Summary of Research and Development -- 2016
ILVSG Presentation. June 2016
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I. INTRODUCTION

This is my 11th annual summary of leading research and developments that have occurred during the past 12 months in the field of blindness and low vision.

I'll take the liberty in several cases of quoting the sources, but for the sake of conversational flow, I'll break the rules of acceptable medical writing and not continually refer to the sources. Sources will, however, be listed with each appropriate topic for those who wish to pursue further information. Studies presented at the 2016 meeting of the Associaion for Research in Vision and Ophthalmology will be referred to as "ARVO".

This year's summary will offer brief descriptions of the work done in the categories of pharmaceutical interventions, anti-VEGF therapies for neovascularization in wet AMD and diabetic retinopathy, combination therapies, treatments for dry macular degeneration and retinitis pigmentosa, stem cell and gene therapy, bionic implants, surgical procedures, new technology, health and nutrition, daily living, and low vision devices.

II. PHARMACEUTICAL INTERVENTIONS

RXI-109 May Reduce Retinal Scarring

lowvision.preventblindness.org/research-and-developments/rxi-109-may-reduce-retinal-scarring/

One of the most serious causes of vision loss is development of scar tissue on, in, or under the retina. People can develop retinal scarring from severe myopia, ocular histoplasmosis syndrome, and wet age-related macular degeneration (AMD). Scarring results from inflammation, caused by irritation of the retina. Severe occurences can cause swelling of the retina, wrinkling of the surface tissue, or even retinal detachment.

Scarring cannot usually be safely removed. This means that, even if the underlying cause is successfully treated, vision remains obstructed or distorted. The presence of scarring can also prohibit qualification for clinical trials of future treatments like stem cell transplantation and genetic replacement.

The best approach to the problem, then, might be to prevent scarring in the first place. This is being studied by RXI Pharmaceuticals, a company in Marlborough, Massachusetts. On August 12, 2015, they announced the start of a Phase 1/2 trial in Ophthalmology to evaluate the safety and clinical activity of RXI-109, a compound that targets connective tissue growth factor (CTGF), a key regulator in scar formation.
The company has been researching RX-109 for use in the skin, and now they have received approval by the FDA to apply it to retinal scarring resulting from neovascularization in wet macular degeneration. By blocking the retina's natural response to inflammation, one of the most serious ramifications of the disease could someday be eliminated.

Iluvien Similar to Anti-VEGF Drugs as Treatment for Diabetic Retinopathy
lowvision.preventblindness.org/research-and-developments/iluvien-similar-to-anti-vegf-drugs-as-treatment-for-diabetic-retinopathy/

On February 16, Dr. Charles Wykoff announced to the American Academy of Ophthalmology annual meeting that Iluvian (fluocinolone acetonide) treatment, after 1.3 injections over 3 years in the FAME trials, "significantly reduced progression to prolific diabetic retinopathy from 31% to 17%, a similar reduction was observed with monthly anti-VEGF treatments."

Iluvian (Alimera Sciences) is a drug implant devised for treatment of diabetic macular edema (DME). It is a corticosteroid that has demonstrated effectiveness in the treatment of DME without the need for monthly injections. Tiny implants injected into the eye's vitreous gel release the steroids into the retina over a period of years, greatly relieving the burden of multiple clinic visits.

Due to the high risk of cataract development and glaucoma, extended-release steroid treatments are limited to adults without elevated

intraocular pressure and those who either have undergone, or are scheduled for, cataract surgery.

Iluvian is also being studied as a treatment for dry AMD, but concerns by the FDA about safety and manufacturing standards have slowed its progress toward clinical trials.

High Dose Statins May Be Effective In Treating Dry AMD
lowvision.preventblindness.org/research-and-developments/high-dose-statins-may-be-effective-in-treating-dry-amd/

Researchers at Massachusetts Eye and Ear/Harvard Medical School and the University of Crete have found that high doses of statins (cholesterol-lowering medications) can effectively reduce the number of soft drusen deposits in retinas of people with dry age-related macular degeneration (dAMD). The findings from their phase I/II clinical trial were published in the recent issue of EBioMedicine. Their hope is that this research will provide a foundation for an effective means of preventing progression to the advanced stages of a disease which currently has no effective treatment.

