The 119th annual meeting of the American Academy of Ophthalmology (AAO), held from November 14 to 17, 2015, in Las Vegas, Nevada, attracted 28,000 attendees. We review key scientific sessions on endophthalmitis, new patient education videos, and ongoing research activities.

New Information on Endophthalmitis

The AAO’s Intelligent Research in Sight (IRIS) registry is used by more than 10,000 physicians to benchmark quality of care and patient outcomes. It contains data on 17.6 million patients and 60 million patient visits.

IRIS has revealed important new information about endophthalmitis, a rare complication of cataract surgery and intravitreal injections for wet age-related macular degeneration (AMD), the AAO announced at the meeting. According to IRIS data, there is no statistically significant difference between endophthalmitis rates for injections of compounded anti–vascular endothelial growth factor (VEGF) treatments for wet AMD, including off-label bevacizumab (Avastin, Genentech), and drugs manufactured specifically for that indication, such as ranibizumab (Lucentis, Genentech) and aflibercept (Eylea, Regeneron). Wet AMD is the leading cause of blindness among older Americans. The difference in infection rates between the two types of treatment was 0.01%. The IRIS registry provides data on 1,084,306 injections from 2013 to 2014.

Bevacizumab, ranibizumab, and aflibercept are considered to be safe and effective for the treatment of wet AMD. Before bevacizumab can be used off-label for ocular injections, it must be repackaged into smaller doses.

“These data disprove previous assertions made in reference to federal compounding legislation that no compounded product should ever be injected into the eye because of an elevated risk of infection,” said George A. Williams, MD, the AAO’s Secretary for Federal Affairs and Chairman of the Department of Ophthalmology at Oakland University’s William Beaumont School of Medicine in Rochester, Michigan. The new data “could be instrumental in future discussions surrounding federal drug quality and security guidelines that could complicate patient access to compounded Avastin,” he added.

In another presentation, Anne L. Coleman, MD, PhD, an ophthalmology researcher and Professor at the University of California at Los Angeles, described an analysis of IRIS registry and Medicare data in patients who had undergone cataract surgery in combination with anterior vitrectomy. The latter procedure is commonly used to disentangle the vitreous—the clear, jelly-like substance that fills the eye—from an intraocular lens or other structures.

Dr. Coleman suggested that further research could focus on the use of prophylactic antibiotics when anterior vitrectomy is combined with cataract surgery. The data in the IRIS registry could make such an investigation possible, she said.

“While common eye procedures, such as cataract surgery, are extremely effective, successful, and with very little risk of complication, ophthalmologists will always aim to find ways to lessen these risks, no matter how small,” Dr. Coleman said. “Since these complications are so rare, previously tracking and studying the occurrence and potential contributing factors was challenging. The IRIS registry makes this easier.”

Research Headlines

Eye Drop Advances

In a new study presented at the AAO meeting, five years of treatment with low-dose 0.01% atropine eye drops slowed the progression of nearsightedness in children and caused fewer adverse effects compared with higher doses. The research was led by Donald T. Tan, MD, of the Singapore Eye Research Institute.

In another study, a new eye drop was shown to speed tissue healing. The product, which contains Cacicol (poly[carboxymethylglucose sulfate]), could be used to improve healing in patients undergoing corneal transplants and refractive surgery, according to principal investigator Koray Gumus, MD, of Erciyes University in Turkey. Cacicol is approved in Europe for the treatment of corneal ulcers, but is not available in the U.S.

Trabodenoson for Glaucoma Monotherapy

At the Ophthalmology Innovation Summit, William McVicar, PhD, Chief Scientific Officer at Inotek Pharmaceuticals, announced that the company is about to embark on a phase 3 study of trabodenoson as monotherapy for glaucoma. In addition, Inotek is planning a phase 2 trial of an investigational fixed-dose combination of trabodenoson and latanoprost (Xalatan, Pfizer).

Trabodenoson is the first of a new class of compounds designed to lower intraocular pressure with a mechanism of action that augments the natural function of the trabecular meshwork, the main passageway for transporting aqueous humor out of the eye. Formerly known as INO-8875, the compound is a highly selective adenosine mimetic acting only at the A1 receptor subtype, Dr. McVicar said. This stimulates the release of proteases, which digest and remove accumulated proteins in the outflow path of aqueous humor.
Glaucoma is characterized by high intraocular pressure on the retina, which eventually causes the death of nerve cells that relay visual signals to the brain.

**New Sustained-Release Treatments**

Attendees at the AAO meeting also learned that Envisia Therapeutics is conducting a phase 2a clinical study of a biodegradable, intracameral, sustained-release formulation of travoprost (ENV515) in glaucoma patients. Tomas Navratil, the company’s Vice President of Development, added that Envisia is also developing a biodegradable ophthalmic implant (difluprednate [ENV905]) for the treatment of postoperative cataract inflammation and pain. Envisa expects to submit an investigational new drug application for the implant in the first quarter of 2016.

“We expect that ENV905 will be the first product approved utilizing the PRINT platform and to complete phase 3 clinical studies at the end of 2017. The PRINT nano- and microparticle engineering technology borrows its techniques from the silicone industry, namely lithography printing, wherein we first create a master; and from the master, we create a template or mold, which we can fill with a mixture of polymer and drug or 100% drug, which gives us control over particle size, shape, porosity, surface ligaments, release rate, and all of the key features that one needs to control when it comes to a sustained-release formulation,” Mr. Navratil explained.

**Wet AMD Injectables**

Tyrogenex, Inc., a biopharmaceutical company specializing in VEGF and platelet-derived growth factor (PDGF) inhibitors for wet AMD, has initiated a phase 2 study of its oral compound X-82, a dual VEGF/PDGF inhibitor, in patients who have been treated with aflibercept. The goal of X-82 therapy is to increase the interval between injections of aflibercept or ranibizumab and to reduce the total number of injections needed.

Current injectables often are not administered according to labeling (i.e., on a monthly basis), said Fred Meyer, PhD, CFA, of Tyrogenex. “If they were, they probably would keep patients fairly well maintained over a long period of time. But given the challenges both for patients and the health care system, over time patients start having fewer injections. They start being injected as needed as opposed to on-label, which would be monthly. And with that shift to longer times between injections, there is a fairly predictable and irreversible reduction in vision for those patients. They become unresponsive to the benefits of anti-VEGF therapy. That’s the unmet need that we see. It’s to provide a therapy that better meets the long-term needs of patients and maintains their vision without that irreversible loss. There are also obvious benefits of an oral therapy.”

**VEGF-/PDGF-Inhibiting Compound**

Other new research includes an analysis of squalamine lactate, a small-molecule eye drop, as a treatment for AMD, retinal vein occlusion, and diabetic macular edema. According to Irach Taraporewala, PhD, President and Chief Technology Officer at Ohr Pharmaceutical, the compound’s developer, squalamine lactate is designed to inhibit both VEGF and PDGF and to enhance the anti-VEGF effects of ranibizumab. The compound improved visual acuity in a phase 2 study.

**Patient Education Videos Unveiled**

In another initiative, the AAO debuted 40 new patient education videos. Each video explains treatment options for common eye conditions, along with their benefits and risks, in less than five minutes. Topics include cataract and refractive surgery, glaucoma, oculoplastics, and pediatric ophthalmology. The videos are available in English and Spanish. Ophthalmologists may integrate the videos into their electronic health record systems to meet federal meaningful use requirements, according to the AAO.