

# RESEARCH RESULTS



## HIGHLIGHTS OF THE AGS ANNUAL MEETING

The latest results of clinical trials and research studies presented at the 27th Annual Meeting of the American Glaucoma Society, held March 2 to 5, 2017, in Coronado, California.

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The 27th Annual Meeting of the American Glaucoma Society (AGS) featured important findings from clinical trials and scientific research, with a full day devoted to glaucoma surgery, five symposia, 25 paper presentations, 142 posters,

10 breakfast roundtable discussions, and two workshops. More than 1,100 registrants attended the 4-day meeting and social events. The AGS Lecture “Tools for Teaching—at Home and Afar” was delivered by Wallace L. M. Alward, MD, the author of *Color Atlas of Gonioscopy* and creator of gonioscopy.org. Dr. Alward vividly described his passion for teaching and introduced software tools useful in making teaching modules such as Camtasia (TechSmith) and iBooks Author (Apple).

The prominent topics at this year’s AGS meeting included updates on glaucoma filtration surgery, novel therapies,

imaging, and IOP monitoring. For this article, we selected studies that have the potential to change glaucoma management today or in the near future.

### UPDATES ON OUTFLOW PROCEDURES

#### Primary Tube Versus Trabeculectomy Study

Steven Gedde, MD, presented the 1-year data from the Primary Tube Versus Trabeculectomy (PTVT) study, which compared the safety and efficacy of tube shunt surgery using the Baerveldt glaucoma implant 350 mm<sup>2</sup> (Johnson & Johnson Vision) versus trabeculectomy with mitomycin C (MMC) in patients without a history of intraocular surgery.<sup>1</sup> At 1 year, individuals who underwent trabeculectomy with MMC had a higher success rate than those who underwent tube shunt surgery. The former also had a greater reduction in IOP ( $12.4 \pm 4.4$  vs  $13.8 \pm 4.1$  mm Hg,  $P = .012$ ) and required fewer medications ( $0.91 \pm 1.4$  vs  $2.1 \pm 1.4$ ,  $P < .001$ ).

TABLE. CUMULATIVE PROBABILITY OF FAILURE IN THE PTVT STUDY<sup>1</sup>

|                                                   | Tube Group |              | Trabeculectomy Group |              |
|---------------------------------------------------|------------|--------------|----------------------|--------------|
|                                                   | N          | Failure Rate | N                    | Failure Rate |
| Overall failure rate at 1 year                    | 125        | 17.3%        | 117                  | 7.9%         |
| Failure rates at 1 year based on preoperative IOP |            |              |                      |              |
| IOP < 21 mm Hg                                    | 47         | 36.5%        | 44                   | 9.3%         |
| IOP 21-25 mm Hg                                   | 47         | 9.5%         | 37                   | 5.4%         |
| IOP > 25 mm Hg                                    | 31         | 3.4%         | 36                   | 8.6%         |

Data courtesy of Steven Gedde, MD.

$P = .013$  for the difference in failure rates between treatment groups (log-rank test adjusted for stratum).

$P = .016$  to  $.001$  for the difference in failure rates between the tube subgroup with a preoperative IOP lower than 21 mm Hg and all other subgroups based on randomized treatment and preoperative IOP (log-rank test).

Failure was defined as an IOP higher than 21 mm Hg or not reduced by 20% of baseline or an IOP lower than 5 mm Hg (2 visits after 3 months); need for additional glaucoma surgery; or a loss of light perception vision.

In a subanalysis, the investigators found that patients with lower preoperative IOPs benefited the most from a primary trabeculectomy compared with tube shunt surgery (Table; see *Watch It Now*).

Iqbal Ike Ahmed, MD, reported that there were no significant differences in the rates of intraoperative complications, late postoperative complications, and serious complications among patients enrolled in either arm of the PTVT study.<sup>2</sup> Although postoperative interventions were performed with similar frequency in both groups, the rates of some early postoperative complications (wound leak and bleb encapsulation) and reoperations for complications were higher after trabeculectomy than tube shunt surgery (6% vs 0.8% reoperations in the trabeculectomy and tube groups, respectively;  $P = .024$ ).

