

MODERNOPTOMETRY

CURRENT AND FUTURE GLAUCOMA MANAGEMENT:

An Update on Existing Options
and the Therapeutic Pipeline

A CME/CE activity provided by Evolve Medical Education LLC.

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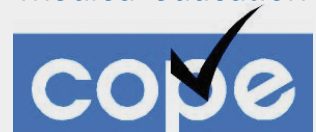


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Current and Future Glaucoma Management: An Update on Existing Options and the Therapeutic Pipeline

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CONTENT SOURCE

This continuing medical education (CME)/continuing education (CE) activity captures content from a virtual round table discussion that occurred on March 5, 2019.

ACTIVITY DESCRIPTION

Topical pharmacologic therapy is the mainstay primary treatment for patients with primary open-angle glaucoma (POAG) and ocular hypertension. Unfortunately, many patients need to be on multiple medications and different classes of drugs before there is adequate intraocular pressure (IOP) control. And for some patients, visual field loss will progress despite adequate IOP control. Until recently, no new topical pharmacologic treatments had been approved in the United States for more than a decade. Two new formulations were approved in late 2017. Ophthalmologists and other health care providers may not be familiar with potential new treatments for glaucoma, the latest clinical studies evaluating treatment nor the mechanism of action of topical medications.

TARGET AUDIENCE

This certified CME/CE activity is designed for specialists and other allied eye care practitioners involved in the management of glaucoma and associated disorders.

LEARNING OBJECTIVES

Upon completion of this activity, the participant should be able to:

- **Explain** how novel therapeutics differ in their methods of action from other topical medications.
- **Evaluate** the safety and efficacy of latanoprostene bunod for ocular hypertension and POAG.
- **Describe** how a healthy eye manages IOP in contrast with an unhealthy eye.

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- PLEASE RATE YOUR CONFIDENCE ON YOUR ABILITY TO APPLY UPDATES IN THE TREATMENT OF OPEN-ANGLE GLAUCOMA AND OCULAR HYPERTENSION IN THE CLINIC. (BASED ON A SCALE OF 1 TO 5, WITH 1 BEING NOT AT ALL CONFIDENT AND 5 BEING EXTREMELY CONFIDENT.)**
 - 1
 - 2
 - 3
 - 4
 - 5
- PLEASE RATE HOW OFTEN YOU INTEND TO APPLY ADVANCES IN THE MANAGEMENT OF OPEN-ANGLE GLAUCOMA AND OCULAR HYPERTENSION IN THE CLINIC. (BASED ON A SCALE OF 1 TO 5, WITH 1 BEING NEVER AND 5 BEING ALWAYS.)**
 - 1
 - 2
 - 3
 - 4
 - 5
- WHAT IS THE PRIMARY IOP-LOWERING MECHANISM OF ACTION AT PLAY IN RHO-KINASE INHIBITORS?**
 - They lower IOP by suppressing aqueous humor production
 - They lower IOP by relaxing the trabecular meshwork
 - They lower IOP by increasing aqueous outflow through the uveoscleral outflow
 - They lower IOP by decreasing episcleral venous pressure
- YOU ARE TREATING AN ASIAN PATIENT WITH NORMAL-TENSION GLAUCOMA, CENTRAL FIELD DEFECTS, AND AN IOP OF 17 MM HG IN BOTH EYES. THE PATIENT ADMITS THAT THEY ARE UNLIKELY TO REMEMBER DROPS, BUT PREFERS MEDICAL THERAPY OVER LASER TREATMENT. WHAT IS AN EVIDENCE-BASED APPROACH TO TREATMENT IN THE FIRST-LINE SETTING?**
 - Latanoprostene bunod
 - Selective laser trabeculoplasty (SLT)
 - Dorzolamide
 - Trabeculoplasty
- WHICH OF THE FOLLOWING ARE REPORTED ADVERSE EVENTS FROM COMBINATION NETARSUDIL/LATANOPROST THAT MAY BE A LIMITING FACTOR FOR USE?**
 - Conjunctival hemorrhage
 - Instillation site pain
 - Cornea verticillata
 - Hyperemia
 - All the above
 - None of the above
- PUBLISHED LITERATURE NOTES THE AVERAGE INTRADAY IOP VARIABILITY IN GLAUCOMA PATIENT WITH WELL-CONTROLLED DISEASE IS _____.**
 - 2 mm Hg to 3 mm Hg
 - 3 mm Hg to 5 mm Hg
 - 5 mm Hg to 6 mm Hg
 - More than 6 mm Hg
- BASED ON RESULTS OF THE LIGHT STUDY, EFFECTS OF A FIRST SLT LAST AN AVERAGE OF _____ IN MOST EYES.**
 - 1 year
 - 2 years
 - 3 years
 - 4 years
- SLT CAN LOWER IOP BY WHAT PERCENTAGE IN THE FIRST-LINE SETTING?**
 - 25%
 - 20%
 - 30%
 - 15%
- IN THE MERCURY 2 TRIAL, THE COMBINATION NETARSUDIL/LATANOPROST LOWERED IOP BY AN ADDITIONAL _____ OVER NETARSUDIL MONOTHERAPY OR LATANOPROST MONOTHERAPY.**
 - 5 mm Hg
 - 2 mm Hg to 3 mm Hg
 - 3 mm Hg to 4 mm Hg
 - 1 mm Hg to 3 mm Hg
- A PATIENT IS CURRENTLY ON A PROSTAGLANDIN, BUT THE IOP IS 15 MM HG, WHILE THE TARGET PRESSURE IN THE LOW TEENS. THE PATIENT HAS REPORTED AN ALLERGY TO BRIMONIDINE, AND GETS CONFUSED WHEN HE HAS TO TAKE MULTIPLE DRUGS FIRST THING IN THE MORNING. WHAT IS THE MOST ACCEPTABLE AGENT TO ADD TO THE PATIENT TO REACH TARGET IOP?**
 - Netarsudil QHS
 - Dorzolamide TID
 - Timolol BID
 - Pilocarpine BID
- THE VOYAGER PIVOTAL TRIAL DEMONSTRATED AN EFFICACY ADVANTAGE OF LATANOPROSTENE BUNOD OVER LATANOPROST OF _____ ON AVERAGE.**
 - 0.38 mm Hg
 - 1.12 mm Hg
 - 1.23 mm Hg
 - 2.04 mm Hg
- THE PHASE 3 JUPITER STUDY ON LATANOPROSTENE BUNOD ENROLLED JAPANESE PATIENTS WITH OPEN-ANGLE GLAUCOMA AGED \geq 20 YEARS WITH A MEAN BASELINE IOP OF 19.6 MM HG IN STUDY EYES. WHAT DID THE 4-WEEK RESULTS AND YEAR 1 OUTCOMES FIND?**
 - Mean IOP reductions of 22% in the treated eye, maintained through year 1
 - No difference in mean IOP reduction in the study eye, but statistically significant differences by year 1
 - Mean IOP reductions of 22% in the study eye, but a regression at year 1
 - Statistically significant IOP reductions of in the study eye, but unacceptable side effects for 22% of patients

Current and Future Glaucoma Management: An Update on Existing Options and the Therapeutic Pipeline

The treatment of glaucoma has undergone a renaissance in recent years with the advent of minimally invasive glaucoma surgery (MIGS) and a novel class of drugs known as Rho-kinase (ROCK) inhibitors. These advancements are great news for the 3 million Americans who have some form of this chronic disease^{1,2} as many patients will have visual field loss despite adequate intraocular pressure (IOP) control. Patient compliance remains a significant challenge in glaucoma treatment, but recently approved once-daily agents and combination treatments may help minimize this. Even more importantly, newly approved agents may prove more effective than current treatments, possibly ushering in a new era of disease-modifying therapy.

