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Retina Rumble: Debating Modern Treatment Options

Announcer:

Welcome to CE on ReachMD. This activity, titled Retina Rumble: Debating Modern Treatment Options is provided by Prova Education.

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Dr. Goldberg:

Currently, there are no head-to-head studies between second-generation treatments for retinal disease, so how are you choosing among them in your practice? Watch our experts debate the pros and cons of current agents to help you decide treatment options.

This is CE on ReachMD, and I'm Dr. Roger Goldberg. With me today are 2 great friends and retinal experts, Dr. Yasha Modi and Dr. Christina Weng.

Dr. Modi:

Yeah, great to be here. Looking forward to it.

Dr. Weng:

Thanks for having us, Roger.

Dr. Goldberg:

This is a neat experience, because I've put together 3 cases, and Christina and Yasha have not seen these cases before, and I'm going to let them duke it out, so to speak, and help us think through these various cases.

So the first case is a patient with treatment-naïve wet AMD. She's an 85-year-old Caucasian woman. She comes in complaining of 3 weeks of blurred vision in the left eye. I had last seen her 7 years earlier when I diagnosed her with intermediate AMD in both eyes. She was 20/30 in the right eye, 20/250 in the left eye—the eye of interest here—pseudophakic in both eyes.

And here's her imaging. And what we see here, I've got a color fundus photograph, an angiogram, and the OCT, but we see a very large pigment epithelial detachment with subretinal fluid, subretinal hemorrhage at the inferior rim of that PED, and a lot of intraretinal fluid. So pretty impressive case, lots of exudation, large PED, and subretinal hemorrhage.

Christina, we'll start with you. Tell me how you think about this case and which agent to select.

Dr. Weng:

Yeah, great case. Obviously, very extreme presentation here. And first of all, Roger, I follow my intermediate dry AMD patients more

frequently than every 7 years. But we know that patients sometimes get lost to follow-up, and they do sometimes present once they have something very massive happen, like this hemorrhage here.

For this patient, I'm considering her age of 85 and also some features that we're seeing here on her imaging, including a pigment epithelial detachment. You mentioned there's a lot of fluid, including intraretinal fluid, which we know is particularly sinister in this condition. And she also looks like she has some subretinal hyperreflective material as well, along with the hemorrhage, as you said.

So, for me, my mind automatically turns to some of our second-generation agents, including faricimab and aflibercept 8 mg. And the reason I lean towards these are several reasons. We've seen from the pivotal studies that they are noninferior to their comparator arm, which was aflibercept 2 mg in both sets of trials. But they can offer the potential for longer durability in patients.

Additionally, there's been post hoc analyses, particularly with faricimab, showing that it might have better control of patients with prominent pigment epithelial detachments, hyperreflective foci, which I see a few of here, as well as SHRM, compared to aflibercept 2 mg. But I do want to highlight that we don't have a head-to-head. It doesn't mean that aflibercept 8 mg wouldn't also be a great choice here.

And I also like the potential for longer durability. When you think of an 85-year-old patient, we know those patients oftentimes are not able to come alone to the clinic. They often need family members as well. And additionally, you know that disease that's this aggressive is going to need pretty frequent treatment, at least initially. And so I like the fact that these second-generation agents may offer longer durability, even if we're hitting these patients hard to start.

Dr. Goldberg:

Christina, that was great. Yasha, tell me, what are your thoughts on this case.

Dr. Modi:

So, Roger, I think I got to go old school on this one, because one of the things that I'm particularly worried about is the height of the pigment epithelial detachment. And when you see something like this, what is immediately concerning to me, especially when you see that sort of hyperreflective material under the RPE, is the risk of RPE tear.

And when you look at the natural history versus laser versus anti-VEGF, the risk of RPE tear goes up sequentially as you go from observation to laser to anti-VEGF. Now interestingly, when you look at the rates, if you go back to the original ranibizumab studies then the aflibercept study, and if you go to the most recent one, which was TENAYA and LUCERNE, there was an increased rate of RPE tear with faricimab relative to that of aflibercept 2 mg.

So I agree completely with Christina that the value here is ultimately trying to get them to a long-duration medication. But I would argue I'd probably start with bevacizumab. I would probably start there, eventually try and get rid of that type 1, type 2 neovascularization. Mostly what you're going to see is resolution of SHRM, intraretinal fluid, but hopefully a theoretically lower rate of potential RPE tear. And then once the height of the pigment epithelial detachment is a little bit lower, that's probably when I would shift over to the exact same thing that Christina was saying with either faricimab or aflibercept 8 mg.