Drusen in the retina are similar to cholesterol deposits in the blood vessels, which has led scientists to look at cholesterol-lowering drugs for AMD patients. Previous studies, however, have not shown a significant effect of cholesterol medications on drusen. The possible answer, according to these researchers, is to increase the dosages beyond the normal amount.

Twenty-three patients with dry AMD marked by soft lipid deposits in the outer retina were prescribed a high dose (80mg) of atorvastatin, the generic name of the statin marketed as Lipitor® and several generic equivalents. Of the 23 patients, 10 experienced an elimination of the deposits under the retina and mild improvement in visual acuity.

As the next step for this line of research, the investigators plan to expand to a larger prospective multicenter trial to further investigate the efficacy of the treatment in a larger sample of patients with dry AMD.

III. ANTI-VEGF THERAPY FOR NEOVASCULAR CONDITIONS

One of the miracles of the 21st century has been treatment for central vision loss caused by uncontrolled blood vessel growth and leakage in the back of the retina. Called “neovascularization” this has been treated successfully since 2004 with chemicals that block the responsible growth factors. They are referred to as “anti-V-E-G-F”, or “anti-VEGF” drugs. Those most commonly used are Lucentis, Eylea, and off-label Avastin, all of which require periodic injections into the back of the eye. Comparisons of these anti-VEGF drugs continue to show no significant differences among them, and benefits of switching among them as necessary are still being realized. Most importantly, follow-up studies continue to show long-term effectiveness of anti-VEGF treatments.

AMD Since Anti-VEGF

CATT Research Group. Five-year outcomes with anti-vascular endothelial growth factor treatment for neovascular age-related macular degeneration: The Comparison of Age-Related Macular Degeneration Treatments Trials. Ophthalmology. May 2, 2016.
DOI: 10.1016/j.ophtha.2016.03.045

This National Eye Institute (NEI) study confirms that anti-VEGF treatments have greatly improved the prognosis for patients with the wet form of age-related macular degeneration (AMD) during the past decade.

In the study of nearly 650 people, half still had vision 20/40 or better, typically good enough to drive or to read standard print, after five years of treatment with anti-VEGF drugs that are injected into the eye. The authors of the study say those outcomes would have been unimaginable about 10 years ago, prior to the drugs’ availability. At that time, laser coagulation and photodynamic therapy were the only treatments for wet AMD.

Researchers looked at people with wet AMD who had regular treatment with drugs designed to block VEGF. After five years, 50 percent of them had 20/40 vision or better, 20 percent had 20/200 vision or worse, and the rest were in-between. In the U.S., state drivers’ licenses generally require 20/40 vision in at least one eye. A best-corrected vision of 20/200

in both eyes is considered legally blind for the purpose of federal disability benefits.

Maureen G. Maguire, Ph.D., the study's principal investigator, reported to ARVO that "Although anti-VEGF treatment has greatly improved the prognosis for patients overall, we still need to find ways to avoid poor vision in these patients and to decrease the burden of ongoing treatment".

Research is still moving forward to find cures for the dry form of AMD that can develop into wet AMD. For information about those potential treatments, see A Guide to Research in Dry AMD on the Living Well With Low Vision website at lowvision.preventblindness.org.

In vitro anti-VEGF agent safety profile: apoptosis in ARPE-19 cells treated with ranibizumab, bevacizumab, aflibercept and ziv-aflibercept

ARVO Posterboard #: B0235
Abstract Number: 5029 - B0235
Authors:Deepam Rusia, et al

The use of anti-VEGF (anti-vascular endothelial growth factor) therapy has dramatically altered the prognosis of eyes with wet AMD. However, chronic use of anti-VEGF medications may have an effect on progression of cell degeneration, known as geographic atrophy. The purpose of this study was to compare the effect of different concentrations of anti-VEGF drugs on death of cultured sight cells.