— Inder Paul Singh, MD, Moderator

Note: This roundtable discussion was conducted before the FDA approved netarsudil and latanoprost ophthalmic solution (Rocklatan, Aerie Pharmaceuticals) for the treatment of open-angle glaucoma or ocular hypertension.

UNDERSTANDING MECHANISM OF ACTION IN NEW GLAUCOMA TREATMENTS

Q | Inder Paul Singh, MD: I've noticed in the past few years there has been a reemphasis on mechanism of action (MOA) in the treatment of glaucoma. This is partly due to the development of MIGS, which has revolutionized surgical glaucoma management,³ because the devices all work on a slightly different part of the outflow pathway.⁴ Some devices work by increasing trabecular outflow (iStent Micro-Bypass,⁵ Kahook Dual Blade,⁶ Trabectome⁷). Others increase the uveoscleral, suprachoroidal, or supraciliary outflow (CyPass Micro-Stent [withdrawn from the market in August 2018],⁸ iStent^{9,10}), increase the subconjunctival outflow (XEN-45¹¹, InnFocus MicroShunt¹¹), or reduce aqueous humor (endoscopic cyclophotocoagulation¹²).

MIGS devices need to be tailored to the patient, their disease type, and their target pressure. Pharmaceutical companies are finally coming around to this and understanding that we have to address the actual mechanism of pathology causing patients' IOP to rise. How do you incorporate an MOA discussion into your practices?

Constance Okeke, MD, MSCE: I agree there is now a significant amount of attention placed on understanding the MOA in terms of how these treatments are working as opposed to just how much they are working. MOA helps us understand the different MIGS devices in terms of what each can do and if they should be stand-alone or symbiotic. Just like with our combination pharmaceuticals, I think we can leverage multiple MOAs with MIGS surgeries and laser treatments. What long-term impact that will have on the patient and their disease, we are still trying to figure that out.

Michael Chaglasian, OD, FAAO: It's a great time to be a glaucoma practitioner. We now have a novel class of drugs

(ROCK inhibitors) that function by relaxing the trabecular meshwork (TM),¹³⁻¹⁵ and two new molecules in our armamentarium: latanoprostene bunod¹⁶ and netarsudil.¹⁷ This is an area of the pathophysiology of glaucoma that we've never before been able to attack. We've had to bypass it with uveoscleral outflow, beta blockers, and other agents to decrease aqueous humor production. In my mind, latanoprostene bunod and netarsudil have opened up new doors and will likely have significant advantages to patients in the long-term. They have given us a bigger playing field. I can now select products that are just as safe and effective as other topical products. These topicals impact even more distal pathways as well as episcleral venous pressure and outflow channels.

Tony Realini, MD, MPH: The addition of new drugs that work where the problem is—in the TM—is an important step forward in glaucoma pharmacology. What remains to be seen is how well these drugs add to our existing options. Often, drugs with complementary MOAs don't work as well together as we might expect. One example is prostaglandins and beta blockers, which add so poorly that the various fixed combinations of these products were never approved in the United States. A drug that adds significantly to a prostaglandin would fill a tremendous unmet need in glaucoma.

Dr. Singh: How do you select the patients who receive latanoprostene bunod?

Dr. Okeke: When latanoprostene bunod first became available, I had a waiting list of patients in whom I wanted to switch to this new drug from their prostaglandin analogs (PGAs). I had some good responses with that switch; some IOPs lowered by 2 mm Hg or 3 mm Hg, while some other patients had lowered IOPs by up to 6 mm Hg. I also had a number of patients with virgin eyes who had

great responses to treatment with latanoprostene bunod as a first-line agent. Some of them would have used two medications, but now I'm using just one, which is wonderful for compliance.

Latanoprostene bunod has also been shown to work in patients with lower baseline pressures. The phase 3 JUPITER study¹⁸ enrolled Japanese patients with open-angle glaucoma (OAG) who were at least 20 years old and had a mean baseline IOP of 19.6 mm Hg and 18.7 mm Hg in study eyes and treated fellow eyes, respectively. By week 4, mean reductions in IOP from baseline were 22.0% and 19.5% in study and fellow eyes, respectively, and reductions were maintained through year 1.

In my own practice, I have had some patients with low pressures who were progressing on a PGA, and I was able to get them down to pressures in the single digits after switching to latanoprostene bunod. Some of these patients had consistent pressures of 7 mm Hg. I think there's a lot of opportunity for latanoprostene bunod in the first-line setting as well as a switch.

DR. CHAGLASIAN: Formulary restrictions direct me to use generic medications as first-line agents, so I haven't had quite as much success with branded latanoprostene bunod (Vyzulta) in this setting. Most of my clinical experience with latanoprostene bunod has been with switches. Ideal patients are those who are on a PGA, tolerating it very well, and between 2 mm Hg and 4 mm Hg away from their target pressure. I try to use a single agent whenever possible to help with patient compliance, which makes latanoprostene bunod a natural switch.

I first start patients with a sample to see how they respond and confirm they are reaching their target pressure and tolerating it well. Then we'll go through the steps for prior authorization. It's a process, but patients understand that I am working to get them the best medications and to incorporate different MOAs to help control their disease.

DR. SINGH: Access to any new drug on the market is always a challenge. Samples help test the drug and ensure it will work in that particular patient. A number of my patients have had success with commercial coupons. Prior authorizations are sometimes a necessary evil. If a prior authorization is necessary, it's important to explain that the drug has a novel MOA, and that it's helping the patient reach their target pressure when PGAs have failed to do so, and there is no generic equivalent. Even though Vyzulta adds a nitric oxide component, it's been classified as a prostaglandin, so the additional explanation to get a prior authorization is usually needed.

The VOYAGER study compared latanoprostene bunod to latanoprost and showed a 28-day advantage for latanoprostene bunod of about a 1.23 mm Hg on average, but 42% of people had an IOP reduction of 2 mm Hg or greater.¹⁹ A significant number of patients will have an additional reduction. Multiple studies have shown that for every 1 mm Hg drop in IOP, the risk of disease progression decreases by 10%.²⁰⁻²³ Not everyone will benefit from latanoprostene bunod, but enough patients will that it's worthwhile to make the switch and see what happens.

