Study treatments show promise for wet AMD

New approaches may ease burden of repeated eye injections

For two and a half years, David Hall has been making monthly trips from his home in Astoria, Ore. to Casey Eye Institute in Portland for treatment of his wet age-related macular degeneration. At first, the 83-year-old got regular injections in his right eye to stabilize his condition, the standard of care for patients with his form of the disease.

“Hearing that I had wet AMD was frightening,” said Hall, who said the diagnosis brought back memories of his sister-in-law’s own struggles losing sight to the disease.

But for the last two years, Hall has been able to avoid the shots and still maintain his vision. As a participant in the first study of an ocular implant for wet AMD, a steady dose of medication slowly released into his affected eye has stabilized his condition.

The implant study, which has shown positive results, is one of several inventive approaches being developed as a more long-lasting alternative to current treatments.

“Although treatments for wet AMD are very effective, the need for repeated injections to manage active disease — as often as monthly — can be burdensome, especially for older adults who have mobility problems or do not want to burden their family or friends for transportation,” said Andreas Lauer, M.D., a retina specialist and principal investigator of the study at Casey.

The surgically implanted port, slightly longer than a grain of rice, continuously emits ranizumab (Lucentis) into the eye’s vitreous. When needed, the implant’s

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A note from the director

In this issue, we report on two clinical trials that have potential to alter the treatment landscape for wet macular degeneration. Findings from both studies show that these approaches may last longer than the current treatment, which involves regular eye injections as often as every four weeks.

If you are one of the thousands of patients undergoing treatment for wet AMD, this news is heartening. These and other promising therapies for macular degeneration are the result of decades of painstaking medical research conducted at the Macular Degeneration Center and other institutions throughout the world.

Although the search for safe and effective cures takes time, there is much reason for optimism. A transformative gift from philanthropist John Wold and his family (also described in this issue) will enable us to expand our work and hasten the discovery of new treatments. We also are deeply grateful to the many donors and friends who so generously support our efforts in tackling this disease. Thank you for joining us on this exciting journey!

Early research points to link between AMD and gut

Findings from a pilot study at Casey Eye Institute suggest a possible connection between advanced age-related macular degeneration and alterations in the gut microbiome, the community of bacteria and other microscopic organisms that live in our intestinal tract. Phoebe Lin, M.D., Ph.D., a physician-scientist specializing in retinal and inflammatory eye disease, compared the microbiome of study patients with advanced AMD to healthy controls without the disease. She and her team found differences between the two groups, with AMD patients having increased amounts of several strains of intestinal bacteria and less of others than healthy participants.

The researchers also noted changes in the intestinal bacteria in study patients taking AREDS2 eye supplements and in those with a certain gene mutation associated with AMD. “These alterations in the intestinal tract may explain why individuals develop advanced AMD,” said Dr. Lin, explaining that it may affect "some of the biochemical pathways known to be involved in the disease, such as the immune system."

Dr. Lin said she plans to continue her investigations using newer methods of analysis and conducting more in-depth and longitudinal clinical studies. “While this early research is promising, more work is needed to learn how the gut microbiome and other factors may trigger this disease.”
reservoir is refilled in the clinic in a minimally-invasive, sterile procedure.

Called LADDER, the Phase 2 study compared the effects of three different concentrations of Lucentis in the implant to injections of the same drug. It also looked at the amount of time until a patient first needed a refill of the medication. Lucentis, one of the primary drugs used for wet AMD, blocks the growth of abnormal blood vessels. Vision can be damaged when these fragile blood vessels leak fluid and blood, eventually scarring tissue in the eye’s retina.

The study found that the majority of participants went six months or longer between the time the device was implanted and the first required refill, according to Genentech, the clinical trial’s sponsor. It also found that study patients given the highest dose of Lucentis had similar vision outcomes as those who received monthly eye injections.

Hall said his eyesight has remained stable since joining the study and he has yet to need a refill of the medication.

“This is the first therapeutic option for wet AMD in which patients aren’t required to get injections,” said Dr. Lauer. “By extending the time in between doctor visits, patients may find it easier to get the necessary treatments to maintain or improve their vision,” he said, adding that Genentech is planning a Phase 3 clinical trial of the implant. Participants must be able to make monthly study visits and meet other eligibility requirements.

Treatments with more staying power

While some medical researchers are focusing on designing sustained-release delivery systems like the implant, others have turned their attention to developing more long-lasting agents to treat wet AMD. In July, scientists announced positive results of a study of an investigative drug called abicipar pegol. The phase 3 clinical trial, called SEQUOIA, was conducted at Casey and other sites in the U.S. In SEQUOIA, patients newly diagnosed with wet AMD were randomly divided into three groups. Over two years, they received eye injections of the study medication in either eight or 12-week regimens while a third group received injections of ranizumab (Lucentis) every four weeks.

