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Glaucoma: Therapeutic Advances on the Cutting Edge

Announcer:
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Dr. Ramulu:
This is this is CME on ReachMD, and I’m Dr. Pradeep Ramulu.

Dr. Gaddie:
And I’m Dr. Ben Gaddie.

Dr. Ramulu:
So, to get started, Dr. Gaddie, of course it’s very important to diagnose glaucoma early, but we really want to diagnose it early in the people who are most at risk of losing vision in their lifetime and becoming functionally impaired. Can you talk about which patients you consider to be high risk?

Dr. Gaddie:
Sure. We have several landmark clinical trials that help kind of guide our context in this area. The Early Manifest Glaucoma Trial really showed the importance of identifying glaucoma early and lowering intraocular pressures as soon as possible, and the Ocular Hypertension Treatment Study really showed us the importance of which patients are most at risk for glaucoma. And on the flipside, the Advanced Glaucoma Intervention Study shows the results of waiting too late to start treatment. So we have some nice context.

Really, there’s two reasons why patients are considered glaucoma suspects in my opinion. The first is they have elevated intraocular pressure that may be detected at a comprehensive eye exam or suspicious optic nerve head cupping that is found by the practitioner during examination. Those are really the two main triggers that lead people to become a glaucoma suspect. But more than anything, we’re looking at patients that have elevated intraocular pressure. We look at ethnicity. African Americans, Hispanic, Latino population has a much higher incidence and prevalence of glaucoma. We look at—things like corneal thickness and corneal hysteresis really give us a hint at which patients are at most risk for developing glaucoma.

Dr. Ramulu:
Thank you for that great response. So I think increasingly we’re having a lot of new ways to treat glaucoma and to diagnose it, so can you maybe talk about some of the recent advances, especially in pharmacologic treatment, for our patients with glaucoma?

Dr. Gaddie:
Sure. It really is a nice time for innovation in glaucoma. If you think back historically, we really haven’t had any new molecular compounds in glaucoma since the prostaglandins debuted in 1996, so it was definitely time for some innovation.

One of the first agents we have is netarsudil. Netarsudil is a Rho kinase or sometimes referred to as a ROCK inhibitor. And the way

that these compounds work is they decrease intraocular pressure by increasing trabecular outflow. It also has an effect by decreasing the episcleral venous pressure, which is a very important pathway in glaucoma, and it also has a norepinephrine transporter effect, which in essence causes a decrease in aqueous production. So we're hitting on a lot of the main pathways involved in glaucoma. It causes direct relaxation of the trabecular meshwork cells actually via nitric oxide signaling, and we think that Rhopressa, or netarsudil, works by decreasing the downstream nitric oxide signaling via the cyclic GMP pathway, so a great new agent. And the side effects really are hyperemia, which is very common in our glaucoma medicines today, corneal verticillata, which is really just something that is seen by the practitioner and not by the patient. We do have some blurred vision as a reported adverse event with this medication as well as small petechial conjunctival hemorrhages. I've experienced all of these in clinical practice, but one of the nice aspects of this drug from an efficacy standpoint is it does show some nice benefit in patients with lower baseline intraocular pressure in the realm of normal-tension glaucoma. So those are the attributes of netarsudil.

They also have a product that's combined with a prostaglandin, with latanoprost, and it's known as Rocklatan, and really the same profile as netarsudil except with the added benefits of a prostaglandin analog. So all of the attributes and mechanism of action plus uveoscleral outflow all in a once-a-day, combined, fixed-dose combination. And it was found that the fixed-dose combination was slightly more efficacious than using the individual components in separate bottles.

And then we have latanoprostene bunod, which is Vyzulta, and this is a very unique drug. The Vyzulta is actually an organonitrate, and it's chemically linked to latanoprost. And when the corneal esterases—when the drop hits the surface, the corneal esterases break it down into the prostaglandin free acid and the nitric oxide moiety. And we think that this helps increase trabecular outflow via trabecular endothelial cells relaxing. Basically, this is an upstream nitric oxide signaling cascade, and again, via a very similar pathway as Rho kinase inhibitors via the cyclic GMP pathway. For this particular innovative medication, there really are very few side effects aside from what we see with the prostaglandin class, which is nice. A very low rate of hyperemia statistically and clinically and really a pretty safe profile.

And then we also have Xelpros, a new formulation latanoprost. And it's the same mechanism of action of the prostaglandin class, but it does not contain benzalkonium chloride, which many of our patients have some sensitivities to the various preservatives.

Dr. Ramulu:
Yeah, those are great comments. I think there's really a place for all three of these in your practice. Obviously, I think we've all seen the benefits of preservative-free formulations in some of our patients who are just highly intolerant of medications, and so Xelpros is definitely going to have an important role.

I've been impressed by both Vyzulta and Rhopressa. I think Rhopressa, while it does cause some conjunctival hyperemia, it really has been able to get the pressure lower in some people who are even on multiple medications and who are otherwise headed towards surgery, and so I think there are some patients who are very appreciative of the ROCK inhibitors and this method. And you do see some people who respond quite well to Vyzulta as well and can really avoid going on to procedural therapy because of it, and I think they're highly appreciative of these new innovations.