### InnFocus MicroShunt

Made from a nonreactive polystyrene and featuring an outer diameter of 250  $\mu\text{m}$ , the InnFocus MicroShunt (Santen; not FDA approved) may provide an alternative to conventional trabeculectomy in some patients. Paul Palmberg, MD, presented data collected over 4 years in the Dominican Republic and 2 years in France from patients who underwent implantation of the device.<sup>3</sup> The MicroShunt is implanted 3 mm from the corneoscleral limbus via a 25-gauge needle tract with adjunctive MMC. The IOP reduction was 55% from baseline, with a mean level of

11.2 mm Hg at the final visit. There was a 61% reduction in the number of glaucoma medications, and 62% of patients were free of drops postoperatively. No serious adverse events occurred during either study period, and patients who developed transient hypotony or choroidal detachment had a resolution of their complications at 3 months.

## WATCH IT NOW

Steven Gedde, MD, shares the 1-year results of the PTVT study.



In this episode of Glaucoma Today Journal Club (GTJC), Richard Lewis, MD, discusses Rhopressa's mechanisms of action.



James Brandt, MD, comments on the Bimatoprost Ring in this GTJC episode.



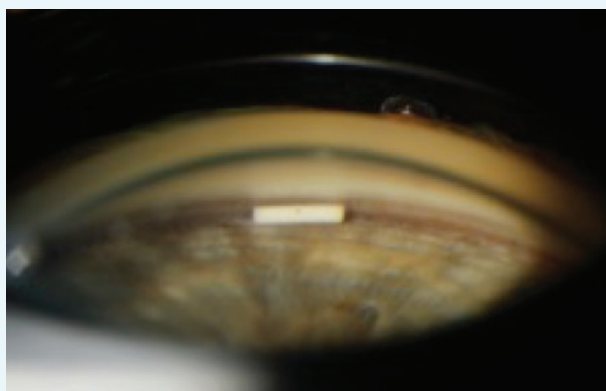
## AT A GLANCE

- The Primary Tube Versus Trabeculectomy (PTVT) study reported lower IOPs in patients who underwent trabeculectomy compared with tube shunt surgery, especially among those with lower preoperative pressure measurements.
- A microshunt may provide a safe alternative to traditional glaucoma filtration surgery in some patients.
- New medical therapies for glaucoma include drugs targeting novel mechanisms of aqueous outflow and sustained-release devices.
- Imaging provides detailed information about how the lamina cribrosa responds to IOP in advanced glaucoma and how blood vessels in the optic nerve head change in early disease.
- IOP monitoring beyond applanation tonometry in the clinic may become a new tool to help identify patients at risk of visual field progression.

(Figures 1 and 2 courtesy of Allergan.)



**Figure 1.** The Bimatoprost Ring and a US quarter for size comparison.



**Figure 2.** Gonioscopic view of Bimatoprost SR in the angle.

## NEW MEDICAL THERAPIES FOR GLAUCOMA

### Mercury 1

Netarsudil (Rhopressa 0.02%; Aerie Pharmaceuticals; not FDA approved) is an inhibitor of Rho kinase and norepinephrine transporter. The agent has three mechanisms of action: it increases aqueous outflow, reduces aqueous production, and lowers episcleral venous pressure (see *Watch It Now*).<sup>4</sup> Sanjay Asrani, MD, presented the 3-month interim results of the Mercury 1 phase 3 trial, which compared the efficacy of netarsudil/latanoprost ophthalmic solution (Roclatan 0.02%/0.005%; Aerie Pharmaceuticals) to its individual components.<sup>5</sup>

In patients with open-angle glaucoma or ocular hypertension, the fixed combination dosed every day after noon achieved a significantly greater IOP reduction than netarsudil or latanoprost alone; 44% of patients on the fixed-combination medication had a diurnal IOP of 15 mm Hg or less compared with 23% and 25% of patients treated with netarsudil or latanoprost, respectively. The most common side effects of the fixed-combination medication were conjunctival hyperemia (53% in the combination group, 41% in the netarsudil group, and 14% in the latanoprost group) and conjunctival hemorrhage (11%, 14%, and 0.4%, respectively), both of which were mild and sporadic.

