The current proliferation of new options for the surgical management of glaucoma may be just the beginning.

BY JONATHAN S. MYERS, MD

At a time when many surgeons are pondering how to incorporate microinvasive glaucoma surgery (MIGS) into a treatment algorithm, researchers are contemplating entirely new options and directions for MIGS-based therapies. Two videos that capture the excitement and possibilities of this era are “MIGS of Tomorrow” by Devesh K. Varma, MD, of the Prism Eye Institute in Toronto and “Gene-based Therapies” by Paul Kaufman, MD, from the University of Wisconsin (see Watch It Now).

MIGS OF TOMORROW

Dr. Varma compares the development of MIGS to that of cardiac stents and convincingly argues that a similar blossoming of directions and options of MIGS-based therapies is underway. His review of current and upcoming MIGS-based treatments highlights many of the most exciting and innovative ideas.

Dr. Varma notes the promising results of a prospective, randomized trial of the iStent Inject (Glaukos) as a stand-alone procedure versus two medications, with the IOP of more than 90% of eyes controlled at 18 mm Hg or less at 1 year in the iStent Inject group (two devices inserted). The recently released 3-year outcomes data on the InnFocus MicroShunt (Santen) are also impressive, with persistently low pressures over the course of follow-up.

Several companies are working on drug delivery devices. The iDose by Glaukos is a depot delivery system, and a phase 2 trial of iDose-delivered travoprost has completed enrollment. Ivantis is looking at drug delivery options for the Hydrus, and Allergan may find possibilities for the Xen45 stent as well.

Imaging of the supraciliary space has suggested that the size of the lake created by a supraciliary shunt may be related to IOP reduction.

At a glance

- Researchers are contemplating new options and directions for therapies based on microinvasive glaucoma surgery (MIGS).
- Glaukos has reported completion of a phase 2 trial with the iDose, and Ivantis is looking at the Hydrus for drug delivery. Allergan may find possibilities for the Xen45 stent as well.
- Alcon is developing the Cypass VX to allow the concurrent injection of a viscoelastic to enlarge the lake at the time of the MIGS device’s placement. Ivantis and Glaukos are also investigating IOP sensors, creating possibilities of therapeutic devices that adjust treatment based on IOP.
- MIGS-based delivery of gene therapy is under investigation. A one-time intervention based on gene therapy may decrease IOP for a prolonged period, reducing problems with adherence.
In addition, Ivantis and Glaukos are investigating IOP sensors, creating the possibility of therapeutic devices that adjust treatment based on IOP.

**GENE-BASED THERAPY**

Drug delivery by MIGS may be more broadly applicable. MIGS-based delivery of gene therapy is already under investigation by Dr. Kaufman and coworkers (see Watch It Now). Dr. Kaufman’s video is a great primer on the opportunities and challenges of gene-based therapy to reduce eye pressure. He notes that a one-time intervention based on gene therapy may reduce IOP for a prolonged period, thereby decreasing adherence problems. Potential targets for intervention may be completely distinct from the genes that cause glaucoma, much in the way that lowering IOP by aqueous suppression is completely separate from the pathology of reduced outflow that leads to elevated IOP.

Topical Rho kinase inhibitors have been shown to lower IOP by increasing outflow through their effects on trabecular meshwork cell contraction and cell junctions. Targeting mechanisms to inhibit the Rho kinase pathway, researchers have shown that gene therapy can be used in vitro to lead cells to overexpress C3, an exotoxin of *clostridia*, or caldesmon. In live animals, adenoviral-delivered gene therapy vectors have led to gene expression in the anterior chamber for 2 years or more, but attempts to deliver genes for the overexpression of C3 and caldesmon in live animals have not been successful, because the cells somehow turn off these genes. Dr. Kaufman notes that the broad delivery of target genes to all of the cells in the anterior segment may be partially responsible. Recent work using a modified MIGS delivery system to allow dosing of the gene therapy vectors directly to the trabecular meshwork and Schlemm canal may avoid these issues.  

4 Terete Borras, PhD, of the University of North Carolina recently published an in-depth review of gene therapy for glaucoma that demonstrates the staggering pace of development of novel approaches to the management of glaucoma.  

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