Dr. Gaddie:
Dr. Ramulu, let me ask you about the Durysta bimatoprost implant. I know you've been working with that in your clinics. What's your experience with that?

Dr. Ramulu:
Yeah, we're just getting it off the ground and we're setting it up. I mean, I think it's a little bit different than what we've done before for treating glaucoma. I think we're used to either procedures that are either more laser-based or operations or otherwise just prescribing eye drops, but I think Durysta is a little bit different. It's an intracameral injection of bimatoprost. It's scheduled as a few injections into the anterior chamber over the course of the first year. Each injection can last for several months and have an effect which is comparable to bimatoprost eye drops—just a little bit worse, but just as good as timolol. And I think for our patients who really don't want to take drops every day and who maybe have failed laser trabeculoplasty or are averse to it for other reasons, or who have physical limitations where they have difficulty putting eye drops in their eyes because of movement disorders or arthritis, I think this is a great new option for those individuals to be able to get their therapy without having to go to something just as invasive as surgery.

Dr. Gaddie:
When I was reviewing the data, I thought it was pretty interesting that there was a small subset of patients that really had an extended duration of effect. What do you make of that, those that are kind of super responders that can last one or two years with just one single implant?

Dr. Ramulu:

Yeah, I think it's a great point. I think some of the other innovations that are happening in glaucoma relate to home tonometry, and it would be great if maybe we could match up the administration pattern of Durysta with home tonometry so maybe we could take advantage of those people who are readily getting those prolonged responses.

Dr. Gaddie:
Yeah, great point.

Dr. Ramulu:
For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Pradeep Ramulu, and I'm joined by Dr. Ben Gaddie. We're discussing clinical innovations in glaucoma therapy and how to apply them in clinical practice.

So, Dr. Gaddie, thanks for going through those pharmacological innovations. Can you also talk about some of the clinical innovations that are coming up in glaucoma treatment, especially with regards to new sustained-release formulations? What does the future hold for us?

Dr. Gaddie:
Sure. I think that the future is very bright in terms of glaucoma innovation. We just mentioned the Durysta, the implantable, biodegradable implant. We also have a whole host of other polymer-degradable implants under investigation, including the ocular ring, which is a ring that goes around the actual eyeball itself and slowly elutes, in this case, bimatoprost. We have contact lenses that are under investigation that elute medications. I think they are starting with a prostaglandin analog, so the patient would wear a daily, disposable contact lens that elutes the drug into the ocular surface. We also have a goggle system under investigation where a patient would wear effectively what looks like a pair of swim goggles. And you can preset the pressure that you want the patient to have, and they wear the goggles for several hours a day. And it maintains the intraocular pressure that's set without any pharmacological or surgical intervention, which I know I have a lot of patients that are maybe averse, don't like taking medications, don't like the thought of surgery or laser, so that may be an excellent opportunity as well. And we have a lot of preservative-free innovations on the horizon. You mentioned earlier the fact that many of our patients are sensitive to preservatives in glaucoma medications. Well, there is a lot of innovation to take that preserve medicine in a bottle and make it nonpreserved when it hits the ocular surface. Now, that's not necessarily new in eye care, but I think in glaucoma there is a lot of opportunity for further innovation in that area.

Dr. Ramulu:
I think those are great points. And as somebody who has somewhat of a referral-based practice, I think the most common reason that I get somebody referred is they're getting worse, but I think the second most common reason is either adherence or nontolerance of medications. And so having all these new technologies which are going to really give ourselves some better options for how to deal with our nonadherent or medication-intolerant patients is really going to be a real boon for us, and we really look forward to what's coming in the future.

Well, thank you, Dr. Gaddie, this has been a very valuable conversation. If you wouldn't mind maybe sharing with our audience one final take-home message that you want them to remember from our discussion?

Dr. Gaddie:
Sure. I think the take-home message for me is that the two hardest parts of managing glaucoma are making the diagnosis, which isn't always a black-and-white type of decision, and then the second most difficult thing is telling if someone is progressing or changing to glaucoma. That's the most important role we play in surveilling glaucoma. And now more than ever, we're going to have a lot more options to keep our patients from having to go from eye drop therapy to surgical intervention with the tube or a trab-type procedure. We have a lot of intermediary gap steps now which will allow us to control patients and really hopefully delay or completely postpone the need for incisional surgery.

Dr. Ramulu:
That's great, Dr. Gaddie. I think from my standpoint my biggest takeaway is that it's increasingly becoming more important that we educate ourselves on all the various options that are available to our patients. I think it's not as easy for us to present options to people as before, where there were maybe only one or two options for their treatment. And now, with so many of them available, I think we have to be very thoughtful and very deliberate in how we customize our therapy for each individual patient.

Well, thank you all. Unfortunately, that's all the time we have for today, so I wanted to thank our audience for your participation, and thanks to you especially, Dr. Gaddie, for joining me and sharing with us all of your valuable insights. It was great speaking with you today.

Dr. Gaddie:
Thank you.

Announcer:
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