I also like that latanoprostene bunod is once a day, which really helps with compliance. Latanoprostene bunod is a single molecule with two active metabolites, both of which have their own MOA.^{24,25} It

is metabolized into latanoprost and a moiety that donates nitric oxide, giving it a dual MOA. Latanoprost works on the uveoscleral pathway to increase aqueous humor outflow, while the nitric oxide increases trabecular outflow.²⁶ The real benefit is you're opening up multiple MOAs—the TM and the uveoscleral pathway.

The truth is, we don't know why it works. My theory is that by relaxing the TM, we are helping enhance the outflow and perhaps preventing further collapse over time (Figure 1). Nitric oxide is an endogenous signaling molecule that is naturally generated by nitric oxide synthases²⁶ and regulates many functions throughout the body.²⁷ Nitric oxide triggers production of cyclic guanosine monophosphate (cGMP) by guanylate cyclase-1 (GC-1), and cGMP activates protein kinase G (PKG).²⁸ Activated PKG can phosphorylate numerous targets with multiple downstream effects, including inhibition of Rho A, thus preventing inhibition of myosin phosphatase by ROCK. In addition to inhibition of Rho A, activated PKG can directly activate myosin light chain phosphatase. Subsequent dephosphorylation of the regulatory light chain of myosin by myosin light chain phosphatase prevents actin-myosin interaction, promoting cell relaxation. This in turn leads to a widening of the intercellular spaces in the juxtacanalicular trabecular meshwork and Schlemm canal, thus facilitating conventional aqueous humor outflow and relieving IOP.²⁹⁻³⁴

Therefore, by increasing flow through the TM and canal, we might be halting the disease pathology. Contrast this to beta blockers that work by reducing the aqueous outflow,³⁵ which may translate into further collapse of the TM over time. This could be why we see tachyphylaxis.^{36,37} The TM actually has a pumping mechanism, demonstrated by Murray Johnstone et al. Therefore, a stiffening of the meshwork beams caused by decreased flow through the TM could result in a decrease in this pump mechanism, thereby further collapsing the beams.

DR. OKEKE: Time and research will tell us more, but it's exciting to think that these drugs affecting the TM are changing its structure. Theoretically, there should be a long-term, real dynamic change to these tissues so that patients may actually benefit on another level.

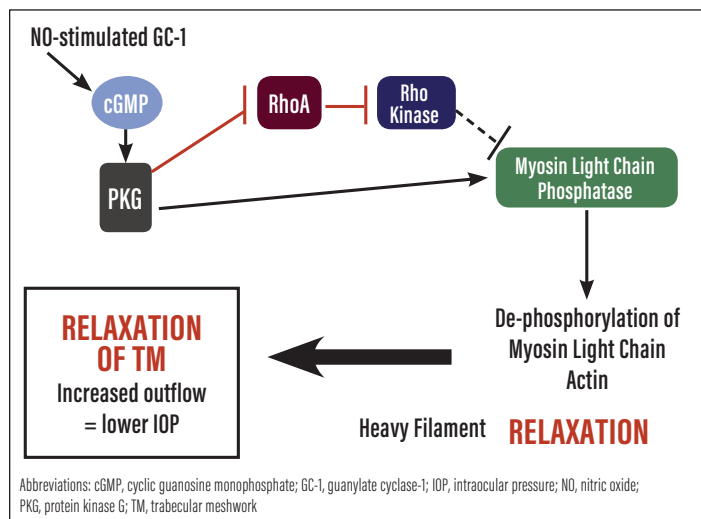


Figure 1. A simplified rendition of the cGMP modulation of IOP through increase in aqueous humor outflow.²⁸

And, if one continues using the medicine, at some point their TM could become so strong that there could be theoretical reversal of damage and modification of the disease. It's nice to think we are doing something beyond just lowering pressure; we may be resolving the underlying disease.

DR. CHAGLASIAN: The science behind nitric oxide is pretty well documented in the way that the nitric oxide inhibits both the ROCK and the calcium signal pathways intracellularly in the TM.²⁶ It speaks to the science behind the molecule and how latanoprostene is a great addition to our glaucoma medications. I agree that time will tell about the true histological changes, improvements in TM structure, and a real relaxation of cellular structure and increased permeability. But for now, the science on nitric oxide and its pathway channels in the cell is quite strong and certainly enough for me to use it in the first-line setting or a switch for patients who have not achieved target pressure.

CHALLENGES AND SOLUTIONS FOR INCREASED PATIENT COMPLIANCE

Q | DR. SINGH: The success of pharmacologic agents hinges on patients taking them. Have you experienced any compliance or tolerability issues with latanoprostene bunod?

DR. OKEKE: I've been pleasantly surprised that the tolerability is very good. Many patients I've switched to latanoprostene bunod report more tolerability, less redness, and less hyperemia than with their previous agent. Once-daily dosing is great for compliance. I've been happy to see the majority of the patients tolerate the medication quite well.

DR. CHAGLASIAN: My patients have also done really well with latanoprostene bunod. We know from the APOLLO and LUNAR studies that the adverse events and side-effect profile was essentially the same as a typical PGA therapy (Table).^{38, 39} Both studies compared latanoprostene bunod to timolol. In a pooled analysis, 21.6% of 811 patients in the latanoprostene bunod arm and 12.5% of 271 patients in the timolol arm experienced at least one ocular treatment-emergent adverse events (TEAEs).⁴⁰ Most were mild to moderate in severity. The most frequently reported TEAEs were conjunctival hyperemia, eye irritation, and eye pain. I have not seen an increase in side effects from nitric oxide in my patients.

DR. SINGH: Compliance is still one of the biggest issues that faces the medical management of glaucoma. Studies have shown that up to 60% of patients are noncompliant,⁴¹⁻⁴⁴ which is why it is so exciting to get patients off multiple drops. Any time you add a second or third medication to their regimen, compliance becomes extremely challenging. It's difficult to get patients to stay on medications long-term and go back for refills. My goal is to keep patients on the smallest number of bottles as possible.

DR. OKEKE: I've had some patients with well-controlled pressure on beta blockers or a PGA combination, but were still having

TABLE. MOST COMMON OCULAR ADVERSE REACTIONS IN APOLLO AND LUNAR* 38-40

Adverse Reaction	LBN (n = 811)	Timolol, 0.05% (n = 271)
Conjunctival hyperemia†	5.9%	1.1%
Eye irritation	4.6%	2.6%
Eye pain	3.6%	2.2%
Ocular hyperema	2.0%	0.7%
Instillation site pain	2.0%	1.8%
Abbreviation: LBN, Latanoprostene bunod.		

* Pooled data from all tested time points in the APOLLO and LUNAR studies; ocular adverse reactions occurring in ≥2% of study eyes.
† Included moderate or severe ocular hyperemia.

challenges keeping up with their regimen because the morning routine was too difficult and they'd forget a dose. I suggested switching to latanoprostene bunod to see if their pressures would at least be consistent. In some, they were actually lower. I was extremely pleased with that—being able to offer a simple alternative to patients struggling with compliance.

