

# Enrollment Completed for US Investigational Study of the Xen Gel Stent

Enrollment is complete for the US investigational study of the Xen 45 Gel Stent (AqueSys), per a news release. According to the company, the stent is the first glaucoma device to achieve an IOP reduction similar to traditional subconjunctival trabeculectomy and tube shunt procedures through a minimally invasive technique with less associated surgical and postoperative risk.

The prospective, multicenter, single-arm clinical trial to be conducted at 12 sites in the United States is designed to evaluate the safety and performance of the Xen 45 Gel stent in subjects with refractory glaucoma. The company plans to collect 12-month data on all subjects and to submit them to the FDA to seek market clearance.

"Enrollment was completed within the study's prescribed time frame," Ron Bache, CEO of AqueSys, said in the news release. "We are pleased to achieve this milestone and look forward to obtaining all of the results and pursuing US market clearance. With commercialization going very well in Europe and our recent approval in Canada, the Xen Gel Stent is well positioned for success in the US."

AqueSys recently received a class 3 medical device license for the Xen Gel stent from Health Canada, permitting its sale in the country, according to a news release. AqueSys has chosen Salient Medical Solutions as the Canadian distributor, and commercialization is expected to begin immediately. AqueSys began commercial activities for the Xen in Europe in 2014, where it is CE Mark approved. To date, more than 1,800 stents have been implanted.

"AqueSys has reinvented the approach to subconjunctival outflow," Iqbal Ike Ahmed, MD, said in a news release. "It's the same space surgeons have trusted for close to 100 years, but we've never had a minimally invasive procedure to get access to it. This offers the advantage of a simpler and safer way of doing a well-recognized procedure. The mechanism of action of the Xen allows for a target pressure in the low teens, which makes it suitable for a broad range of glaucoma stages. I've used it with and without cataract surgery with similar efficacy."

At the Annual Meeting of the American Glaucoma Society, Dr. Ahmed presented the results of 57 eyes of 57 patients implanted with the Xen 45 with adjunctive mitomycin C.<sup>1</sup> The mean follow-up at the time of Dr. Ahmed's presentation was  $12.5 \pm 5.8$  months. The mean preoperative IOP was  $26.7 \pm 5.1$  mm Hg (stan-



dard deviation). The mean postoperative IOP was  $14.3 \pm 4.7$  mm Hg at 3 months ( $n = 57$ ),  $13.8 \pm 4.1$  mm Hg at 6 months ( $n = 56$ ),  $12 \pm 2.9$  mm Hg at 12 months ( $n = 55$ ),  $12.5 \pm 3.5$  mm Hg at 18 months ( $n = 46$ ), and  $13.1 \pm 3.7$  mm Hg at 24 months ( $n = 33$ ). At all time points, the postoperative IOP was lower than the preoperative IOP ( $P < .0001$ ). The mean postoperative glaucoma medications were reduced from a mean of  $3.5 \pm 1.5$  preoperatively to  $0.5 \pm 0.4$  at 12 months and  $0.8 \pm 0.5$  at 24 months ( $P < .001$ ). Six eyes (11%) required postoperative needling. Three eyes (5%) required re-operation for additional glaucoma surgery. No eyes lost 2 or more lines of visual acuity postoperatively, and there were no cases of persistent hypotony.

According to the company, the device stands alone as the world's first minimally invasive, standardized ab interno approach to subconjunctival outflow. It is implanted using a disposable injector with a small 27-gauge needle preloaded with the stent. Once in place, the soft, permanent gelatin stent is designed to minimize known complications related to synthetic materials. The proprietary technology reportedly uses physics to control aqueous fluid flow to lower IOP significantly yet protect against the hypotony associated with current subconjunctival procedures.

"My initial impression of the Xen 45 Gel Stent, based on my experience as a clinical investigator in a trial for patients with refractory glaucoma, is excitement," William J. Flynn, MD, said in a news release. "I eagerly await adding it to my clinical practice. The Xen 45 stent procedure is unique among glaucoma surgeries; it is minimally invasive yet results in an effective filtering bleb that is safer and more comfortable for patients."

*Dr. Ahmed is a consultant to AqueSys.*

1. Ahmed IK, Shah, M, Sheybani A. Use of a 45- $\mu$ m ab interno subconjunctival gel-stent with adjunctive mitomycin-C for the treatment of uncontrolled open angle glaucoma. Paper presented at: The 2015 AGS Annual Meeting; February 27, 2015; Coronado, CA.