Dr. Goldberg:

And the thinking there, Yasha, is kind of start with a little bit of a, quote unquote, weaker agent, and maybe you don't have a contraction of the CNV quite as rapidly that might precipitate an RPE tear. Is that the thinking for starting bevacizumab?

Dr. Modi:

That's exactly right. We actually learned that from TENAYA and LUCERNE, where the rate of RPE tear was higher. So Christina brought up a great point was that faricimab has a sort of a more impactful impact on pigment epithelial detachments. Now, weirdly, in that particular post hoc analysis, it was really serous pigment epithelial detachments that did better than fibrovascular pigment epithelial detachments. But needless to say, when you couple that in addition to the fact that there was increased risk of RPE tears, that sort of does provide some rationale to the idea that it is a more effective or intense medication. And, arguably, once that risk of RPE tear is a little bit lower at month 1 or 2, that's probably when it's a good time to start using that medication.

Dr. Goldberg:

Great point. Let me shift gears a little bit away from the PED. We also have a subretinal hemorrhage. And when you see subretinal hemorrhage like you do in this case—now granted, it's not a foveal subretinal hemorrhage, it's extrafoveal—but does this impact your treat-and-extend algorithm? I know many of us are considering with the next-generation agents going to 3- or 4-week steps as we extend them. But in the case with a subretinal hemorrhage, do you do a 1- or 2-week step, or does it enter your thinking at all?

Dr. Weng:

Roger, I'll take that. When I have subretinal hemorrhage, even if it's not involving the central macula, I generally will put those patients on strict monthly treatment to start until the hemorrhage has largely resolved, and then I'll begin extending. I think that hemorrhage warrants aggressive treatment. And so even regardless if I'm using a first- or a second-generation anti-VEGF agent, that's what I tend to do.

We don't have great data to guide exactly how we should handle these. And I know there's a variety across the community, but I'd be curious to hear what Yasha does.

Dr. Modi:

So, Roger, we're presuming the case of a sort of theoretical massive submacular hemorrhage involving the fovea. Is that what you're asking us about?

Dr. Goldberg:

No. In this case, as you can see at the inferior edge, and you can see it in the color fundus photograph and on the fluorescein angiogram where there's some blockage, that's some subretinal hemorrhage that's present. Again, it's not right in the center, it's peripheral. It's not massive, it's small. But does that enter into your equation at all as you think about how you're going to kind of titrate the interval between injections?

Dr. Modi:

In this particular case, it probably doesn't. I think what I'd like to see is the height of the pigment epithelial detachment sort of shallow and hopefully in the absence of an RPE tear. If it was subfoveal in terms of the hemorrhage, then probably I would do monthly treatment until we ended up with total resolution before extending them out.

And, then finally, it's some data that I'd love to see but it doesn't currently exist yet, but if you extrapolate from DME, there was a lower rate of epiretinal membrane formation with faricimab relative to that of aflibercept 2 mg. And the idea is, there's some potential prevention of gliosis or fibrosis that's occurring. And in that case, if I was worried about subfoveal hemorrhage that colocalizes to type 2 neovascularization, I would probably want to use an anti-gliotic medication. And while we don't have definitive evidence of that, probably faricimab has the best chance of having the least amount of fibrotic proliferation.

Dr. Goldberg:

And so translating that into day-to-day practice, if you see SHRM, are you more likely then to go with an anti-gliotic agent like a faricimab? Is that the implication?

Dr. Modi:

I would love to see more definitive data. I think we're still waiting to see whether or not there's a change in the resolution of SHRM in the TENAYA and LUCERNE study between faricimab and that of aflibercept. So the answer is out. But just given that sort of weak signal in DME, I think there is some plausibility as to why we should at least consider it, and why we should move forward with post hoc analysis to better understand that.

Dr. Goldberg:

Yasha, those are all great points. Let me just toss up one additional question here. We've talked a lot about the effect of faricimab versus 2-mg aflibercept on resolution of RPE detachments and also RPE tears. What do we know about 8-mg aflibercept versus 2-mg aflibercept when it comes to sub-RPE fluid and the risk of RPE tears from the PULSAR study?