I had one patient with newly diagnosed glaucoma and pressure in the mid-30s. He was up front with me about not being good with instilling his drops consistently. I suggested starting with latanoprostene bunod and explained its benefits: dual MOA, safe, tolerable, and only once-daily dosing. He was able to achieve pressures in the teens on the medication. It was very encouraging and exciting to know I could consider latanoprostene bunod as a first-line option; that's how efficacious it is. We have some super responders, up to 9 mm Hg, who respond even higher than what was noted in APOLLO and LUNAR.^{38,39} Those studies looked at the average across many patients. Just knowing that some individuals have a pronounced response to this medication makes me want to try it.

That said, we can be discouraged from using these new drugs because sometimes there is extra effort in getting prior authorizations. But these efforts are important—they show there is a demand for these medications. Eventually, insurance companies will see that demand and start to change the formulary level and allow it to be more accessible to more people.

DR. REALINI: Adherence is probably the biggest limitation to topical medical therapy for glaucoma. Glaucoma is generally without symptoms and our medications do not make anything perceptibly better for patients. Quite the opposite. In a medically controlled glaucoma patient, the only symptoms of their disease are the side effects of therapy. In the recent LiGHT study comparing selective laser trabeculoplasty (SLT) to medical therapy as first-line interventions for newly diagnosed glaucoma, both groups had comparable mean IOP and number of visits at target IOP, but the progression rates were almost 3-fold higher in the medication group and all 11 trabeculectomies performed in the study were in the medication group—evidence that some patients only took their medication the night before their study visits.⁴⁵

DR. CHAGLASIAN: As we saw in the JUPITER study,¹⁸

latanoprostene bunod has been a big help for our patients with normal or low pressures. I had one patient with pressures hovering around 18 mm Hg to 19 mm Hg. She initially tried a generic PGA and did not respond well. I gave her latanoprostene bunod and she came back 5 mm Hg points lower, bringing her IOP down to 13 mm Hg. I was glad I was able to offer her something that was safe and efficacious without prescribing multiple medications or something more invasive.

DR. SINGH: As we get closer to episcleral venous pressure, which can be anywhere between 8 mm Hg and 13 mm Hg it becomes harder and harder to get these pressures lower, especially with the aqueous suppressants.^{46,47} Some patients do well on a beta blocker and PGA but aren't consistent with their beta blocker. Anywhere from 40% to 50% of my patients have pressures less than 21 mm Hg, so there's definitely a need here.

Has anyone noticed a trend of lowering pressure further over time with latanoprostene bunod?

DR. OKEKE: I can't say that I've noticed a lowering trend, but I have noticed consistency.

CLINICAL APPLICATION OF NETARSUDIL

Q | DR. SINGH: Netarsudil is a potent ROCK inhibitor that is an amino isoquinoline amide that also inhibits the norepinephrine transporter.^{17,25,48} Its been shown to have three novel MOAs that lower IOP.⁴⁹⁻⁵¹ The relaxation of the TM and contraction of ciliary muscle lead to an increase in aqueous outflow through the conventional pathway.⁴⁸ Additionally, netarsudil reduces IOP by decreasing episcleral venous pressure and decreasing aqueous humor production.⁵² Its efficacy has been compared to both timolol and latanoprost. In the ROCKET trials, which compared netarsudil and timolol, patients in the netarsudil arm achieved a reduction in IOP ranging from 3.9 mm Hg to 4.1 mm Hg, while patients in the timolol arm had IOP reduction of 3.5 mm Hg to 4.6 mm Hg (Figure 2).⁵⁰ It also offers consistent IOP reduction in patients with a low baseline pressure.⁵⁰

Bacharach et al compared netarsudil to latanoprost, and found that netarsudil was actually less effective than latanoprost by approximately 1 mm Hg in patients with IOPs of 22 mm Hg to 35 mm Hg. However, netarsudil had similar efficacy to latanoprost in patients with a baseline IOP less than 26 mm Hg.⁵³

I tend to use netarsudil in the second-line setting or as an addition to a PGA. For me, the ideal patient is someone with a pressure in the low to mid-teens and needs additional IOP reduction. Sometimes needing IOP near 10 mm Hg or below. How have you incorporated netarsudil in your treatment paradigms?

DR. REALINI: I tend to use netarsudil in patients who need very low, single-digit target pressures. If we have the ability to lower episcleral venous pressure, then we're making lower target pressures potentially accessible with medical therapy.

DR. OKEKE: I agree—I've found netarsudil tends to work well in patients with lower IOPs, and it has been successful in additional

pressure reduction when used as an adjunct. It's a strong adjunct, even in the first-line setting, and I've also seen it work as a standalone agent. It is also useful postsurgery, when the patient needs additional pressure reduction due to steroids. It's great for patients with a history of uveitis and macular edema.

Netarsudil definitely has a role in glaucoma management, especially in synergy with the other medications. Maybe you've tried latanoprostene bunod and it didn't give you the results you wanted. If you add netarsudil in those patients, you may get 2 or 3, or sometimes more, points of IOP lowering activity.

DR. CHAGLASIAN: Netarsudil is a great alternative when you don't want to use topical, nonselective beta blockers and when you want to stay away from brimonidine because a patient has an allergy or sensitivity to those products. Because netarsudil is dosed in the evening, most of my patients are on a PGA first and then netarsudil is added adjunctively; that way they are taking their glaucoma medications only one time a day. That helps with compliance.

DR. SINGH: The phase 3 MERCURY 1 trial compared patients (n = 718) treated with combination netarsudil/latanoprost with patients treated with its individual components.⁴⁹ Patients had a maximum baseline IOP between 20 mm Hg and 36 mm Hg. The study found that 82% of patients on netarsudil/latanoprost achieved an IOP of 18 mm Hg or less compared with 57% of patients with netarsudil monotherapy and 68% of patients with latanoprost monotherapy. In MERCURY 1, there wasn't a significant difference between netarsudil and latanoprost when you were looking at achieving target pressures in the lower teens. At the higher pressures, latanoprost performed better than netarsudil. I think its success at lower pressures is part of the MOA with the episcleral venous pressure. It's difficult to achieve a pressure that low just with outflow only to the uveoscleral pathway.