The study showed abicipar pegol to be similarly effective after six or eight injections compared to 13 injections of ranizumab in their first year. Allergan and Molecular Partners, the drug’s developers, plan to seek FDA approval of the study drug sometime next year.

“It’s exciting to know that safe and effective treatments are on the horizon that may lead to fewer visits to the eye doctor,” said retina specialist Christina Flaxel, M.D., principal investigator of the study at Casey and director of the Macular Degeneration Center.

Other medical breakthroughs are also in the pipeline to extend the treatment benefits of wet AMD, said Dr. Lauer. For example, scientists are investigating the use of nano technology, in which minute particles slowly release a macular degeneration drug as it gradually breaks down.

For now, study patients like David Hall are gratified they can contribute to scientific advances in macular degeneration research. The only drawback from his repeated visits, he joked, is that the eye charts are getting boring. “They’re not very attention-getting,” he said with a chuckle. “There’s no story line or plot.”
Meet our new providers

Merina Thomas, M.D., and Alan Labrum, O.D., are focused on providing top quality care for macular degeneration.

Merina Thomas, M.D., credits a medical outreach trip to southern India for sparking her interest in ophthalmology. “After seeing how eye problems can profoundly affect quality of life, I decided to pursue ophthalmology,” said Dr. Thomas, who completed her residency at the Illinois Eye and Ear Infirmary at the University of Illinois and a fellowship in vitreoretinal surgery at the University of Michigan’s Kellogg Eye Center.

Her decision to become a retina specialist was shaped early on in her medical training. Between her third and fourth year of medical school at Vanderbilt University, she conducted a year-long study evaluating a home monitoring device for patients at high risk of wet macular degeneration. Used daily, the device is designed to detect early signs of the disease before visual symptoms are noticed.

“I became interested in macular degeneration because it is so common yet has such a huge impact on the lives of patients and their families,” said Dr. Thomas, who conducted the NIH-supported project at the Wilmer Eye Institute at Johns Hopkins University. Now that the multi-year follow-up is completed, she expects to publish the investigation’s results in the coming months. While at Casey, she also hopes to build on her research by using optical coherence tomography angiography – a revolutionary imaging technology developed by OHSU scientists – in conjunction with home monitoring systems to detect disease as early as possible.

Dr. Thomas said it is Casey’s friendly, family atmosphere and reputation for patient-centered care that first attracted her here. “As a retina specialist at an academic medical center, I look forward to not only taking care of patients, but talking to them about medical advancements to fight this disease.”

Dr. Thomas practices at Casey Eye Institute’s offices in Portland, Vancouver and Longview.

For more information or to make an appointment, please call 503-494-7891.

Alan Labrum, O.D., says he was drawn to the field of vision rehabilitation because it suits his personality. “I like to sit down and talk to patients and build a relationship with them — and that’s especially important when caring for people who are dealing with visual disabilities.”

Dr. Labrum joins clinical director John Boyer, O.D., at OHSU Casey Eye Institute’s Vision Rehabilitation Center, where he provides full vision exams and designs personalized plans to help individuals manage their vision loss. Those plans may include demonstrating and prescribing visual aids and adaptive technologies, recommendations for better lighting and contrast, and teaching patients to do familiar tasks in new ways.

After earning his optometry degree from the Illinois College of Optometry, the Vancouver, B.C. native moved to northern British Columbia to practice primary optometry care. Finding that services for people with visual disabilities are limited — especially in rural areas — he returned to Chicago to complete a residency in vision rehabilitation and ocular disease from the Illinois College of Optometry and Chicago Lighthouse.
Two gifts totaling $7.5 million from the late philanthropist John S. Wold and his family will help establish a new macular degeneration center at OHSU Casey Eye Institute.

“The Wold family's generous investment will accelerate and build on Casey’s decades of research in macular degeneration. We are incredibly grateful for their support,” said David Wilson, M.D., director of the Casey Eye.

In June, the Wold Foundation of Wyoming made a gift of $2.5 million to combat macular degeneration, the leading cause of legal blindness in older Americans.

Combined with $5 million that John S. Wold donated in 2015, the Wold Foundation’s gift will build and support the Wold Family Macular Degeneration Center. The center will be part of the new building next to Casey’s existing facility.

The Wold Family Macular Degeneration Center will allow Casey to expand its pioneering work to better understand the disease and develop more effective treatments. The center will create a collaborative space with today’s most advanced medical technologies, bringing together experts in genomics, as well as gene and stem cell therapy. The center also will enhance patient care, offering state-of-the-art clinical and support services under one roof.

John S. Wold, who died in 2017 at age 100, was a businessman, geologist, inventor and former U.S. congressman. He suffered from age-related macular degeneration for the last 20 years of his life.