Dr. Weng:

So Roger, I think you're alluding to some of the post hoc analyses that have been done from the PULSAR study, which is the pivotal study that led to the approval of 8-mg aflibercept for neovascular AMD. And, similar to what we just covered earlier in the post hoc

analyses with TENAYA and LUCERNE, there also seemed to be better control of PEDs with the aflibercept 8-mg arms compared to aflibercept 2 mg.

So, again, we don't have head-to-head between these 2 second-generation agents. But there also, again, seems to potentially be a signal there. And it makes you wonder, is it because of the increased molar dosing? Aflibercept 8 mg is 4 times the dose of aflibercept 2 mg. Maybe it's actually that part of it that is actually addressing the PED component. And that's what makes it tough to know exactly how to tease out the anti-angiopoietin-2 aspect of the bispecific faricimab compared to its anti-VEGF-A aspect. It's hard to tease those out, and we're still learning more.

Dr. Goldberg:

Yeah, those are great comments. Thank you, guys, so much.

Let me switch gears a little bit. I'm now going to talk about a case of treatment-naïve DME, the other major retinal vascular disease that we see every day, every hour in clinic. And this is a patient presented to me, 73-year-old Caucasian woman, non-insulin-dependent diabetic. She's 20/160 in the right eye, 20/100 in the left eye. She's got 2+ NS, but no PSC cataract.

I apologize because I don't have an angiogram, but I'm going to show you her fundus photos, which show here extensive exudation and hard exudates, lipid hard exudates, including through the central macula, through the fovea. And I can tell you, she did not have PDR on the FA. And here's her OCTs of the right and left eyes. So she's got tremendous exudation, intraretinal fluid, hard exudates, including right through the center of the fovea.

And I think we started with Christina last time. So let me, Yasha, start with you this time. Here's a patient, bilateral treatment-naïve DME, kind of with a lot of exudation. What's your approach here?

Dr. Modi:

It's remarkably sad to me that this is treatment naïve and this is her first presentation. I mean, when you look at that hard exudation at the fovea that's unfortunately a feature of chronicity. It also carries a poor prognostic factor, no matter what anti-VEGF medication you consider.

The caveat is that we are starting to look at biomarkers when it comes to the second-generation anti-VEGFs, and the only data to date supporting a faster resolution of hard exudates, relative comparing 1 medication to the other, was faricimab relative to that of aflibercept 2 mg.

And so I think in this case, it would be certainly very reasonable to consider steroids early in this case. But I think the data really supports the use of faricimab very early out of the gate. And I probably would start there and sort of assess a response. And it's really critical that this patient understands that this is something that needs to be chronically administered. I wouldn't be in a rush to get treatment extension here. I'd really try to work on anatomic improvement.

And then finally, one last point, which is what I do very much in my clinic, is I always check blood pressure. When I see a patient with this level of presentation, I'm also worried about a superimposed hypertensive retinopathy or even a choroidopathy. The RPE and the ellipsoid zone look pretty good, but I still think it's worthwhile to check.

Dr. Goldberg:

Great comments. Christina, what are your thoughts here? A lot of hard exudates. And in your answer, when you see some of these turbid cystic spaces where it's not just clear fluid but kind of a hazier gray on the OCT, do you worry about almost precipitation of the hard exudates and worsening hard exudate, particularly in a case like this where there's already a lot to begin with?

Dr. Weng:

I was actually just going to point that out, Roger, when you see that turbidity in these intraretinal cystoid changes on the OCT, I certainly worry, because it's sometimes an uphill battle because you can get them drier, but then you end up with a clustering of all the precipitates from all of the exudates that can sometimes land in the fovea, and the patient may not end up having substantial visual acuity improvement, even though they thin out a lot. So it does make me concerned.

I'll be honest, I echo what Yasha said. For patients like this with a lot of exudation, you can also see a lot of hyperreflective foci. I think we have more data supporting faricimab in this case. But again, because we don't have a head-to-head to aflibercept 8 mg, it doesn't mean that that wouldn't necessarily work just as well.

But I'll tell you, I like to incorporate steroids in patients like this. And I know that they already have 2+ nuclear sclerosis, but those are something that can be taken care of down the line. And that's something that I always remind viewers to consider, because it doesn't have to be an either/or decision. You can use those in combination. So that's probably what I would recommend for this patient.

Dr. Goldberg:

I saw Yasha nodding his head too. What is it about this case that both of you think maybe this is one where you might want to consider a steroid earlier in the course of treatment?