The MERCURY 2 trial (n = 750) evaluated IOP at 90 days in three arms: combination netarsudil/latanoprost; netarsudil monotherapy; or latanoprost monotherapy.^{50,54} Results were similar to MERCURY 1: the combination of netarsudil/latanoprost lowered IOP by 1 mm Hg to 3 mm Hg beyond the comparators. More patients in the

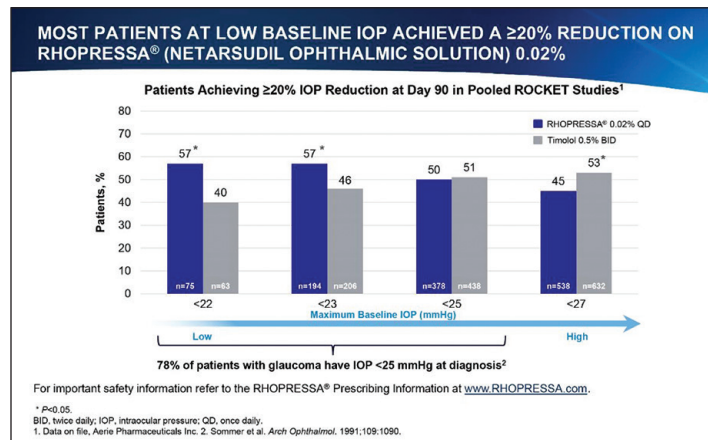


Figure 2. IOP reduction data of netarsudil compared with timolol at day 90 in pooled ROCKET studies.¹⁷

latanoprost/netarsudil group achieved IOPs of 14 mm Hg or less than the latanoprost 0.005% group.

It's going to be interesting to see what combination netarsudil/latanoprost does to the treatment landscape for first-line glaucoma treatment. How do you think netarsudil/latanoprost will change the treatment landscape?

DR. OKEKE: I have used the combination of netarsudil/latanoprost as a first-line treatment and saw some significant eye pressure reduction in patients who were in their mid-30s and as young as early teens. The potential for significant pressure reduction is there, but the side-effect profile is going to play a role. Latanoprostene bunod's side effects are more comparable to the other PGAs, whereas the hyperemia is much higher in netarsudil/latanoprost. Pooled results of the MERCURY 1 and MERCURY 2 trials on the combination reported adverse events such as conjunctival hyperemia (59%), instillation site pain (20%), cornea verticillata (15%), and conjunctival hemorrhage (11%).⁵¹ The majority of it is mild, but it is present. Hyperemia could be a deal breaker for some patients. That said, I think there is strong potential for netarsudil/latanoprost to be a front runner in terms simplifying a regimen when patients' pressures are high.

DR. REALINI: I think the limiting factor with netarsudil/latanoprost is justifying its cost; what is the IOP-lowering advantage over less expensive generic latanoprost? Right now, the combination has been statistically proven to be better than latanoprost.⁵⁵ Similarly, latanoprostene bunod is statistically more effective than latanoprost, but only by a small margin, and its cost is significantly more than generic latanoprost. For the near future, the barrier to using these drugs will initially relate to market access. Over time, if the health care and insurance industries perceive a benefit to this added efficacy, coverage will reflect and facilitate their use.

DR. SINGH: Can netarsudil and latanoprostene bunod be used successfully in combination? While there are no trials to evaluate this, does anyone have anecdotal evidence to share?

DR. CHAGLASIAN: I have a number of patients who are on both and I have seen additional pressure reduction. There must be different mechanisms in how these drugs approach the ROCK pathway. You're doubling down on the MOA, which achieves some nice results. I'd like to continue to look at it scientifically as opposed to my anecdotal information and really examine all the ways we can attack this disease.

DR. SINGH: I think we will see clinicians adding netarsudil to latanoprost to see how that works separately from the approved combination. I agree that hyperemia may be an issue and it will help determine if they can switch over to the single-bottle netarsudil/latanoprost combination for simplicity. Although hyperemia can be a limiting factor, the phase 3 trials have shown hyperemia was mild in a majority of patients and was not seen at every visit. We have also dealt with hyperemia within the PGA class for years. No doubt cost and access will be an issue as with all new medications.

DR. REALINI: I don't worry too much about the hyperemia with netarsudil, since I'm using it largely as adjunct to a PGA. If the patient has already acclimated to the hyperemia associated with a PGA, then we've fought and won that battle. The incremental hyperemia with netarsudil is negligible and clinically not significant in most patients.

PATIENT SELECTION

Q | DR. SINGH: What are the characteristics of a patient who would have success with latanoprostene bunod?

DR. CHAGLASIAN: I've found that latanoprostene bunod works well in Asian women with normal-tension glaucoma, central field defects, and pressure in the high teens. I don't reserve it exclusively for those patients by any means, but the nitric oxide component seems to be a great addition to a PGA by itself in those patients.

DR. OKEKE: I tend to use latanoprostene bunod as a first-line treatment in patients who have high pressures. I had a patient about age 40 with a pressure in the 30s who I was able to get down to the upper teens on latanoprostene bunod alone. I had another patient with low-tension glaucoma who was progressing on combination medication after an iStent, and had been on prostaglandins before the iStent procedure. I decided to put him on latanoprostene bunod, and his pressures went into the single digits and have been maintained there for more than 9 months. So, yes, there is potential for latanoprostene bunod to work with high pressures as well as low pressures.

Another one of my patients was on a beta blocker in the morning and a PGA in the evening. I switched them to latanoprostene bunod for a simplified regimen, and they've had stable pressures since. I've also had patients who are switched over from latanoprost and achieved up to a 6 mm Hg additional reduction with the switch to latanoprostene bunod.

DR. CHAGLASIAN: Does anyone recommend a branded PGA for older patients?

DR. SINGH: I do, but not everyone will get branded PGAs because of the cost issues. For me, the PGA is the foundation. It's your baseline for everything you do, whether you add a drop or perform a SLT. I prefer consistency in the inactive ingredients, and I've noticed differences between the various versions of generic latanoprost. I've had patients come in whose pressures have spiked up to 5 mm Hg and it turns out they were given a different generic latanoprost. Of course, that is not the case with all generics—and we need generics—but I strive for long-term consistency. I explain to the patient that the drug they are prescribed is their decision, but that I advocate for the branded version because the results can be different. My goal is to give the patient enough knowledge to make an informed decision.

DR. CHAGLASIAN: I'm going to play devil's advocate to that. Studies looking at diurnal curves in well-medicated patients have shown that the average intraday variability is 5 mm Hg to 6 mm Hg in well-controlled, stable patients.⁵⁶ Seeing a visit-to-visit, every 3- to 4-month fluctuation of 3 mm Hg to 5 mm Hg is entirely consistent

with the disease and entirely consistent with the stable patient. I'm not sure I would blame that on a generic medication.

DR. SINGH: I agree that fluctuating IOP is inherent to the disease process of glaucoma. However, a study on three different versions of generic latanoprost showed there was up to a 10% difference in efficacy between them.⁵⁷ Not every generic works as well as the branded version; there's too much variability. We should minimize fluctuation as much as possible, so I prescribe the branded version whenever possible. There could be no difference in some cases, but I don't want to take that chance.

DR. OKEKE: I also try to prescribe brand medications first. My focus is on patient compliance. Sometimes a branded drug I select is too expensive, so I switch the patient to another brand name that better meets their budget. My last choice is to start the monogeneric, unless I know that cost is going to be the rate-limiting step, and I want to have them on something versus nothing. I have had patients in whom I have switched from brand to generic come back with spikes in pressure of up to 6 mm Hg. I haven't, however, seen that much variability in patients on branded drugs. I try branded medications first, while being sensitive to what the patient can afford, and develop a regimen that works for them. I heavily utilize copay cards and patient assistance programs.