The medications studied were Lucentis, Avastin, Eylea, and ziv-aflibercept (essentially a low cost but unapproved anti-VEGF drug similar to Eylea). Only ziv-aflibercept demonstrated significant increase in cell death rates at standard clinical concentrations. At 2x standard concentration and higher, Eylea and Avastin produced higher cell death rates. Exposure to Lucentis caused no significant increase in cell death at any of the tested concentration levels.

A 2-year study comparing the efficacy and safety of brolucizumab vs aflibercept in subjects with neovascular age-related macular degeneration: testing an alternative treatment regimen
ARVO Posterboard #: B0224
Abstract Number: 5018 - B0224
Authors:Pravin U. Dugel, et al

Many wet AMD treatment options target a molecule called vascular endothelial growth factor (VEGF), which stimulates blood vessel growth and survival. One of the greatest unmet needs in the treatment of patients with neovascular AMD is reducing treatment burden, as current treatment options typically require repeated injections. Brolucizumab is a potential new anti-VEGF therapeutic option that is under clinical development for the treatment of patients with neovascular AMD. Brolucizumab is smaller than other available anti-VEGF neovascular AMD treatment options; the smaller size may allow delivery of a much higher dose, resulting in a potentially longer duration of effect and the potential for a reduced number of injections. This study showed a potential of brolucizumab for 12-week dosing, which could address a significant unmet need in the treatment of patients with wet AMD by reducing treatment burden.

OPT-302 Enters Phase 2A Trials for Wet AMD
lowvision.preventblindness.org/research-and-developments/opt-302-enters-phase-2a-trials-for-wet-amd/

Opthea Limited, a developer of novel biologic therapies for the treatment of eye diseases, has randomized and dosed the first patient in the Phase 2A dose expansion clinical trial of OPT-302 for wet AMD. OPT-302 is a soluble form of vascular endothelial growth factor receptor 3 (VEGFR-3) or ‘Trap’ molecule, that blocks the activity of two proteins called VEGF-C and VEGF-D that cause blood vessels to grow and leak.

The Phase 2A dose expansion study will enroll about 30 subjects with wet AMD. The subjects will be randomized in a 1:1 ratio to two treatment groups of OPT-302 given as monotherapy or in combination with Lucentis®. The drug will be administered by intravitreal injection on a monthly basis for 3 months. Primary analysis data from the Phase 2A study is anticipated by the end of 2016.

IV. SUSTAINED DRUG THERAPY FOR WET (NEOVASCULAR) CONDITIONS

Comparison of the regimens of "Treat and Extend" and "As Needed" Treatment With Anti-VEGF Drugs

An example of a "Treat and Extend" regimen is treatment intervals that are sequentially lengthened by two weeks, starting at four weeks, until signs of abnormal neovascularization recur.

An example of an "As Needed" regimen is monthly evaluation with retreatment in case of reoccurrence of retinal bleeding or fluid accumulation.

Several reports this past year have shown no significant differences in outcomes of comparisons between "Treat and Extend" and "As Needed" methods of treatment. This continues to be doctor's choice.

Future Sustained Drug Delivery Methods for Choroidal Neovascularization

At the annual meeting of the American Academy of Ophthalmology, Dr. Peter Kaiser described six alternative methods being looked at for delivery of anti-VEGF drugs.

One method is to put the drug into a biodegradable macromolecule, or polymer, that slowly releases the compound.

Another method is storing the drug in multilayer liposomes, which are tiny bubbles in the body that are made of the same material as a cell membrane. As the lipid layer breaks down, the drug is released.

