let’s see. Oh, this is sort of ... I mean, it’s similar, and I know we’ve asked you this before—at least I think we have. Do intraocular injections for the treatment of exudative AMD accelerate non-exudative AMD, and, in particular, geographic atrophy? I’m not sure if that’s a misconception or if there’s some truth to it ... whether getting the injections for wet AMD actually might put you more at risk for GA.

**DR. DAVID LIAO:** Right. So, there has been this discussion out there, and certainly in studies that have followed people with wet AMD; they have seen an increase in geographic atrophy with repeated intraocular wet AMD injections. So, whether the injections themselves are an actual cause is debatable. We don’t know exactly what’s causing it. It may be that regression of the wet AMD has something to do with it, or perhaps the medicine is removing some support for the RPE cells there. We don’t know exactly. We do try to minimize injections for this and other reasons so that we’re not treating too much, but we’re treating enough to keep the wet AMD under control. But I think the answer will come in coming years as we get these medications on the market and people will receive treatment for both at the same time, most likely, and we’ll be able to see whether this medication has an effect on that type of geographic atrophy. It may be a separate type of disease, but we don’t know at this point.

**MS. DIANA CAMPBELL:** Sure. I imagine if they’re going in relatively frequently for injections, their doctors are also looking at that other eye to identify any worsening of vision loss.

**DR. DAVID LIAO:** Oh, yes. Yeah, so definitely in the fellow eye, the other eye, that can be a different issue, but even with eyes with the same ... in the same eye with wet macular and dry macular at the same time, they'll be checked quite frequently.

**MS. DIANA CAMPBELL:** Very good. So, you know, a question that we receive all the time when we talk about AMD is the AREDS vitamins, and I know, or I'm pretty sure I remember, that they're most helpful in early to intermediate AMD. And so, this person has a question about having GA in both eyes and wants to know if increased vitamin intake can slow things down.

**DR. DAVID LIAO:** Right. That's a common question, and from the big studies that were done, the main point of the AREDS vitamins are to decrease your risk of converting to wet AMD. Really hasn't shown a big effect on conversion to geographic atrophy or the spread of geographic atrophy, though. Yeah.

**MS. DIANA CAMPBELL:** Okay. Okay, very good. Let's see. I think that covers the questions that I have. Okay. So, we'll move on, and I want to take this opportunity to mention that BrightFocus has a fact sheet about geographic atrophy that covers some of the topics we discussed today. If you would like us to mail this to you free of charge, please leave your information on the voicemail at the end of the Chat; and remember, you can order a transcript in the same way. Let's see ... a couple of notes in addition before we conclude. Next month, on October 26, we'll have a fantastic discussion with Sally Temple and Jeffrey Stern about adult stem cell therapy targets for dry AMD treatment. I know I've received so many questions about this, so mark your calendars. This should be really exciting as well. And I'm also thrilled to share that on October 12, we will host our first-ever BrightFocus Glaucoma Chat. I know there are many of you out there that actually have both AMD and glaucoma, so we'd love to welcome you to that. Okay, so to close out, Dr. Liao, I can't thank you enough. This discussion has answered so many questions we've received. I know I'll probably get more. I might reach out to you to figure out how to address that. But before we conclude, are there any final thoughts or remarks you'd like to share with us?

**DR. DAVID LIAO:** Yeah, well, it's been a pleasure being back, and I think it's good to get the word out. We're definitely in an exciting time where we're going to start to see new therapies come out for geographic atrophy, and hopefully, we'll get more and more out there and be able to offer more things to patients. And it's definitely a good time in geographic atrophy, and as you mentioned earlier, I do want to thank all the patients that were involved in the clinical trials because they are really the ones that have helped bring these drugs to approval so we can help other people with them. So, thank you to those people, and we'll stay tuned, and hopefully, there will be many new treatments coming out in the near future.

**MS. DIANA CAMPBELL:** Absolutely. And this whole talk has been from the angle of the patient perspective, but I imagine it must be so nice for you as a doctor to finally have something to tell the folks that you haven't been able to treat yet. I imagine that must be very rewarding for you as well.

**DR. DAVID LIAO:** Yes. Yeah, we never like to send someone home without trying to make them better, so this will be very good.

**MS. DIANA CAMPBELL:** Wonderful. Well, thank you so much for your time. We'll definitely try and bring you back next year at some point. And on behalf of BrightFocus Foundation and of the audience, we appreciate you so much and thank you for educating us today about dry AMD and GA.

**DR. DAVID LIAO:** Thanks for having me. It's my pleasure.

**MS. DIANA CAMPBELL:** All right. Best to you. This concludes today's BrightFocus Chat, and we will return on October 26. Thank you so much for listening 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](http://www.BrightFocus.org). Available resources include—

[Geographic Atrophy \(GA\) \(brightfocus.org\)](http://brightfocus.org)

[Retinal Imaging Techniques for Macular Degeneration | BrightFocus Foundation](#)

[Potential Breakthrough Drug for Geographic Atrophy Awaiting FDA Approval | BrightFocus Foundation](#)

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[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](#)

[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—**

- BrightFocus fact sheet about geographic atrophy
- pegcetacoplan, Apellis Pharmaceuticals
- Zimura, Iveric Bio
- danicopan, Alexion Pharmaceuticals
- gene therapy treatment for GA in development at Gyroscope Therapeutics