## Micropulse Cyclophotocoagulation Technique “Reboots” a Traditional Glaucoma Therapy

Micropulse transscleral cyclophotocoagulation (mTSCPC) is a promising new treatment for glaucoma that offers a safe and effective alternative to standard transscleral cyclophotocoagulation, according to a poster presented by Nathan Radcliffe, MD, and colleagues at the 2015 American Glaucoma Society Annual Meeting in Coronado, California.<sup>1</sup>

The study evaluated the outcomes of 48 eyes of 45 patients who underwent mTSCPC with an 810-nm laser and MicroPulse P3 device (both products from Iridex). The patients received retrobulbar anesthesia followed by two 50- to 90-second mTSCPC treatments over the superior and inferior hemispheres, sparing the most temporal clock hour. The investigators performed the procedure with the laser on MicroPulse mode and a duty cycle of 31.3% (0.5-millisecond laser bursts followed by 1.1-millisecond rests, repeated throughout the 50- to 90-second laser application per hemisphere). Topical steroids were prescribed postoperatively, and patients' IOP was monitored.

The investigators reported a significant reduction in mean baseline IOP from  $25.8 \pm 1.3$  mm Hg (standard error of the mean) to  $17.1 \pm 2.1$  mm Hg 3 months postoperatively. The mean percentage change in IOP was 21.6% at week 1 ( $P < .001$ ), 30% at month 1 ( $P = .002$ ), and 29.8% at month 3 ( $P = .027$ ). The mean number of ocular hypotensive medications required to control IOP dropped from  $3.3 \pm 0.3$  (standard error of the mean) at baseline to  $2.4 \pm 0.3$  3 months postoperatively, resulting in an overall mean reduction of  $0.91 \pm 0.3$  ( $P = .018$ ).

In terms of safety, no cases of visually significant hypotony, macular edema, or phthisis bulbi were observed. One patient lost more than 2 lines of visual acuity from the worsening of a pre-existing cataract.

“Standard transscleral cyclophotocoagulation is a glaucoma therapy that is highly versatile and very efficacious but has lacked the ideal safety profile,” Dr. Radcliffe told *Glaucoma Today*. “Micropulse laser delivery is a new technology that breaks up continuous laser delivery into a rapidly alternating on-and-off cycle. This technique reduces thermal spread (collateral damage) and may possibly enhance biologic or noncoagulative tissue effects. In our series of 45 patients who underwent a mTSCPC, we saw a 30% pressure reduction with significant medication reduction and an excellent safety profile. This therapy provides new options to a wider spectrum of patients.”

In other news from the company, Iridex announced the first commercial sales of its Cyclo G6 laser system, which is designed to treat patients diagnosed with a range of glaucoma disease states. The Cyclo G6 system includes a laser dedicated to glaucoma treatment along with a family of single-use probes, namely the newly patented MicroPulse P3 disposable probe.

*Dr. Radcliffe is a consultant to Iridex.*

1. Radcliffe N, Vold S, Kammer JA, et al. MicroPulse trans-scleral cyclophotocoagulation (mTSCPC) for the treatment of glaucoma using the MicroPulse P3 device. Poster presented at: The 2015 AGS Annual Meeting; February 27, 2015; Coronado, CA.

## Rhopressa Shows Preliminary Evidence of Disease-Modifying Activity in Glaucoma

According to preclinical research by Aerie Pharmaceuticals, their leading drug candidate, Rhopressa, may block the effect of fibrosis-promoting proteins on cells of the trabecular meshwork that are associated with elevated IOP in glaucoma patients, per a news release. The research found that the drug suppressed the activity of the profibrotic proteins transforming growth factor  $\beta$ -2 and connective tissue growth factor on human trabecular meshwork cells in an in vitro model. This is the first study to show that Rhopressa—a novel once-daily—triple-action eye drop that lowers IOP in glaucoma patients, has the potential to modify the course of glaucoma by arresting fibrosis. Researchers from Duke University collaborated with Aerie on the study.

Another recent preclinical study by Aerie indicated that Rhopressa may increase the perfusion of the trabecular meshwork with aqueous humor, which has the potential to positively affect the overall health of the tissue. This research was performed in conjunction with Duke University and Boston University.

“The Rhopressa findings indicate a specific mechanism by which disease modification could be achieved in glaucoma,” Casey Kopczynski, PhD, Aerie’s chief scientific officer, said in a news release. “We are grateful to our collaborators at Duke University and Boston University for their contributions to this compelling research. Due to the progressive nature of glaucoma, new therapies are needed that directly target the diseased trabecular meshwork to block or reverse its deterioration, and we believe Rhopressa has excellent potential to address this unmet need.”