A third method being studied is a micropump, which can slowly release drugs into the eye as often as every hour over a period of 4 to 9 months. It is attached unseen to the side exterior of the eyeball, and it delivers drugs to the interior of the eyeball through a tube permanently inserted through the white covering of the eye. The reservoir is filled in the clinic and can be programmed wirelessly. Similar to the micropump,

Genentech is conducting trials with Lucentis, wherein a refillable port-delivery system releases the drug slowly over 3 to 4 months.

Gene therapy may also be able to provide unlimited release of medications. A virus containing the gene for human pigment epithelium-derived factor (PEDF) has shown evidence of being able to stop disease progression when injected directly into the eyes of patients with wet AMD.

Another possible drug delivery method is by means of an implanted capsule that acts like a miniature factory for production and distribution of a drug. Called Encapsulated Cell Technology, Neurotech Pharmaceuticals has already enrolled the first patient in their Phase 2 clinical trial using the technology to deliver a protein called NT-503. The company plans to report top-line data from their Phase 2 program in the first half of 2017. More information about the trial may be found at: http://lowvision.preventblindness.org/research-and-developments/long-term-treatment-for-wet-amd-enters-phase-2-trials/

Finally, the blood vessel layer of the retina can itself act as a depot for medication. A microcatheter or microneedle can be used to inject drugs into the space above that layer.

To conclude this category, here are two other delivery methods that are receiving attention:

Extended Release of anti-VEGF Biologics from Biodegradable Hydrogel Implants for the Treatment of Age Related Macular Degeneration
ARVO Posterboard #: A0164
Abstract Number: 527 - A0164
Authors:Gary Owens, et al

The purpose of this study was to demonstrate the ability to produce extended release intravitreal implants for the release of genetically-engineered anti-VEGF proteins. These proteins are stored in biodegradable capsules. The study data succeeded in establishing proof of concept, potentially bypassing the need for monthly intravitreal injections.

Sustained Delivery of Ranibizumab: The LADDER Trial of the Ranibizumab Port Delivery System
ARVO Posterboard #: A0167
Abstract Number: 530 - A0167
Authors:J J. Hopkins, et al

The phase 2 LADDER trial is evaluating the Ranibizumab (Lucentis) Port Delivery System (RPDS) a refillable implant enabling sustained delivery of Lucentis in patients with wet AMD. The primary objective of the LADDER trial, now in Phase 2 trials, is to determine the time until a patient first requires their first implant refill. Sustained delivery of Lucentis in the RPDS has the potential to significantly reduce treatment burden by requiring less frequent dosing for patients with wet AMD. LADDER anticipates enrolling 220 patients at up to 55 US sites.

Delivery of drug molecules to treat visually impairing ocular diseases is currently the most challenging task to the pharmaceutical scientists and retinal specialists. As we have seen, a number of sustained drug delivery methods are being researched, and to add to the list, we are also seeing drug-loaded contact lenses, and even a polymeric wafer placed beneath the eyelid. Advances in delivery methods will continue to occur along with the development of new agents. Time will tell which of these will prove to be most effective, but the day of the needle may be soon passing.

V. ALTERNATIVE DELIVERY METHODS

No cure yet exists for wet AMD, but three FDA-approved therapies (Lucentis, Eylea, and off-label Avastin) are slowing the progress of the disease and reducing the amount of vision loss. These medications are highly successful, but they must be injected directly into the eye, and the treatment often needs to be repeated. In addition to sustained release methods to relieve this burden, oral medications and eye drops are also being studied.

X-82 Oral Medication May Reduce Number of Intravitreal Injections for Wet AMD
lowvision.preventblindness.org/research-and-developments/x-82-oral-medication-may-reduce-number-of-intravitreal-injections-for-wet-amd/

An oral medication under study is X-82. This drug in tablet form has been administered to 35 patients and evaluated for preliminary safety and efficacy. All patients either maintained or improved vision with few or no intravitreal injections needed. Phase 2 trials are now being conducted at 22 clinical sites in the U.S. and 5 sites in the U.K.

