SUSTAINED DRUG DELIVERY: REAL-WORLD EXPERIENCES

Surgeons describe their initial cases and the insights gained using a new pharmaceutical solution for glaucoma.

BY GAGAN SAWHNEY, MD; ROMAN KRIVOCHENITSER, MD; BLAKE K. WILLIAMSON, MD, MPH; AND STEVEN R. SARKISIAN JR, MD

GAGAN SAWHNEY, MD

The first patient of mine to receive the bimatoprost implant 10 mcg (Durysta, Allergan) was a Black woman in her 70s who is monocular. Vision was no light perception in her right eye and counting fingers in her left eye. She was on maximum tolerated medical therapy, including a prostaglandin analogue, a Rho kinase inhibitor, and aqueous suppressants. Her IOP ranged from 15 to 17 mm Hg, and she had a 0.95 cup-to-disc ratio and significant visual field loss. Our target IOP for her was in the range of 10 to 12 mm Hg, given her advanced optic nerve cupping.

I had several discussions with the patient about surgical intervention, but she was hesitant to undergo surgery due to having only one seeing eye. However, because of her limited vision in this eye, she had difficulty identifying her eye drops and properly administering them. Additionally, she did not have access to family members who could assist. When the bimatoprost implant was launched, I was excited by the prospect of helping this patient to decrease some of these obstacles by implanting a sustained-release medication and taking compliance out of her hands.

Initially, I thought the patient might be hesitant about this treatment option because it involves an injection. I have found that most patients with glaucoma want to do everything in their power to keep their IOP as low as possible and prevent progression. *Surgery*, however, can be a scary word, and often patients are reluctant to accept the potential risks associated with an invasive glaucoma procedure. When I spoke to the patient about the bimatoprost implant, however, she was intrigued by the simple, straightforward nature of the treatment and the fact that it entailed a procedure less invasive than surgery. Hence, she was highly motivated to proceed.

I mentioned to the patient that the bimatoprost implant is currently indicated for a one-time injection but that the effect may last between 6 months and 2 years, as evidenced by the FDA trials. More important, the patient and I discussed that, if we could lower and stabilize her IOP and also alleviate some of her challenges associated with drop use, her glaucoma and her well-being could improve as a result.

I chose to do the injection in our minor procedure room. Because of the patient's monocular status, we wanted to take as much caution as possible. We cleaned her eyelids with a povidone-iodine swab and placed a drop of povidone-iodine on the ocular surface to prevent infection. I used a lid speculum to maximize exposure. The implant was being placed in the patient's left eye, so I sat somewhat temporally because I am a right-handed surgeon. I injected the implant into the superotemporal quadrant, and the pellet released and floated to the inferior angle without complications. I noted some subtle leakage through the injection site, so I applied pressure for about 1 to 2 minutes to ensure that the wound self-sealed.

At 2 weeks postoperative, the patient's IOP was around 10 mm Hg. This indicated that, even though she had been taking a prostaglandin before the procedure, the intracameral sustained-delivery implant was having a greater effect. This presumably was because of the implant's 24-hour release of medication and the elimination of any variables affecting the patient's drop usage.

ROMAN KRIVOCHENITSER, MD

My first case with the bimatoprost implant 10 mcg was performed on June 23—the same day the treatment option became available to US providers. Our practice was one of the first in the country to gain access to the device. My first patient was an 81-year-old woman with primary open-angle glaucoma. She had been treated with topical bimatoprost 0.01% (Lumigan, Allergan) for several years and had well-controlled IOP before becoming my patient. She was well educated about glaucoma and understood the importance of keeping her IOP under control.

Once the bimatoprost implant gained FDA approval, I discussed the treatment as a potential option for this patient and felt she was a perfect fit. She had been tolerating bimatoprost drops for several years with good IOP control and excellent compliance. However, she was struggling with drop administration and frequently needed early refills, further exacerbating the cost of her glaucoma treatment. We both recognized that a sustained drug delivery option could resolve some of these issues for her.

In educating the patient about the bimatoprost implant, I was forthright and honest about the data we had available at the time and shared with her some results from the ARTEMIS trials. I told the patient that the bimatoprost implant is an FDA-approved delivery device that contains the same medication she was already taking. The patient was fully informed of the risks but was confident in the procedure and the ease of placement of the device.