### Sustained Drug Delivery

The Bimatoprost Ring (Allergan) is a preservative-free ocular ring placed topically by a physician that releases bimatoprost for up to 6 months (Figure 1).<sup>6</sup> James Brandt, MD, presented the pooled results from two open-label extension studies from prior phase 2 studies (see *Watch It Now*).<sup>7</sup> One hundred fifty-six subjects were enrolled. The inserts were replaced at regular intervals and reduced IOP by between 4 and 6 mm Hg from postwashout IOP over more than 1 year of follow-up. The ring remained in the fornix of the eye in 92.3% of patients during the follow-up period. Adverse events were generally mild and consisted mainly of eye discharge and punctate keratitis. No significant eyelid or orbital issues were observed.

Donald L. Budenz, MD, MPH, reviewed other sustained drug delivery systems (see *Watch It Now*).<sup>8</sup> These included biodegradable implants in the anterior chamber such as ENV515 (travoprost XR; Envisia Therapeutics), which is in phase 1/2 trials, and the bimatoprost sustained-release implant (bimatoprost SR; Allergan; Figure 2), which is in phase 3 trials.

### IMAGING

As optic nerve head imaging becomes more sophisticated, researchers are using this tool to explore the pathophysiology of glaucoma. In a study presented by Harry Quigley, MD, investigators used spectral-domain optical coherence tomography to assess the response of anterior lamina cribrosa depth to changes in IOP.<sup>9</sup> The researchers imaged glaucoma patients before and after IOP reduction, which was achieved with laser suture lysis after trabeculectomy. The change in anterior lamina cribrosa depth related to overall lower IOP levels but not to the IOP difference before and after laser suture lysis. The change was mostly observed in eyes with early glaucoma, whereas the anterior lamina did not move in eyes with advanced disease. Furthermore, the regions of the lamina cribrosa corresponding to less glaucomatous damage moved more than those with greater damage. According to the investigators, the lamina cribrosa in eyes with advanced disease appeared stiffer, and regions of the lamina responded differently to IOP, suggesting that clinicians can image the anterior lamina cribrosa to assess the biomechanical state of the optic nerve head.

In a different study, Vikas Chopra, MD, and colleagues examined retinal vessel density in 56 eyes using swept-source optical coherence tomography angiography.<sup>10</sup> They found a stepwise decrease in vessel density from normal eyes to eyes with preperimetric glaucoma to those with mild glaucoma. This pattern was observed in the optic nerve head as well as the papillary and peripapillary regions. The investigators concluded that retinal vascular changes can develop early in glaucoma, before visual field changes become apparent.

(Courtesy of Kaweh Mansouri, MD, MPH.)

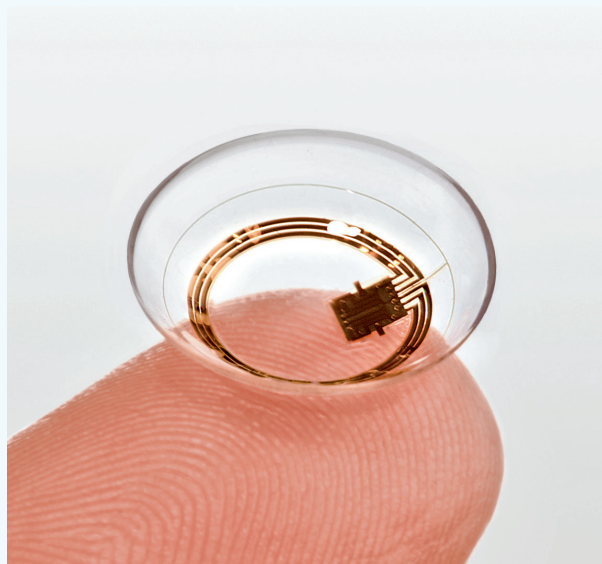


Figure 3. The Triggerfish contact lens sensor.