FUTURE OF DRUG DELIVERY

Q | DR. SINGH: Novel sustained-release drug-delivery systems are currently under investigation and include Bimatoprost SR (Allergan), designed to lower IOP in patients with OAG for up to 4 months; the Bimatoprost Ocular Ring Insert (Allergan), a ring-shaped device that releases bimatoprost over the course of 6 months; the OTX-TP sustained-release travoprost insert and OTX-TIC, a travoprost implant (Ocular Therapeutix); and the iDose Travoprost sustained-release implant (Glaukos).^{58,59}

Allergan recently announced top-line data from its phase 3 trial (n = 594) on Bimatoprost SR, which lowered IOP by 30% over 12 weeks and was well tolerated.⁶⁰ Glaukos has released interim phase 2 data for the iDose delivery system (n = 74) that found a 30% reduction in IOP over 12 months. No adverse events of hyperemia were reported to date.⁶¹ Ocular Therapeutix reached its target enrollment in a phase 3 study on OTX-TP, and top-line efficacy data are expected soon.⁶²

What are your thoughts on sustained-release drug delivery and how it can change practice?

DR. REALINI: We've been waiting for sustained-release drug delivery systems for a long time. We certainly know that adherence is an important part of glaucoma therapy and a real challenge for our patients; up to 60% of patients are not compliant with even single-dose regimens.⁴¹⁻⁴⁴ When we make those regimens more complex by adding more medications, compliance rates drop further.

That said, I think a sustained-release system will need to offer something more than comparable efficacy to topical therapy in order to drive adoption. Not many of my patients would opt for

frequent intraocular injections of a drug they can more safely use in drop form, and I suspect commercial payors will not broadly support a switch to injectable over topical therapy. There may be a role in patients who are known to be nonadherent to topical therapy, but we are not very good at identifying those patients.

DR. OKEKE: In terms of adoption, it will really come down to the practicality of the different options. For example, the Bimatoprost Ocular Ring Insert sounds very simple because it's placed in the eyes similarly to a contact lens, and it's easily removable; it doesn't seem invasive. More than 300 patients participated in the phase 1 and 2 clinical trials and 90% said the ring is comfortable. It lowered IOP by 4 mm Hg to 6 mm Hg over 6 months.⁶³ The question is, how long does it really last? Will it require fewer office visits or more compared with drops? I agree that sustained-release devices will be a slow uptake, but one of these will surface as the most practical. I think a lot of that will be determined by how invasive the procedure is, how long it lasts, and the number of office visits required.

DR. CHAGLASIAN: We know from our retinal colleagues that patients with age-related macular degeneration will tolerate regular and frequent ocular injections. But how many of those patients would tolerate an injection if a topical formulation was available? We may have a hard time selling patients on an implant and procedure when glaucoma medications are available as drops.

However, there are the benefits of sustained release as we've just mentioned. Overall, we now know there is not much of a difference in efficacy between the sustained-release devices and the drops.⁶⁰ In theory, a sustained-release product should provide more consistent 24-hour IOP reduction with less IOP fluctuation and thus less disease progression over time. Data from the Advanced Glaucoma Intervention Study reported that subjects with low mean IOP and high fluctuation were more likely to show visual field progression.⁶⁴ One of our general therapeutic targets in glaucoma is to minimize IOP fluctuation, though further study needs to confirm this information.

SELECTIVE LASER TRABECULOPLASTY IN THE FIRST-LINE SETTING

Q | DR. SINGH: How often do you use SLT as first-line treatment?

DR. REALINI: I use SLT in the first-line setting 95% of the time. When I diagnose a patient with glaucoma and tell them they need pressure reduction, I present two options. The first option is eye drops, which are safe, effective, and well-tolerated but require daily dosing and come with side effects. The alternate option is SLT, which is just as effective at lowering IOP as PGAs⁶⁵⁻⁶⁸ and lasts 3 years or more in most patients.⁴⁵ It takes 5 minutes in the office, is safe, is not painful, and works for 85% of patients.^{69,70} I explain that if it works, they don't have to bother with daily drops. I also tell them that if I was diagnosed with glaucoma tomorrow, I'd want SLT. Most of my patients go with the therapy I'd select for myself.

DR. OKEKE: I'm a strong advocate of SLT, and I use it as a first-line treatment in at least 50% of my patients. The treatment is great,

and it really works. I've had it last in some patients for up to 5 years. When discussing SLT with patients, I describe it as a light energy treatment in the form of laser and gauge their interest. If they are clearly scared of the laser option, then we try the drops first and give them more information about SLT to be considered at a later time. SLT needs to be considered more often as a first-line option.

DR. CHAGLASIAN: I think it's incumbent upon us to make recommendations to our patients. If a patient has just been diagnosed with glaucoma, maybe they don't fully understand the concept of SLT. They have no frame of reference for making this decision. They don't have a year of glaucoma fellowship and 20 years of experience treating glaucoma. If you, as a physician, believe that SLT is better for them than medical therapy, we need to say so.

DR. SINGH: You're absolutely right. I think you have to advocate for what you believe in. I use SLT in the first-line setting in about 50% to 60% of patients. I don't offer it as much as a first-line option as I should because I'm in a habit of prescribing drops and assuming that's what the patient wants. That mind set has started to change and I'm offering SLT more and more as a first-line treatment.

We also need to encourage our colleagues to initiate the conversation with patients about SLT and at least offer SLT in the first-line setting. Studies have shown that the efficacy of SLT decreases as the number of medications the patient takes increases.⁷¹ In virgin eyes, SLT could lower IOP by 30%,⁷² and repeating the procedure may result in outcomes similar to the initial treatment.⁷³ However, if a patient is on maximal medications and 10 years have gone by since the initial diagnosis, medical therapy has suppressed aqueous production and enhanced outflow to the point that the effect of SLT is reduced.^{73,74} The LiGHT study, published in the March 2019 issue of *The Lancet*, concluded that SLT is not only more effective and safer than drops, but can also save money in health care costs.⁴⁵ Patients who received SLT had better and more stable eye pressures and there was also less need for glaucoma surgery and cataract extractions compared to the drops group.

FUTURE DIRECTIONS IN GLAUCOMA MANAGEMENT

Q | DR. SINGH: What do we still need in terms of diagnostics and treatment in the management of glaucoma?

DR. OKEKE: It would be great to have a diagnostic tool that could evaluate the flow and tell us exactly where the blockage is located. Maybe the blockage is in more than one place. Maybe the outflow system is still working and the issue is the TM or Schlemm canal. If we had that, we'd be able to select the best treatment, whether that's medication, SLT, or surgery. But for now, we are doing a lot of guesswork. We'd be able to do so much more for our patients if we were able to really key into the problem.