Dr. Modi:

Well, we know from the DME studies of YOSEMITE and RHINE that no matter what, when you start injecting them, whether it's aflibercept 2 mg or faricimab, for the first 3 months you get an increase in the amount of exudation before it finally kind of makes that curve and starts headed in the correct direction.

And exactly to Christina's point is, are you going to increase the amount of exudation at the level of the fovea? Is that going to result in sort of a fibrotic nodule at the end of all of this? And that's where potentially steroids may have a role. We don't know the answer to that.

There are some post hoc analyses showing improved outcomes in patients with hard exudates. Most of those are European studies, and there are also non-control studies. But certainly, I think that's probably the reason why Christina and I are both also adding steroids into the armamentarium pretty early in this case.

Dr. Goldberg:

I will add—and I'm curious to hear what you guys think—when in the PHOTON study, which was the 8-mg aflibercept study, they broke out the baseline retinal thickness by quartiles. And when you look at quartiles 1 and 2, the milder disease, both 2-mg and 8-mg honestly worked great. And there I think of 8-mg really as the durability agent. But when they looked at the 4th quartile, the most swollen retinas—and I would put this in that 4th quartile category—they got equally dry. But then the rebound of fluid, when you waited from the 4-week visit to 8 weeks after that last loading dose, they didn't rebound nearly as much, suggesting that you're able to kind of maintain a drier retina longer with 8-mg versus 2-mg aflibercept.

Do you find that compelling here in a case like this? And how do you talk about durability in general? Obviously, they're presenting with very severe disease and frankly advanced vision loss. When are you starting that conversation and thinking about the durability aspect of these agents?

Dr. Weng:

Yeah, I think that's so important, Roger. Yasha said at the beginning that this patient was surprisingly late in their presentation and presenting for the first time with this level of disease. And so that already sort of bodes poorly for future adherence to treatment and visits. So I'm definitely thinking about trying to use the longest durability treatment that I can offer them.

And certainly aflibercept 8 mg is one that comes to mind. You mentioned some of the studies that have been looked at. But even though patients in the second year we saw in PHOTON could potentially get out to every 24 weeks, I never lead with that when I speak with patients. I always tell them it's very likely that we'll treat you on a monthly basis initially until we get this under better control and then potentially extend you out.

And it's really exciting that we now have that dosing flexibility, a recent addition to the aflibercept 8-mg label to allow us to treat monthly for harder-to-treat patients. And we all have a small proportion of our patients who are like that and fall into that category and this may be one of them.

And that every-4-week ability to treat with aflibercept 8 mg really comes from an ongoing phase 3b study called ELARA.

So ELARA is an ongoing phase 3b study looking at eyes that had been previously treated. And interestingly enough, for diabetic

macular edema, even though this patient is treatment naive, not one that's been previously treated, but in the readout that they've shared so far, for those that were treatment-experienced after having 7 monthly injections over the course of that first 6 months, they actually gained nearly 3 letters and another 50 μ m of improvement in their CST.

And so that's really surprising, because a lot of times when we see treatment-experienced patients in these studies, we're happy to just maintain them, right? But here we actually saw continued gains in their vision as well as their anatomy. And it makes me wonder, if we are treating that frequently for patients that are maybe treatment naive, for example, maybe we could also gain the same benefits, if not even more.

So it's definitely something that we're continuing to learn about. And like I said, that's an ongoing study. But it makes me happy to know that on the label now we can use aflibercept 8 mg on a monthly basis if needed.

Dr. Modi:

And Christina, to follow that up, there's also some evidence even in the real world that when you start, you don't get this incredible response right out of the gate in diabetic macular edema.

If you look at the TAHOE study, one of the cool features of that study is that they broke it down to outcomes after 3 injections, 6 injections, and 9 injections. And what you see is that the visual acuity, especially for those who are previously treatment naive, their vision gets better and their CST continues to go down at 6 months relative to 3 months and then 9 months relative to 6 months.

So I think coming out of the gate, hitting it hard, this is somebody who I would really say you're likely going to be on every-4-week injections for the foreseeable future. We are in a really tough spot with those hard exudates, but we have to be very aggressive in terms of the treatment.

Dr. Goldberg:

The way I translate that is don't give up hope. Don't just say, "Oh well geez after 3 injections we didn't see a lot of improvement or vision improvement." But sometimes it takes time, and I try to transmit that hope as well to these patients. Fortunately, this patient ended up doing very well and it got to about 20/40 after she ended up having her cataracts removed. So in the end she did very well, but it was a process. It took about 2 years to get there.

