RT NEWS

SEPTEMBER 2018

VOL. 13, NO. 6 | RETINATODAY.COM

# AFLIBERCEPT LABEL NOW INCLUDES 12-WEEK DOSING INTERVAL FOR AMD

The US FDA in August approved an updated label for aflibercept (Eylea, Regeneron), adding every-12-week injection frequency as an alternative dosing strategy for patients with neovascular age-related macular degeneration (AMD). The previous labeling recommended injection once every 8 weeks after three initial monthly injections, and the new labeling retains that recommendation but adds this language:

"Although not as effective as the recommended every 8 week dosing regimen, patients may also be treated with one dose every 12 weeks after one year of effective therapy. Patients should be assessed regularly."

Regeneron's supplemental biologics license application to the FDA was based on second-year data from the phase 3 VIEW 1 and 2 trials, in which patients with wet AMD were treated with a modified 12-week dosing schedule, with doses given at least every 12 weeks and additional doses as needed.

## GENE REPLACEMENT THERAPY WAS EFFECTIVE IN CANINE MODEL OF RP

A gene therapy strategy that simultaneously suppresses a mutant gene and delivers a normal replacement copy was effective in saving photoreceptor cells and preventing vision loss in a canine model of autosomal dominant retinitis pigmentosa (RP).[1] The therapy is mutation-independent, researchers said, targeting a section of the rhodopsin gene (*RHO*) that is separate from where mutations are located.

The researchers, at the University of Pennsylvania and the University of Florida, noted that progress has been made in gene therapy treatment of autosomal recessive and X-linked RP, but "translation to the clinic has stalled" in attempts to treat the most common form of autosomal dominant RP, caused by more than 150 mutations in the *RHO* gene.

In this work, the researchers combined in a single adeno-associated virus vector a short-hairpin RNA that targets human and canine *RHO* in a mutation-independent manner with replacement complementary DNA made resistant to RNA interference. In a naturally occurring canine model of *RHO* autosomal dominant RP, subretinal injections of the vector led to nearly complete suppression of endogenous canine RHO RNA. At the same time, the human replacement RNA produced up to 30% of normal RHO protein levels.

Imaging showed that photoreceptors in treated areas were protected from retinal degeneration, and long-term follow-up for more than 8 months indicated that structure and function were preserved.

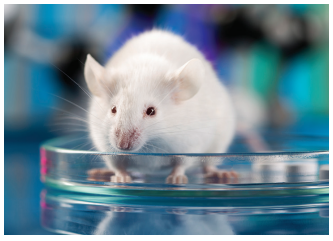
"The efficacy of this gene therapy in a clinically relevant large-animal model paves the way for treating patients" with this form of RP in a clinical trial, the researchers concluded.

1. Cideciyan AV, Sudharsan R, Dufour VL, et al. Mutation-independent rhodopsin gene therapy by knockdown and replacement with a single AAV vector [published online ahead of print August 20, 2018]. *Proc Nat Acad Sci U S A*.

## VISUAL RESPONSES RESTORED IN MOUSE MODEL OF BLINDNESS

A gene therapy approach that wakes up dormant stem cells and reprograms them to generate rod photoreceptor cells showed evidence of vision restoration in a mouse model of congenital blindness.[1]

An international team of researchers used a two-stage method to reach their goal: First, they used gene transfer of beta-catenin to reactivate the cell cycle in Müeller glial (MG)



cells in the mice; then, they used gene transfer of transcription factors to cause the awakened cells to develop into rod photoreceptors. The MG-derived rods restored visual responses throughout the visual pathways in the mice, from the retina to the primary visual cortex.

The authors noted that, in zebrafish, MG cells can replenish damaged retinal neurons to restore vision, but in mammals MGs do not spontaneously perform this function. MG cells do, however, proliferate in response to retinal injury. They hypothesized that this repair capability of MG cells could be exploited to restore vision in mammalian retinas.

The results of their work "provide evidence of vision restoration after de novo MG-derived genesis of rod photoreceptors in mammalian retinas," the authors said.

1. Yao K, Qiu S, Wang YV, et al. Restoration of vision after de novo genesis of rod photoreceptors in mammalian retinas [published online ahead of print August 15, 2018]. *Nature*.

## SOME EYE CONDITIONS ASSOCIATED WITH ALZHEIMER DISEASE

People with certain ophthalmic diseases may be at increased risk for developing Alzheimer disease (AD), according to recent research. In an analysis of data from participants in the Adult Changes in Thought study, significant links were seen between AD and three conditions—established diagnosis of AMD, recent diagnosis of glaucoma, and established or recent diagnosis of diabetic retinopathy.[1]

Investigators at the University of Washington and colleagues analyzed data from a cohort of 3,877 randomly selected patients in the ongoing study, comprising more than 30,000 person-years of follow-up. In the period studied, 792 cases of AD occurred. Adjusted hazard ratios were computed for developing probable or possible AD for recent (within 5 years) and established (> 5 years) diagnoses.

The investigators noted that the relationship between these ophthalmic diseases and AD may provide important insights into shared pathologic pathways. ■

1. Lee CS, Larson EB, Gibbons LE, et al. Associations between recent and established ophthalmic conditions and risk of Alzheimer's disease [published online ahead of print August 2, 2018]. *Alzheimers Dement*.

# BRIEFS

## > RETINAL CELL REPLACEMENT THERAPY ANIMAL TESTING TO EXPAND

In studies to date, in vitro pretreatment of cells with 4 mg/mL of an anti-aging glycopeptide (AAGP, ProtoKinetix) retinal cell replacement therapy resulted in a substantial increase of cell survival over a 4-week period following transplantation into the subretinal area of immunocompromised rabbits with retinal degeneration. A new study will evaluate AAGP in two animal models over a longer period of time to test whether the AAGP-treated cells continue to develop into retinal cells to potentially restore vision in humans.

**bit.ly/Brief0918a**

## >> AAV-CNGB3 GRANTED FAST TRACK DESIGNATION FOR ACHROMATOPSIA

The FDA has granted fast track designation to MeiraGTx's AAV-CNGB3 gene therapy product candidate for treatment of achromatopsia caused by mutations in the *CNGB3* gene. AAV-CNGB3 is designed to be delivered to the cone receptors at the back of the eye via subretinal injection to restore cone function.

**bit.ly/Brief0918b**

## >>> JOSEPH GORDON NAMED US PRESIDENT OF BAUSCH + LOMB

Bausch + Lomb has named Joseph Gordon US president. In this role Mr. Gordon will report to chairman and CEO of Bausch Health, Joseph C. Papa, and will oversee the fully integrated US eye care business.

**bit.ly/Brief0918c**

## >>>> BASCOM PALMER RANKED NO. 1 FOR 17TH TIME

Bascom Palmer Eye Institute of the University of Miami Health System has been ranked No. 1 in ophthalmology in 2018-2019 by *US News & World Report* for the 15th year in a row and for the 17th time since the publication began surveying US physicians for its annual "Best Hospitals" rankings 29 years ago.

**bit.ly/Brief0918d**