Eye Drops for Wet AMD Enter Phase 3 Trials
lowvision.preventblindness.org/research-and-developments/positive-interim-results-from-phase-ii-study-of-eye-drops-for-wet-amd/

Ohr Pharmaceutical announced in April that the first patient had been enrolled in a Phase III clinical trial of the company's lead drug candidate "Squalamine", also known as OHR-102, for the treatment of wet AMD.

The study is examining the potential of Squalamine, when administered as part of a combination therapy, to significantly improve visual acuity in patients. The first of two randomized, double-masked, placebo-controlled trials will include approximately 165 centers in the United States and Canada with a target enrollment of 650 treatment subjects newly diagnosed with wet AMD.

VI. COMBINATION THERAPIES FOR NEOVASCULARIZATION

Triple Therapy with Zeaxanthin Lessens Burden of Treatment for Wet AMD
journalretinavitreous.biomedcentral.com/articles/10.1186/s40942-015-0019-2

Combining anti-VEGF injections with other therapies can also help to relieve the treatment burden by stretching the time between treatments.

As far back as 2007, triple therapy for wet AMD has been shown to be superior to injection of a single anti-VEGF drug. And now, this study has

found that triple therapy supplemented with oral zeaxanthin is even better.

Scientists found that a combination Avastin, photodynamic therapy with verteporfin, intravitreal corticosteroids, and ingestion of 20 mg of the carotenoid, zeaxanthin, had potentially groundbreaking results. Of particular note was the finding that the addition of oral zeaxanthin decreased the number of injections by 5-fold, decreased the costs by 5-fold, and decreased the incidence of neovascular AMD in the second eye over two years from 36% to 7%.

Two- year results of a randomized prospective sham-controlled study comparing proton beam irradiation combined with ranibizumab with ranibizumab monotherapy for exudative age-related macular degeneration.
ARVO Posterboard #: A0332
Abstract Number: 4427 - A0332
Authors:Senad Osmanovic, et al

These findings indicated that the addition of proton beam therapy, a specific type of targeted low dose radiation treatment, may complement current standard of care therapy to combat wet AMD. Interim analysis at 2-years show no significant safety concerns combining proton beam irradiation with anti-VEGF therapy. And the study showed that there was less need for re-injection. Complete 2 year follow-up data will be presented to determine whether these interim findings are sustained.

New Combination Therapy Treats Retinal Damage in Diabetics
lowvision.preventblindness.org/research-and-developments/new-combination-therapy-treats-retinal-damage-in-diabetics/

Diabetic retinopathy is a rapidly growing global epidemic, occurring in approximately one-third of all diabetic patients. And In greater than 50% of patients, the disease poses a threat to both eyes. In February of this year, Aerpio Therapeutics announced promising results from their study of AKB-9778 as a treatment for diabetic retinopathy. The drug alone improved underlying retinopathy by 10.0% and in combination with Lucentis, it improved the condition by 11.4% compared to 8.8% of patients receiving Lucentis alone.

Similarity of Anti-VEGF Drugs Confirmed For DME Treatment
Wells JA et al. for the Diabetic Retinopathy Clinical Research Network. "Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema: Two-year Results from a Comparative Effectiveness Randomized Clinical Trial." Ophthalmology, February 27, 2016.

In other diabetes news from early 2016, this rigorous clinical trial found that individuals with diabetic macular edema, whose visual acuity is 20/50 or worse, gained more improvement with Eylea than with Avastin. Aside from that, no significant difference was found among the three anti-VEGF drugs (including Lucentis) in subjects with 20/32 or 20/40 vision at the start of treatment. NEI Director Dr. Paul Sieving commented that "This . . . confirms that Eylea, Avastin, and Lucentis are all effective treatments for diabetic macular edema," and that "Eye care providers and patients can have confidence in all three drugs."

Dr. John A. Wells, lead author of the study, said the results showed "little advantage of choosing Eylea or Lucentis over Avastin when a patient's loss of visual acuity from macular edema is mild."