### IOP MONITORING

A continuous, 24-hour, IOP-related profile can be generated with the Triggerfish (Sensimed; FDA approved but not available in the United States; Figure 3). This contact lens sensor records dimensional changes of the eye in response to IOP.<sup>11</sup> Gustavo De Moraes, MD, presented a multicenter study to assess IOP-related parameters associated with visual field progression in treated glaucoma patients.<sup>12</sup> The researchers assessed 55 IOP-related parameters generated by the sensor in 445 patients with open-angle glaucoma. The investigators created a predictive model that included the number of large peaks while patients were awake, mean peak ratio at night, wake-to-sleep slope, and other parameters. This model had an area under the receiver operating characteristic curve of 0.798 for the prediction of slow versus fast visual field progression. The 24-hour recording from the device may help clinicians identify patients at risk of glaucomatous progression. (For more on IOP microsensors, see *Watch It Now*.) ■

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2. Ahmed II, Gedde S, Lim S, et al. Surgical complications in the Primary Tube Versus Trabeculectomy (PTVT) study during the first year of follow-up. Paper presented at: The 27th Annual AGS Meeting; March 2, 2017; Coronado, CA.
3. Palmberg P, Battie J, Riss I, et al. Two-center results of a SIBS-based micro shunt at 1 to 4 years. Paper presented at: The 27th Annual AGS Meeting; March 2, 2017; Coronado, CA.
4. Bacharach J, Dubiner HB, Levy B, et al. Double-masked, randomized, dose-response study of AR-13324 versus latanoprost in patients with elevated intraocular pressure. *Ophthalmology*. 2015;122(2):302-307.
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6. Brandt JD, Sall K, Dubiner H, et al. Six-month intraocular pressure reduction with a topical bimatoprost ocular insert: results of a phase II randomized controlled study. *Ophthalmology*. 2016;123(8):1685-1694.
7. Brandt J, Dubiner H, Benza R, et al. Reduction in IOP from a sustained-release bimatoprost ring: pooled results from 2 open-label extension (OLE) studies. Paper presented at: The 27th Annual AGS Meeting; March 3, 2017; Coronado, CA.
8. Budenz DL. Sustained drug delivery for glaucoma treatment. Paper presented at: The 27th Annual AGS Meeting; March 3, 2017; Coronado, CA.
9. Quigley H, Bedrood S, Solano-Moncada F. Biomechanical responses of choroid, posterior sclera, and lamina cribrosa to

## WATCH IT NOW

Donald Budenz, MD, MPH, explores sustained drug delivery for glaucoma management.



[bit.ly/3research0317](http://bit.ly/3research0317)

Donald Budenz, MD, MPH

In this episode of GTJC, H. Burkhard Dick, MD, PhD, discusses microsensors for 24-hour IOP monitoring.



[bit.ly/4research0317](http://bit.ly/4research0317)

Burkhard Dick, MD, PhD  
University Eye Hospital Bochum

intraocular pressure change assessed by OCT in glaucoma eyes. Paper presented at: The 27th Annual AGS Meeting; March 3, 2017; Coronado, CA.

10. Chopra V, Akil H, Huang A, et al. Retinal vessel density from OCTA to differentiate early glaucoma, pre-perimetric glaucoma, and normal eyes. Paper presented at: The 27th Annual AGS Meeting; March 3, 2017; Coronado, CA.

11. Mansouri K, Medeiros FA, Tafreshi A, Weinreb RN. Continuous 24-hour monitoring of intraocular pressure patterns with a contact lens sensor. *Arch Ophthalmol*. 2012;130(12):1534.

12. De Moraes G, Mansouri K, Liebmann J, Ritch R. 24-hour IOP-related profile with a contact lens sensor is associated with visual field progression in treated glaucoma patients: a multicenter study. Paper presented at: The 27th Annual AGS Meeting; March 4, 2017; Coronado, CA.

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