Aerie says, if approved, Rhopressa would become the only once-daily product available that specifically targets

the trabecular meshwork. According to the company, preclinical results have demonstrated that Rhopressa also lowers episcleral venous pressure, which contributes approximately half of IOP in healthy subjects. An additional mechanism reportedly reduces fluid production in the eye and therefore lowers IOP. Biochemically, Rhopressa inhibits both Rho kinase and norepinephrine transporter, according to Aerie.

In the company's phase 2b clinical trial, which was completed in May 2013, Rhopressa reportedly demonstrated a strong IOP-lowering effect, with mean reductions of 5.7 and 6.2 mm Hg on days 28 and 14, respectively. Additionally, the drug demonstrated a consistent mean IOP-lowering effect regardless of the patients' baseline IOPs. According to the company, this finding differentiates the agent from currently marketed IOP-lowering prostaglandin analogues and  $\beta$ -blockers, which have their greatest effect at higher baseline IOPs but lose efficacy as the baseline diminishes, as shown in published studies. In the Roclatan phase 2b trial completed in June 2014, Rhopressa performed with similar results as in its phase 2b trial completed in May 2013 and demonstrated additive efficacy when used in combination with latanoprost.

Enrollment is complete for Aerie's second phase 3 registration trial (Rocket 2) of Rhopressa designed to measure efficacy over 3 months and safety over 1 year. The primary efficacy endpoint is to demonstrate noninferiority of IOP lowering for the drug compared to timolol. Aerie's phase 3 program also includes Rocket 1, a 90-day efficacy registration trial for which data are expected mid second quarter 2015, and Rocket 3, a 1-year safety-only registration trial in Canada.

Pending successful results from the phase 3 registration studies and regulatory approvals, Aerie said it expects to submit a New Drug Application filing by mid-2016. The company plans to commercialize Rhopressa in North American markets and possibly Europe with its own sales force and will seek commercialization partners in other key territories, including Japan, emerging markets, and possibly Europe. Aerie fully owns its product candidates, has no licenses, and has patent protection for both use and composition of matter through 2030.

## PSLT Resulted in Similar Efficacy as SLT After 2 Months

Pattern scanning laser trabeculoplasty (PSLT; not currently available in the United States) is a safe and well-tolerated laser modality with efficacy similar to that of selective laser trabeculoplasty (SLT) in the short term, according to a poster presented by Kaweh

Mansouri, MD, and Tarek Shaarawy, MD, at the 2015 American Glaucoma Society Annual Meeting.<sup>1</sup>

Forty-six eyes of 23 patients with untreated open-angle glaucoma were randomized to undergo PSLT in one eye and SLT in the contralateral eye. Eyes treated with glaucoma medication were washed out 4 weeks prior to the laser treatment. The investigators used the Pascal Streamline 577 (Topcon Medical Systems) device to perform PSLT and the Ellex Tango laser (Ellex) to perform SLT. The Pascal laser is an optically pumped semiconductor laser with a 577-nm wavelength and 5-millisecond pulse duration (vs 532 nm and 3 nanoseconds with SLT). The average pulse energy used was 3.4 mJ, which is approximately one-tenth that of argon laser trabeculoplasty. The power was titrated to blanch the trabecular meshwork at 10 milliseconds, and subvisible treatment was applied with 5-millisecond pulses.

The investigators treated four quadrants in a single session and used the Ocular Latina PSLT gonioscopes. Patients evaluated the comfort level of each laser procedure using the visual analogue scale. The efficacy of the laser treatments was assessed 2 months postoperatively. Complete success was defined as an IOP reduction of at least 20% without medication.

No serious adverse events were recorded. One patient in each group experienced a transient IOP spike of at least 10 mm Hg immediately after the laser intervention. The average duration of treatment was 4.9 minutes for PSLT and 9.6 minutes for SLT.

Patients' comfort levels were higher with PSLT ( $25 \pm 21$  mm) compared to SLT ( $49 \pm 27$  mm;  $P < .0001$ ). For eyes treated with PSLT, the mean IOP dropped from  $20.3 \pm 5.5$  mm Hg at baseline to  $15.4 \pm 5.2$  mm Hg (-24%) 2 months postoperatively without glaucoma medication. For eyes treated with SLT, the mean IOP dropped from  $20.9 \pm 6.4$  mm Hg to  $14.9 \pm 4.4$  mm Hg (-28%) 2 months postoperatively and without glaucoma medication ( $P = .163$  for both PSLT and SLT).