Let me shift gears now to a case of chronic wet macular degeneration, and here I hope to talk a little bit about surgical options for chronic wet AMD. This is an 83-year-old Caucasian gentleman, pseudophakic, history of glaucoma suspect and intermediate AMD prior to presenting here with new-onset wet macular degeneration, 20/60 in the right eye, 20/40 in the left eye. You can see a good size pigment epithelial detachment and SHRM, or subretinal hyperreflective material, some intraretinal fluid as well.

And I gave this patient ranibizumab. And despite being a generation 1 agent, Yasha, he still develops an RPE tear. So this is 5 weeks later. I didn't go with the strongest agent out there and had this RPE tear. But thankfully the fovea was still covered. Vision was actually 20/40. Patient was happy.

And 4 weeks now, this is 4 weeks after ranibizumab number 6, still has this intraretinal cyst right in the fovea. Switched to aflibercept. Four weeks after now their 20th aflibercept, vision is 20/60 in the right eye.

This is a patient who needs chronic therapy. Actually, I'd even tried a period where I was treating every 2 or 3 weeks alternating with a sample agent. At what point and when do you think about the port delivery system for a patient with chronic, frankly needy, high-need wet macular degeneration? And Christina, maybe I'll start with you on this one.

Dr. Weng:

Yeah, definitely I would consider it for this patient. The port delivery system with ranibizumab I think offers several potential benefits particularly for a situation like this.

First of all, this patient has proven to be very needy, trying a lot of different agents already and still needing very frequent treatment. The only thing I guess I might have a little hesitation with is, as you said, they were glaucoma suspect. And we know that with port delivery systems sometimes there are conjunctival issues. But if they're not likely to need any sort of glaucoma surgery in the near future, I think

that this would be the perfect setup.

And I just want to mention one thing too about that RPE rip which is always a dreaded issue. You also wonder sometimes if it's not necessarily just the strength of our anti-VEGF that we're using but maybe because we're bolusing it, right? And so those levels fluctuate so widely. We see that in a lot of the trials where you see that sawtooth thing.

And one of the things that I think is underappreciated about sort of the more continuous type of delivery of therapeutic from options like port delivery system is how you can maintain a more constant level of drug administration. And you wonder if that ultimately may be better for the eye, better for the retina, and maybe even have potential benefits from a visual prognosis standpoint. We've seen hints of that from some post hoc analyses of some of our major anti-VEGF trials.

So I do like the durability aspect of port delivery system. We know that in PORTAL, for example, we have over 5 years of data now rolled over from ARCHWAY that over 90% of patients didn't require any supplemental treatment before those mandated refill exchanges every 6 months.

And then we know from the phase 2 LADDER study as well that patients were able to hit a median of almost 16 months in that study when you let them fly. So this really might be a great option for this particular patient.

Dr. Modi:

Yeah, I think, Christina, you said it beautifully, right, I mean this is exactly the kind of person who would benefit from this.

I do think that it's really important when you are considering the port delivery system that you intensively train to understand all of the steps. Because I think a lot of the complications, like conjunctival erosion and then subsequent endophthalmitis, can arguably be mitigated to some degree by the surgical technique and the way in which we counsel patients.

So I think being really meticulous on 2-layer closure with Tenon's and the conjunctiva is really, really critical. Kind of having that overhang over the limbus is going to be really important.

And then finally just to really counsel patients that after you have this, absolutely no eye rubbing. Any friction over any implant is going to increase your risk of erosions and then put you at risk.

So I've been so impressed after doing port delivery system where I've had a patient who I was giving essentially all of the medications to—afibercept 8 mg, faricimab, and regular aflibercept—and the moment I extended beyond 4 weeks there was fluid. I ended up putting a port delivery system in this patient and I have injected the patient only at the time of the refill at 6 months. But the truth is, she didn't even need the refill injection at 6 months.

So I have a feeling that there's something to be said about where the same patient who got ranibizumab and had fluid at 4 weeks who then gets reformulated ranibizumab ultimately has no fluid for 6 months, it's truly a remarkable medication in the right patient.

So I do think it does require some level of confidence that you are surgically executing to perfection. And I think we have to hold ourselves to the exact same standard we do with epiretinal membrane surgery, and there is absolutely no cutting corners when we take on this surgery.

Dr. Weng:

I agree with all those points.

Dr. Goldberg:

Let me ask a question for both of you here. But number 1, are you cycling through all of the second-generation agents first and really testing the maximum durability that we can get with our current agents before considering port delivery system? That's number 1.