To administer the implant, I placed the patient in the supine position and used a cotton swab to stabilize the eye and provide counterpressure. This was the technique used in the FDA trials as well. In this case, the implant did not fully release from the injector and appeared to be tethered to the needle tip. To disengage the implant, I spun the needle 360° to release the tether. I also found that the wound from the 27-gauge inserter leaked at the end of implantation. Applying 30 seconds of pressure with a Weck-Cel sponge (Beaver-Visitec International) stopped the leak, and I immediately sat the patient upright to help the pellet gravitate to the inferior angle.

UNDERSTANDING THE DURATION OF EFFECT

By Felipe A. Medeiros, MD, PhD

The data on the long-term duration of effect of the bimatoprost implant 10 mcg (Durysta, Allergan) comes from the phase 3 ARTEMIS studies, the 20-month results of which were recently published.[1] In the ARTEMIS studies, approximately 80% of patients remained medication-free 1 year after receiving their last bimatoprost implant. Of note, patients in the studies received a total of three implants, placed every 4 months. Therefore, the long-term duration may be different in patients receiving a single implant, which is the current FDA indication. However, I expect that the duration of a single dose will probably be at least 6 months, with a substantial number of patients potentially experiencing even longer responses. Multiple trials are being conducted to investigate different dosing schemes and to support label expansion in the near future to allow readministration of the implant.

1. Medeiros FA, Walters TR, Kolko M, et al; for the ARTEMIS 1 Study Group. Phase 3, randomized, 20-month study of bimatoprost implant in open-angle glaucoma and ocular hypertension (ARTEMIS 1) [published online June 13, 2020]. *Ophthalmology*. doi:10.1016/j.ophtha.2020.06.018.

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BLAKE K. WILLIAMSON, MD, MPH

A patient who had been coming to me for years and was stable on daily topical bimatoprost (Lumigan) started to have mildly elevated IOPs. When I inquired about her medication use, she stated that her insurance copays had been increasing, so she was using her drops every other day—basically rationing her treatment

to make the bottle last. As a result, her IOP had increased to 23 mm Hg OU, and she had a small nasal step in one eye and some preperimetric optic nerve thinning on OCT in the other eye.

Patient compliance with glaucoma drops is generally poor, and finances are often the primary contributing factor. This patient's disease had been stable when she was using her bimatoprost drops as prescribed, but it started to progress when she began rationing the use of her medication. I wonder how many patients do this and don't inform their providers.

I told the patient that she was a candidate for an implantable medication that would allow her to receive sustained drug delivery at therapeutic levels for several months and possibly longer. My team had run an insurance check before her consultation, so I was able to share with her that this simple procedure would be fully covered by her insurance (other than a $20 copay), and that it would provide sustained treatment for several months or more, without the need for additional drops. The patient was thrilled to have this opportunity. She was hesitant when told that she would be the first patient in Louisiana to undergo the procedure, but I reassured her by citing the safety results of the FDA study.

Placement of the bimatoprost implant 10 mcg is straightforward; any surgeon who can make a paracentesis can perform the procedure. Although the device can be placed at the slit lamp, some surgeons may prefer to do their first few cases in a surgery center or a minor procedure room. With the patient in the supine position, the surgeon simply introduces the needle at the inferotemporal clear cornea and aims directly toward the 6 o'clock position. When the tip of the needle is in the anterior chamber above the inferior iris, the surgeon presses the button on the injector in a controlled, deliberate fashion to release the implant.

This patient did very well with the treatment, and she was quite happy postoperatively when her IOP was in the mid-teens and her daily medication burden had been lifted.

STEVEN R. SARKISIAN JR, MD

On the day the bimatoprost implant became available, I implanted the device in five patients who had similar profiles. They all had a history of selective laser trabeculoplasty (SLT) within the past 2 years, had reasonably controlled or slightly above-target IOP, were taking one to three glaucoma medications, and had normal corneas and open angles. I chose to use the bimatoprost implant in these patients for a variety of reasons, but mostly due to the side effects of their eye drops. Compliance issues related to cost and forgetfulness were also in play. One patient in particular was eager to get off his regimen of three drops because he could not afford the copays.