According to the investigators, a potential limitation of the study is the difficulty in estimating appropriate energy levels with PSLT. Titrating energy to achieve blanching of the trabecular meshwork appears to require a longer learning curve than obtaining "champagne bubbles" with SLT, the authors said.

"Our results show that both SLT and PSLT are efficient treatment modalities, at least in the short term, and can be considered as a first-line treatment in glaucoma patients," Dr. Mansouri told *Glaucoma Today*. "Both laser modalities seem to be similar in IOP-lowering efficacy. In our study, PSLT treatment of 360° was faster (almost twice as fast) than SLT and

better tolerated by most patients. Whether this was due to the shorter treatment duration or other factors is unknown.”

More data are expected to be available this year, Dr. Mansouri said.

*Dr. Mansouri is a consultant to Sensimed and has received funds for research from Topcon.*

1. Mansouri K, Shaarawy T. Randomized, controlled trial to compare safety, tolerability, and efficacy of pattern scanning laser trabeculoplasty (PSLT) to selective laser trabeculoplasty (SLT). Poster presented at: The 2015 AGS Annual Meeting; February 28, 2015; Coronado, CA.

## InnFocus MicroShunt Reduced IOP in a Series of International Patients

Eighty-two patients from France, Japan, Spain, and the Dominican Republic who received the InnFocus MicroShunt (InnFocus) experienced a mean reduction in IOP of 9 mm Hg, according to data presented by Russ Trenary, CEO of InnFocus, at the Glaucoma Research Foundation's New Horizons Forum in San Francisco.

“We are increasingly excited about the results being shown internationally with the InnFocus MicroShunt,” Mr. Trenary said in a news release. “In addition to lowering IOP, we’re seeing an 84% reduction in glaucoma medication, with over 70% of the patients entirely off eye drops after 3 years.”

According to InnFocus, the patented microshunt is made from the innovative SIBS material to control flow. The device reportedly provides a quick and simple method of shunting aqueous humor from the anterior chamber to a diffuse bleb without the use of a scleral flap.

The implant is currently in phase 1 FDA trials at 12 centers in the United States, and the company plans to begin the final FDA phase this year. The device has been implanted alone or in combination with cataract surgery in clinical trials outside the United States.

## Next-Generation Humphrey Field Analyzer Introduced

At the 2015 American Glaucoma Society Annual Meeting in Coronado, California, Carl Zeiss Meditec announced the worldwide launch of the new Humphrey Field Analyzer 3 (HFA3). The device is designed to accelerate flow in the clinic while delivering the same gold-standard testing strategies and patterns. According to the company, test results on the new platform are equal to and interchangeable with results from prior generations of the HFA.

## Online Survey Results January/February 2015

Is cost a viable reason to perform glaucoma surgery first?

|     |       |
|-----|-------|
| Yes | 53.5% |
| No  | 46.5% |

Do you currently participate in the MOC program?

|     |        |
|-----|--------|
| Yes | 33.33% |
| No  | 66.67% |

The HFA3 is the first perimeter to introduce patented Liquid Lens technology, which reportedly saves time, simplifies setup, and reduces the possibility of human error in trial lens correction. According to Zeiss, the HFA3 replaces the manual process with a patented Liquid Trial Lens, which automatically delivers the appropriate refractive correction using measurement information entered into the instrument. The available correction range is -8.00 to +8.00 D sphere and addresses spherical correction only. The Liquid Trial Lens is available on the HFA3 model 860.

The HFA3 streamlines and hastens workflow with an array of new features, including

- RelEye, which allows doctors to instantly review the patient's eye position at any stimulus point. RelEye data are available on the device and when reviewing test results with Forum Glaucoma Workplace. It may reveal common testing problems, such as droopy lids (ptosis) or misalignment of the eye relative to the trial lens holder.
- SmartTouch interface, which reduces the number of steps required for the technician to start a perimetry examination. Faster gaze tracking provides information that helps doctors assess the reliability of test results. The gaze tracker on the HFA3 provides faster initialization and works on a wider spectrum of patients compared to earlier models of the HFA.
- An easy-to-use kinetic graphical user interface with a full 180° field of view.

“The HFA3, together with the other components of the Zeiss glaucoma management offerings, delivers an unrivaled combination of seamless integration and diagnostic performance to eye professionals who diagnose and manage glaucoma,” Ludwin Monz, PhD, president and CEO of Carl Zeiss Meditec, said in the news release. ■