And then number 2, for the patients where you've implanted it, it's keeping them dry, and you've gone through, let's say, the acute postoperative period, what's your follow-up schedule for the patients with port delivery? So kind of 2 questions in there.

Dr. Modi:

So I guess I can maybe start here. I use essentially faricimab and aflibercept 8 mg as sort of the maximum litmus test. I think there's pretty good evidence now that we can say those are our most durable medications. So after I've gone through both and assessed the durability, I sort of talk to patients about, "say, is this something that you'd be interested in doing? And especially if you can go from 4 weeks or 8 weeks out to 6 months." And a lot of patients are really excited about that prospect of going longer, and I think that's been kind of a big sell for getting patients to be on there.

So then the question is, let's go and say you put the port delivery system in and 6 months comes around, are you automatically refilling this patient at 6 months? Or are you going to out 7, 8, 9 months? Well, right now, I don't have enough data in my brain at this window of time beyond 1 refill and I've just, by default, have followed the 6-month refill. But I suspect that probably the next time around I will do a refill and extend and probably get them in at 7 months and refill them, and then probably 8 months.

And, arguably, I'm following them once I know that they've had a treatment response and have not required an injection out to 6 months, I'd say my maximum time I should say that I'm following them is they can't go beyond 3 months. And the rationale for why they're not going beyond 3 months is really to evaluate their conjunctiva, make sure they truly don't have fluid, and they're doing well after surgery.

Dr. Weng:

I agree with everything that Yasha said. I mean, I think that at the end of the day, placing a port delivery system still does require surgical intervention. And so if a patient could respond and we're satisfied with the intervals that they were at for sort of the drugs that do offer the longest durability today—faricimab and aflibercept 8 mg—I would certainly try at least 1 of those before jumping to port delivery system.

That being said, I still think it's a great option. And I think with these ultra-long durability therapeutics, one of the challenges that we're starting to think about and encounter is exactly what Yasha is saying is that we don't necessarily feel comfortable letting patients go super long periods of time without them coming into the office.

I've done a lot of work, Roger, we've had great conversations about home OCT, I think that's really one aspect that could be really important and have a lot of utility in terms of that application to these types of therapies and things coming down the line as well. Tyrosine kinase inhibitors may be here before we know it. Gene therapies might be here before we know it. And at least the home OCT which allows the patients to self-scan from their home every day will at least give us the confidence that they're not reaccumulating fluid even if they don't necessarily come into our office.

That said, I do think the port delivery system has an added aspect in terms of its safety, making sure that there's no conjunctival erosion and retraction, some of the things that we've seen in some of the pivotal studies. And so we will still necessitate a visit for patients to just physically examine them. But certainly, I do think that home OCT has a place in the future for this type of therapeutic.

Dr. Goldberg:

It's also a place where you can build collaboration with your referring doctors. I actually just did a bilateral refill—not on the same day. I will do bilateral injections of bolus anti-VEGFs on the same day, but I don't do bilateral PDS refills on the same day—and she lives about 4 hours away and she was insistent, "I will see you again in 1 year." Her refill interval's about a year. And I said, "look you've got to follow up with your optometrist locally and make sure that they're checking the port to make sure they're okay and if you have any new symptoms, don't hesitate to call and come in." But she was giddy with excitement over not having to come back for a year.

Dr. Modi:

Yeah, Roger, what a great strategy. I love that. It is an incredible opportunity for comanagement.

But home OCT especially when we think about tyrosine kinase inhibitors, the potential for those to get FDA approved, just remember that somewhere between 60% and 2/3 of patients didn't meet requirements for re-treatment which means that about 1/3 of your patients at 6 months are going to ultimately need re-treatment. And how do we know which ones those are going to be? Are they going to be coming to see us regularly? Are we going to be using home OCT?

Conversely, when you think about the port delivery system, 95% of people didn't require any re-treatment between the injections. So arguably the most effective medication we have by far is the port delivery system, but you have to be willing to take on the surgical risk

associated with it.

Dr. Goldberg:

Well guys, this was fantastic. Thank you so much. That's all the time we have today. So I want to thank our audience for listening, and thank you, Yasha and Christina, for joining me and sharing your valuable insights. It was great speaking with you today.

Dr. Weng:

It was fun Roger, thank you. Great to be here with you and Yasha.

Dr. Modi:

Yeah, always a pleasure talking with both of you.

Announcer:

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