DR. SINGH: I couldn't agree with you more. That's a huge need.

DR. CHAGLASIAN: I've been reading a lot about artificial intelligence (AI). From a dreamer's standpoint, I've wondered if we could

harness AI and deep learning to improve our visual field testing, optical coherence tomography, fundus photos, and overall disease management. If I could spend less time analyzing data and recording data, I could spend more time with my patient and talk to them about why they should have SLT first, or why they should go on latanoprostene bunod or netarsudil.

We will see an increase in our patients with glaucoma as the baby boomers age. I'd love to put the data we're collecting to work and use AI to inform me when patients are developing disease and when they're progressing and at what rate.

DR. REALINI: When I see an ocular hypertensive patient, I find the Ocular Hypertension Treatment Study (OHTS) and the European Glaucoma Prevention Study (EGPS) risk calculator invaluable in determining the individual risk of a patient and if we should proceed with treatment.²² In eyes with established glaucoma, however, assessing risk progression is much more difficult. Some patients progress at an IOP of 12 mm Hg, while some patients with an IOP of 24 mm Hg and clear primary OAG don't progress at all. Clearly there's more at play than just IOP in determining progression risk, but we don't have a tool that considers and rates all of those other factors and tells us the patient's true 5-year risk of progression. On a daily basis, I feel like I am sometimes advancing therapy in the wrong people and not advancing it in the wrong people; it's partially guesswork.

I would like to have a validated risk calculator for the progression of established OAG. That would help me with risk assessment, help me determine who to worry about and who not to, who to see more often and who to see less often, and who to test more and who to test less.

DR. SINGH: Has anyone used corneal hysteresis, which is an assessment of the cornea's ability to absorb and dissipate energy, as a predictor of visual field progression?⁷⁵

DR. OKEKE: I've started to use it and find it to be a useful tool. I use it on my patients to get a sense of how aggressive I should be with their treatment, and how closely I should be watching them. A recent study found that measuring corneal hysteresis at initial presentation can help predict the severity of glaucoma. Moderate to severe glaucoma is 2.9 times more likely to occur in eyes with a corneal hysteresis of less than 10 compared with those with a corneal hysteresis of 10 or greater, and suspect or mild glaucoma is more common in eyes with a corneal hysteresis of at least 10.⁷⁶

DR. SINGH: There are more than 700 published papers on corneal hysteresis. It is the only measurement we have to allow us to understand the biomechanical properties of the cornea and likely the lamina. In 2018, Medeiros and colleagues at Duke published a paper in the *American Journal of Ophthalmology* concluding lower corneal hysteresis measurements were significantly associated with increased risk of developing glaucomatous visual field defects over time.⁷⁷ The prospective longitudinal design of this study supports a role of corneal hysteresis as a risk factor for developing glaucoma. In a multivariable model adjusting for age, IOP, central corneal thickness, pattern standard deviation, and treatment, corneal hysteresis was still

predictive of development of glaucoma.

Any final comments on advances in the treatment of glaucoma?

DR. CHAGLASIAN: For every drug that is developed and commercialized, I have a subset of patients for whom it is the right drug. As a clinician on the frontline of defending patients against glaucoma vision loss, I am eternally grateful for the additional treatment options.

DR. SINGH: I think these new outflow drugs are making us more active providers. We are now not only thinking about bringing down the IOP, but how we are actually doing it. It's always beneficial to have more options.

Thank you to the panel for providing your insights and advice on advances in the treatment of glaucoma. ■

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CURRENT AND FUTURE GLAUCOMA MANAGEMENT:

An Update on Existing Options and the Therapeutic Pipeline

Release Date: June 10, 2019
CME Expiration Date: June 15, 2020
COPE Expiration Date: May 7, 2022

INSTRUCTIONS FOR CREDIT

To receive credit, you must complete the attached Posttest/Activity Evaluation/Satisfaction Measures Form and mail or fax to Evolve Medical Education LLC, 353 West Lancaster Avenue, Second Floor, Wayne, PA 19087; Fax: (215) 933-3950. To answer these questions online and receive real-time results, please visit evolvemeded.com/online-courses/1810-supplement-2. You will need to register if you do not already have an account. If you are experiencing problems with the online test, please email us at info@evolvemeded.com. Certificates are issued electronically; please be certain to provide your email address below.

Please type or print clearly, or we will be unable to issue your certificate.

Name _____ MD/DO participant OD non-MD participant

Phone (required) _____ Email (required) _____

Address _____

City _____ State _____ Zip _____

License Number _____

OE Tracker Number _____

DEMOGRAPHIC INFORMATION

Profession	Years in Practice	Patients Seen Per Week (with the disease targeted in this educational activity)	Region	Setting	Models of Care
<input type="checkbox"/> MD/DO	<input type="checkbox"/> > 20	<input type="checkbox"/> (with the disease targeted in this educational activity)	<input type="checkbox"/> Northeast	<input type="checkbox"/> Solo Practice	<input type="checkbox"/> Fee for Service
<input type="checkbox"/> OD	<input type="checkbox"/> 11-20	<input type="checkbox"/> 0	<input type="checkbox"/> Northwest	<input type="checkbox"/> Community Hospital	<input type="checkbox"/> ACO
<input type="checkbox"/> NP	<input type="checkbox"/> 6-10	<input type="checkbox"/> 1-5	<input type="checkbox"/> Midwest	<input type="checkbox"/> Government or VA	<input type="checkbox"/> Patient-Centered Medical Home
<input type="checkbox"/> Nurse/APN	<input type="checkbox"/> 1-5	<input type="checkbox"/> 6-10	<input type="checkbox"/> Southeast	<input type="checkbox"/> Group Practice	<input type="checkbox"/> Capitation
<input type="checkbox"/> PA	<input type="checkbox"/> <1	<input type="checkbox"/> 11-15	<input type="checkbox"/> Southwest	<input type="checkbox"/> Other	<input type="checkbox"/> Bundled Payments
<input type="checkbox"/> Other		<input type="checkbox"/> 16-20		<input type="checkbox"/> I do not actively practice	<input type="checkbox"/> Other

LEARNING OBJECTIVES

DID THE PROGRAM MEET THE FOLLOWING EDUCATIONAL OBJECTIVES?

AGREE

NEUTRAL

DISAGREE

Explain how novel therapeutics differ in their methods of action from other topical medications.

Evaluate the safety and efficacy of latanoprostene bunod for ocular hypertension and POAG.

Describe how a healthy eye manages IOP in contrast with an unhealthy eye.