All five patients were enthusiastic about this new sustained-release treatment option. They received the injection in the first eye on the same day and returned 2 to 3 weeks later for treatment on the other eye. The implantations all went off without complications or complaints. Afterward, several of the patients asked, "Is that it?"

My experience educating patients about the bimatoprost implant has been similar to educating patients about MIGS. Patients often come to see me because they want to hear about new treatment options, and they are often sent to me for a specific technology such as the bimatoprost implant. It is important to remember that these patients have an irreversible, blinding disease with no known cure. If the surgeon does his or her job correctly, the patient should understand the need for continued, lifelong monitoring and treatment. From there, the discussion can center around which treatment or combination of treatments is best. I have always felt strongly that glaucoma is best treated surgically. I prefer to use the phrase *interventional glaucoma* because it is less intimidating than *surgery* for patients, and it more accurately reflects the objective of SLT, the bimatoprost implant, and other sustained-release medication platforms in the pipeline.

Before placing the bimatoprost implant, I inform patients of the possibility of local irritation and redness at the site of the wound. I make clear that there is a risk of conjunctival hyperemia but that hyperemia is far more significant with topical prostaglandin analogues than with intraocular bimatoprost. I also inform patients about the low risk of corneal endothelial cell loss and note that this risk must be balanced by the real risk of optic nerve loss with improper drop use. Further, I mention that it is possible to replace endothelial cells but not a dead optic nerve. Physicians must have courage to be honest with themselves and their patients about the reality of poor compliance with eye drops. Often, the reality of the

situation is way worse than we may believe.

Patients sometimes ask if the bimatoprost implant can be removed if a problem occurs or if they become allergic. Although this is possible, the implant is dissolvable and will be much smaller a few weeks after placement. Moreover, I tell my patients that an allergic reaction is rare because most reactions to glaucoma medications occur from contact sensitivity of the conjunctiva and periocular skin. Often, the preservatives in drops are the culprit, but these toxic preservatives are not needed with an intraocular implant because the eye is sterile inside (unlike the inside of a plastic bottle sitting on a shelf for months). Also, with drops, getting the medication through all of the outer structures of the eye requires massive doses; when placed inside the eye directly via an implant, the dose can be much lower because the implant is right next to the anatomy it is trying to alter.

For surgeons who have yet to use the bimatoprost implant, I would note that the process is easier than perhaps expected and that patients are likely to be happy with the results. The company support is extensive, and Allergan will facilitate a dry lab and instructional videos prior to the surgeon's first implantation.

I have performed all of my bimatoprost implant cases in the office, half with my operating microscope in my procedure room and half at the slit lamp. As a righthanded surgeon, I have done many left-eye injections at the slit lamp for logistical reasons. This approach seems to go smoothly, and it is not unlike doing a paracentesis at the slit lamp; however, it is more involved because the surgeon has to go fully into the eye and may risk hitting the lens if he or she is not experienced being that far inside the eye. These are nonissues for any surgeon trained to do intraocular surgery.

When treating right eyes, I have found it easier to use the operating microscope, sit at the patient's head, and inject with a superotemporal wound, aiming inferiorly while keeping the needle over the iris. It truly is surgeon preference. One advantage of using the slit lamp is that gravity immediately takes the implant into the inferior angle. With the microscope, because the patient is lying down, the implant stays in the middle of the eye until he or she sits up, after which the implant will fall into the inferior angle. Of course, sterile technique is mandatory, and the wound will self-seal within seconds to minutes after the procedure, which can be confirmed with a cotton-topped applicator. The patient is asked to sit up for 1 hour after the procedure.

Going forward, I am debating whether to do these injections back to back in one office session or mix them up into our regular office schedule. I am strongly leaning toward performing them in succession using two rooms in my office, with left eyes at the slit lamp and right eyes in my minor procedure room with the microscope. ■

WATCH IT NOW | CASE FILES FROM THE OFFICE

By I. Paul Singh, MD

Dr. Singh presents two cases in which he discussed the bimatoprost 10 mcg treatment option with prospective glaucoma patients.

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