“Our father never stopped thinking about how he could contribute to making the world a better place,” said his daughter, Priscilla Wold Longfield. “Macular degeneration significantly impacted his life but didn’t dampen his spirit. If anything, his condition made him even more committed to fighting this insidious disease. We can think of no better way to honor his legacy than to support Casey's groundbreaking work in finding a cure for macular degeneration.”
Ongoing clinical trials for AMD at Casey Eye Institute

Metformin for dry macular degeneration
PURPOSE: To determine whether oral Metformin HCL (a diabetes medication) is an effective treatment for slowing the progression of geographic atrophy (late form of dry AMD) in patients with dry AMD. Qualified study patients will be enrolled in a randomized study that lasts 18 months and requires four study visits at Casey Eye Institute. Eligible participants must be 55 or older and have advanced dry AMD in one or both eyes. Candidates cannot have diabetes or currently be taking Metformin. Other eligibility criteria may also apply.

Injectable medication for wet AMD (OPT-302)
PURPOSE: To determine the effectiveness of two different doses of the biologic therapy OPT-302 given in combination with ranizumab (Lucentis) in participants with wet AMD. In a third arm of the study, patients will only receive ranizumab. OCT-302 blocks two different types of vascular endothelial growth factors, which cause blood vessels to grow and leak. Participants in this phase 2 study must have new wet AMD that has not been treated in the affected eye as well as meet other eligibility criteria.

Genetics of Age-Related Macular Degeneration Study
PURPOSE: To find genetic mechanisms associated with AMD, which will lead to more accurate early detection and precise treatments. Researchers are using advanced whole genome sequencing technology to find gene variations in large families and other populations affected by AMD.

For more information about these studies, please call the Macular Degeneration Center at 503-494-3537

Advanced imaging trials
PURPOSE: To test the capabilities of high-speed optical coherence tomography angiography (OCTA) in patients with dry or wet AMD. Investigators are studying whether this new imaging technology can visualize and measure blood vessel growth as well as fluorescein angiography, which involves the injection of a contrasting agent to highlight the problem vessels. The team is also comparing how retinal anatomy and blood flow differ among study patients in early, intermediate and advanced dry AMD.

Diet and vision study (Carotenoids in Age-Related Eye Disease Study 2)
PURPOSE: To learn whether the levels of pigment in the eye’s macula is a risk marker for the development of AMD and loss of retina function with age. The study is also evaluating whether macular pigment declines with age and if so, what factors play a role.

CAREDS 2 is an offshoot of the national Women’s Health Initiative (WHI) and is only open to participants in that study.
Studies with completed enrollment

**Association between advanced AMD and alterations in the gut microbiome**

**PURPOSE:** To learn whether gastrointestinal tract gut bacteria plays a role in the development of advanced AMD. Researchers will also explore the connection between an individual’s genes and the activity of the gut bacteria.

**Ocular implant for wet macular degeneration (LADDER Study)**

**PURPOSE:** To compare the effects of an ocular implant that releases different doses of ranibizumab (Lucentis) to injections of ranibizumab. This approach may decrease the need for frequent injections into the eye.

**Injectable medication for wet AMD (SEQUOIA Study)**

**PURPOSE:** To compare the safety and effectiveness of the study drug abicipar pegol to ranibizumab (Lucentis) in patients newly diagnosed wet AMD. This treatment may be more long lasting than some current therapies for wet AMD.

**Gene therapy for wet AMD (GEM Study)**

**PURPOSE:** To assess the safety and dosing levels of a gene-based treatment, RetinoStat, for wet AMD. In this Phase 1 study, two helpful genes are delivered directly to the retina, where they activate proteins that block abnormal blood vessel growth in a sustained fashion.

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**Ask an expert**

**Q.** I’ve been seeing a lot of articles in the news about stem cell therapy. Is that treatment now available for macular degeneration?

**A.** Stem cells are non-specialized cells that are converted to cells that have a specific function. Although considered a promising approach for restoring vision lost from macular degeneration, stem cell therapy is still in the early stages of research.

At Casey, scientists are focused on creating and transplanting retinal pigment epithelial (RPE) cells in the eye. RPE cells are highly specialized cells that keep the retina’s light-sensing photoreceptors healthy but may become irreversibly damaged by macular degeneration. The hope is that stem cells can be transformed into functioning RPE cells that can be implanted underneath the retina to slow or stop vision loss.

However, questions remain including: Will the transplanted RPE cells integrate and communicate with other cells of the retina as well as native RPE cells; will the immune system tolerate the transplanted RPE cells; and what is the best way to surgically deliver the cell-based therapy?

Unfortunately, there have been cases in which patients suffered severe permanent eye damage after undergoing certain types of stem cell treatment at private clinics. Before undergoing any type of stem cell therapy, make sure it has been approved by the FDA or is being studied in an FDA-approved clinical trial.

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