POSTTEST QUESTIONS

- PLEASE RATE YOUR CONFIDENCE ON YOUR ABILITY TO APPLY UPDATES IN THE TREATMENT OF OPEN-ANGLE GLAUCOMA AND OCULAR HYPERTENSION IN THE CLINIC BASED ON THIS ACTIVITY. (BASED ON A SCALE OF 1 TO 5, WITH 1 BEING NOT AT ALL CONFIDENT AND 5 BEING EXTREMELY CONFIDENT.)**
 - 1
 - 2
 - 3
 - 4
 - 5
- PLEASE RATE HOW OFTEN YOU INTEND TO APPLY ADVANCES IN THE MANAGEMENT OF OPEN-ANGLE GLAUCOMA AND OCULAR HYPERTENSION IN THE CLINIC. (BASED ON A SCALE OF 1 TO 5, WITH 1 BEING NEVER AND 5 BEING ALWAYS.)**
 - 1
 - 2
 - 3
 - 4
 - 5
- WHAT IS THE PRIMARY IOP-LOWERING MECHANISM OF ACTION AT PLAY IN RHO-KINASE INHIBITORS?**
 - They lower IOP by suppressing aqueous humor production
 - They lower IOP by relaxing the trabecular meshwork
 - They lower IOP by increasing aqueous outflow through the uveoscleral outflow
 - They lower IOP by decreasing episcleral venous pressure
- YOU ARE TREATING AN ASIAN PATIENT WITH NORMAL-TENSION GLAUCOMA, CENTRAL FIELD DEFECTS, AND AN IOP OF 17 MM HG IN BOTH EYES. THE PATIENT ADMITS THAT THEY ARE UNLIKELY TO REMEMBER DROPS, BUT PREFERS MEDICAL THERAPY OVER LASER TREATMENT. WHAT IS AN EVIDENCE-BASED APPROACH TO TREATMENT IN THE FIRST-LINE SETTING?**
 - Latanoprostene bunod
 - Selective laser trabeculoplasty (SLT)
 - Dorzolamide
 - Trabeculoplasty
- WHICH OF THE FOLLOWING ARE REPORTED ADVERSE EVENTS FROM COMBINATION NETARSUDIL/LATANOPROST THAT MAY BE A LIMITING FACTOR FOR USE?**
 - Conjunctival hemorrhage
 - Instillation site pain
 - Cornea verticillata
 - Hyperemia
 - All the above
 - None of the above
- PUBLISHED LITERATURE NOTES THE AVERAGE INTRADAY IOP VARIABILITY IN GLAUCOMA PATIENT WITH WELL-CONTROLLED DISEASE IS _____.**
 - 2 mm Hg to 3 mm Hg
 - 3 mm Hg to 5 mm Hg
 - 5 mm Hg to 6 mm Hg
 - More than 6 mm Hg
- BASED ON RESULTS OF THE LIGHT STUDY, EFFECTS OF A FIRST SLT LAST AN AVERAGE OF _____ IN MOST EYES.**
 - 1 year
 - 2 years
 - 3 years
 - 4 years
- SLT CAN LOWER IOP BY WHAT PERCENTAGE IN THE FIRST-LINE SETTING?**
 - 25%
 - 20%
 - 30%
 - 15%
- IN THE MERCURY 2 TRIAL, THE COMBINATION NETARSUDIL/LATANOPROST LOWERED IOP BY AN ADDITIONAL _____ OVER NETARSUDIL MONOTHERAPY OR LATANOPROST MONOTHERAPY.**
 - 5 mm Hg
 - 2 mm Hg to 3 mm Hg
 - 3 mm Hg to 4 mm Hg
 - 1 mm Hg to 3 mm Hg
- A PATIENT IS CURRENTLY ON A PROSTAGLANDIN, BUT THE IOP IS 15 MM HG, WHILE THE TARGET PRESSURE IN THE LOW TEENS. THE PATIENT HAS REPORTED AN ALLERGY TO BRIMONIDINE, AND GETS CONFUSED WHEN HE HAS TO TAKE MULTIPLE DRUGS FIRST THING IN THE MORNING. WHAT IS THE MOST ACCEPTABLE AGENT TO ADD TO THE PATIENT TO REACH TARGET IOP?**
 - Netarsudil QHS
 - Dorzolamide TID
 - Timolol BID
 - Pilocarpine BID
- THE VOYAGER PIVOTAL TRIAL DEMONSTRATED AN EFFICACY ADVANTAGE OF LATANOPROSTENE BUNOD OVER LATANOPROST OF _____ ON AVERAGE.**
 - 0.38 mm Hg
 - 1.12 mm Hg
 - 1.23 mm Hg
 - 2.04 mm Hg
- THE PHASE 3 JUPITER STUDY ON LATANOPROSTENE BUNOD ENROLLED JAPANESE PATIENTS WITH OPEN-ANGLE GLAUCOMA AGED \geq 20 YEARS WITH A MEAN BASELINE IOP OF 19.6 MM HG IN STUDY EYES. WHAT DID THE 4-WEEK RESULTS AND YEAR 1 OUTCOMES FIND?**
 - Mean IOP reductions of 22% in the treated eye, maintained through year 1
 - No difference in mean IOP reduction in the study eye, but statistically significant differences by year 1
 - Mean IOP reductions of 22% in the study eye, but a regression at year 1
 - Statistically significant IOP reductions of in the study eye, but unacceptable side effects for 22% of patients

ACTIVITY EVALUATION

Your responses to the questions below will help us evaluate this CE activity. They will provide us with evidence that improvements were made in patient care as a result of this activity.

Rate your knowledge/skill level prior to participating in this course: 5 = High, 1 = Low _____

Rate your knowledge/skill level after participating in this course: 5 = High, 1 = Low _____

This activity improved my competence in managing patients with this disease/condition/symptom. ____ Yes ____ No

I plan to make changes to my practice based on this activity. ____ Yes ____ No

Please identify any barriers to change (check all that apply):

<input type="checkbox"/> Cost	<input type="checkbox"/> Lack of opportunity (patients)	Other. Please specify: _____
<input type="checkbox"/> Lack of consensus or professional guidelines	<input type="checkbox"/> Reimbursement/insurance issues	_____
<input type="checkbox"/> Lack of administrative support	<input type="checkbox"/> Lack of resources (equipment)	_____
<input type="checkbox"/> Lack of experience	<input type="checkbox"/> Patient compliance issues	
<input type="checkbox"/> Lack of time to assess/counsel patients	<input type="checkbox"/> No barriers	

The design of the program was effective for the content conveyed. ____ Yes ____ No

The content was relative to your practice. ____ Yes ____ No

The content supported the identified learning objectives. ____ Yes ____ No

The faculty was effective. ____ Yes ____ No

The content was free of commercial bias. ____ Yes ____ No

You were satisfied overall with the activity. ____ Yes ____ No

Would you recommend this program to your colleagues? ____ Yes ____ No

Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced through your participation in this activity:

Patient Care

Medical Knowledge

Practice-Based Learning and Improvement

Interpersonal and Communication Skills

Professionalism

System-Based Practice

Additional comments:

I certify that I have participated in this entire activity.

This information will help evaluate this CME/CE activity; may we contact you by email in 3 months to see if you have made this change? If so, please provide your email address below.



MODERNOPTOMETRY