VII. DRY AMD

Delayed Dark Adaptation Predicts Onset of Dry AMD
Delayed Rod-Mediated Dark Adaptation Is a Functional Biomarker for Incident Early Age-Related Macular Degeneration Cynthia Owsley, et al (Ophthalmology online, October 29, 2015, Manuscript no. 2015-1327)

This study from the University of Alabama has found that measurement of the time it takes older adults' eyes to adapt to the dark can predict onset of dry AMD.

Using a computerized dark adaptometer, 325 persons with healthy eyes were each subjected to a flash of light in one eye, and their dark adaptation (DA) time was measured. At baseline, 263 of them had normal DA, meaning that their eyes recovered in under 12.3 minutes. 62 of them had "abnormal DA" with times exceeding 12.3 minutes. Three years later, those with abnormal DA were about 2 times more likely to have developed dry AMD in the tested eye.

These results offer another biomarker for identifying future onset of AMD.

New Drug Under Study for Dry MD
lowvision.preventblindness.org/research-and-developments/new-drug-under-study-for-dry-md/

In January, Ophthotech Corporation announced that the first patient had been dosed in a Phase 2/3 clinical study of Zimura for treatment of advanced dry AMD. Zimura inhibits complement factor C5, believed to be involved in the development of AMD. The Company has also recently initiated a Phase 2 study of Zimura in combination with anti-VEGF therapy for wet AMD patients.

VIII. Minocycline May Slow Damage from Retinitis Pigmentosa
lowvision.preventblindness.org/research-and-developments/trash-collecting-cells-may-accelerate-retinitis-pigmentosa/

Cells called microglia inside the brain, spinal cord and eye, hunt for invaders, capturing and then devouring them. They often play a beneficial role by helping to clear trash and protect the central nervous system against infection. But a new study by researchers at the National Eye Institute shows that they also accelerate damage wrought by blinding eye disorders like retinitis pigmentosa, a disease that destroys peripheral vision.

Researchers studied mice with a mutation in a gene that can also cause RP in people. The researchers observed in these mice that very early in the disease process, the microglia infiltrate a layer of the retina near the photoreceptor sight cells, where they don't usually venture. The microglia then surround a single photoreceptor and ingest it. This is a normal process in healthy tissue, but due to the gene mutation, it is out of control in eyes with retinitis pigmentosa.

A clinical trial is already underway to see if the anti-inflammatory drug minocycline can block the activation of microglia and help slow the progression of RP. Minocycline has been seen in cell culture to also

protect retinal cells from oxidative damage. This finding suggests that minocycline may also play a therapeutic role in the treatment of AMD.

IX. STEM CELL THERAPY

Phase I/II clinical trial of human embryonic stem cell (hESC)-derived retinal pigmented epithelium (RPE) transplantation in Stargardt disease (STGD): One-year results
www.hcplive.com/conference-coverage/arvo-2016/milestone-in-stem-cell-transplant-therapy-for-advanced-age-related-macular-degeneration/P-1#sthash.wX27C1Ed.dpuf

Stargardt disease is the most prevalent juvenile-onset inherited disease of the macula. Defects in the gene ABCA4 lead to accumulation of toxic vitamin A derivatives in the retina, leading to cell degeneration. Science is showing that retinal function may be protected or promoted by replacing those damaged cells with human embryonic stem cells. This research team found that subretinal transplantation of such stem cells appeared safe and well tolerated for up to 12 months in subjects with advanced Stargardt disease. This supports the prospect of further studies to investigate the potential for benefit in less advanced disease.

Stem cell therapy is also being looked at as a potential treatment for dry AMD. A team of researchers at the Karolinska Institute in Stockholm, Sweden, reported the first evidence in a large-eye animal model of geographic atrophy that, once human embryonic stem cells are transplanted, they can integrate within the recipient eye and engage in important functions that support sight cells. They found that the transplanted support cells could continue to rescue sight cells for as long as 8 months. Even though the inner retinas of the animal models were irreversibly damaged, the injected cells preserved the outer retina from damage. And the cells' ability to integrate in patches that can cover a large area makes this approach "very powerful," offering the hope that stem cells could be used as a "safe, efficient, and minimally invasive approach to treat patients suffering from advanced dry AMD."

