

New Trends in Medical Therapy for Glaucoma

Drugs and delivery systems in development offer the hope of better options for individualized treatment.

BY SUNITA RADHAKRISHNAN, MD

Today's patient will most likely start treatment for glaucoma with medical therapy, specifically with a prostaglandin analogue (PGA) taken once at night. If he or she cannot use a PGA or prefers not to, a β -blocker dosed once in the morning is often a suitable alternative. As far as adjunctive therapy is concerned, all classes of medication are effective when added to a PGA.¹ The choice of agent depends on several factors, and there is no one-size-fits-all algorithm. When more than one medication is required to lower IOP, the complexity of the treatment regimen increases, and its tolerability may decrease. These factors affect adherence, as does the method of drug delivery. At present, patients must remember to instill eye drops every day for years on end. If that in itself is not difficult, actually getting the drop into the eye can certainly be challenging.²

The exclusive focus of glaucoma treatment continues to be on lowering IOP, even though this approach is not sufficient in all patients. Despite an expansion in the options for medical treatment, unmet needs remain that new developments will help to address.

CURRENTLY AVAILABLE OPTIONS

In the past few years, new pharmaceutical offerings have expanded eye care specialists' options. A β -blocker-free fixed combination containing brimonidine 0.2% and brinzolamide 1% (Simbrinza; Alcon) was approved in 2013. Its side effects are similar to those of the individual components, and its efficacy is similar to that of a PGA. Advantages of fixed combinations include a lower preservative burden and a simpler treatment regimen.

Tafluprost 0.0015% (Zioptan; Akorn), the only preservative-free commercially available PGA, was approved in 2012. Its efficacy and side effect profile are similar to those of other PGAs. Additional commercially available preservative-free drugs include dorzolamide HCl 2%/timolol maleate 0.5% (Cosopt PF; Akorn) and

timolol maleate 0.5% (Timoptic in Ocudose; Bausch + Lomb). Preservative-free medications are very useful in patients who have ocular surface disease (either preexisting or related to the long-term use of topical medication), but cost, unfortunately, is often a limiting factor.

Although laser trabeculoplasty has been shown to be effective at decreasing medication burden,³ its utilization for this purpose remains low. The FDA's 2012 approval of the iStent Trabecular Micro-Bypass Stent (Glaukos) to be used in combination with cataract surgery may lead ophthalmologists to use microinvasive glaucoma surgery in this setting to minimize patients' dependence on medication. Concerns about the long-term safety and efficacy of these procedures as well as their cost, however, still need to be addressed.

WHAT IS IN THE PIPELINE?

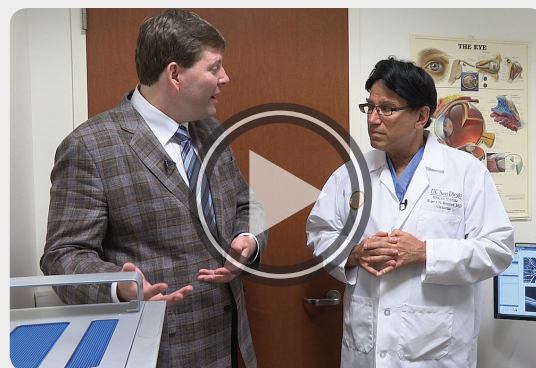
IOP-lowering medications currently in or having recently completed phase 3 trials have novel and often multiple mechanisms of action. Latanoprostene bunod (Vesneo; Valeant Pharmaceuticals and Bausch + Lomb) is a nitrous oxide-donating prostaglandin agonist with a dual mechanism of action: it increases both uveoscleral and trabecular outflow. In a phase 2 trial, once-daily latanoprostene bunod 0.024% reduced IOP to a significantly greater degree than latanoprost with comparable side effects.⁴ The companies expect to submit a new drug application for Vesneo to the FDA this year.

AR-13324 (Rhopressa; Aerie Pharmaceuticals) is a Rho kinase and norepinephrine transporter inhibitor that is believed to lower IOP by the "triple action" of reducing aqueous production, increasing trabecular outflow, and decreasing episcleral venous pressure. In a phase 2 trial, once-daily AR-13324 0.02% lowered IOP by 5.7 mm Hg from the unmedicated baseline.⁵ Another new drug being studied is PG324 0.02% (Roclatan; Aerie Pharmaceuticals), a fixed combination of Rhopressa and latanoprost.

OUTSIDE *the* BOX

by **Glaucoma**
TODAY

Debuting this month, Glaucoma Today Outside the Box (GTOB), provides a fun, casual, and personal look into the world of glaucoma medicine. Hosted by *Glaucoma Today's* (GT's) Chief Medical Editor, Steven Vold, MD, GTOB combines informative interviews on novel surgical techniques, technological advances, and physicians' accomplishments with material relevant to the cover series of each issue of *GT*, human interest stories, and humor. Check out the first episode, in which Dr. Vold and Robert N. Weinreb, MD, discuss the current status of neuroprotection in glaucoma and where this area of research is headed at eyetube.net/series/gt-outside-the-box. Your constructive feedback is welcome at gtletters@bmctoday.com.



Alternative drug delivery systems for glaucoma are an active and exciting area of research. The ability to deliver drugs once every few months instead of instilling eye drops daily would be a welcome change for patients and eye care providers. Among the approaches being pursued are punctal plugs (Ocular Therapeutix, Mati Therapeutics), inserts that rest on the ocular surface (ForSight Vision5), and injectable vehicles for medication (DSM, Envisia Therapeutics, Euclid Systems, GrayBug). The punctal plug delivery system is currently the most studied, and phase 2 trials are ongoing or complete.

Neuroprotective therapy is another unmet need in glaucoma management. Although practitioners typically think of neuroprotection only in patients whose disease is progressing at low IOPs, all glaucoma patients would benefit from IOP lowering *and* neuroprotection if such combination therapies were available. Neuroprotective factors delivered inside the eye via injectable vehicles are currently being studied in animal models of glaucoma (GrayBug). In addition, a phase 1 trial of an intraocular device that releases a neurotrophic factor (NT-501 CNTF Implant; Neurotech) has been completed in patients with primary open-angle glaucoma.⁶

CONCLUSION

It is an exciting time in glaucoma therapy! Currently available agents and new products in the pipeline give eye care providers the hope of offering patients treatment options that are best suited to their specific needs and circumstances. ■

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