Ocata's Stem Cell Trials Entering Phase 2

http://lowvision.preventblindness.org/research-and-developments/ocatas-stem-cell-trials-entering-phase-2/

On another front, Ocata Therapeutics, Inc. (formerly Advanced Cell Technology) announced in 2015 that the first patient had been enrolled in the company's Phase 2 clinical trial using Ocata's proprietary stem cells in patients with dry AMD. The purpose of the trial was to evaluate safety and explore efficacy as compared to a parallel control group. Results were expected early in 2016, but reorganization of the company has delayed the trials. They look forward to concluding this phase of development and expect that the data produced by this study will provide valuable guidance for the design of a Phase 3 program.

An Important Caveat About Ophthalmic Stem Cells

In all of the excitement about the possibility of stem cells someday restoring vision, it is important to remember that current research is focusing mainly on replacement of the pigment epithelial layer of the retina (the RPE), which lies directly below, and provides nutritional support for, the sight (photoreceptor) cells. Replacing the support cells will help only those sight cells that are still functional. If they are no longer able to function, stem cell transplantation will be ineffective. This means that, at this time, people who have reached the advanced stage of macular disease will not benefit from the procedure until further work is done to also replace the sight cells. It will be important, therefore, for people to be diagnosed as early as possible so that they might benefit from stem cell transplantation before the damage is done.

X. GENE THERAPY

Experimental Gene Therapies Still Raising Hopes

Effect of Gene Therapy on Visual Function in Leber's Congenital Amaurosis (James W.B. Bainbridge, Ph.D., et al, 10.1056/NEJMoa0802268, April 27, 2008)

Wills Eye Hospital has announced that it has treated the first RESCUE trial patient in the United States enrolled in an FDA-approved gene therapy

vision research study. A product called GS010 (GenSight Biologics), can be injected right into the eye and, in a sense, “re-wire” or lower the patient’s risk for getting the disease. The patient has Leber’s Hereditary Optic Neuropathy (LHON), a rare, genetic eye disease, passed on by the mother and affecting 35,000 patients worldwide.

Patients with vision related disorders are considered ideal candidates for gene therapy, because the product can be injected directly into the eye. The first experimental treatment for LHON, also known as Leber’s congenital amaurosis (LCA), was injection of the rpe65 gene in 2008. The procedure showed some success by researchers from the University of Pennsylvania School of Medicine and University College London. In that study, one patient improved from an acuity of 20/2000 to 20/710. Three others showed no acuity improvement, but did improve in other areas of visual function.

If successful, research such as this will open doors for future patients with other eye diseases for which no cures presently exist.

Inactivation of VEGFR2 using CRISPR/Cas9 provides superior inhibition to the anti-VEGF drugs
ARVO Posterboard #: B0230
Abstract Number: 5024 - B0230
Authors:Xionggao Huang, et al

Earlier, we discussed the importance of using combination therapies and extended release methods to extend the time between injections of anti-VEGF drugs for wet AMD and similar conditions. Gene editing may be another way to do that. A gene editing procedure, called CRISPR for short, allows scientists to actually cut out damaged parts of our DNA and replace them with healthy sections from another gene. And now a system called CRISPR/Cas9 (again, for short) has been demonstrated to be a simple and efficient tool for genome editing and protein depletion in cultured human cells and mice. The goal of this project was to explore a novel approach for silencing the VEGF pathway. And the method was shown to be superior to the anti-VEGF drugs Lucentis and Eylea for suppressing the signaling pathway. This provides a novel opportunity to use gene therapy to inhibit unwanted blood vessel development in the retina.

AVA-101 May Extend Time Between Wet AMD Treatments

In 2014, Avalanche Biotechnologies postulated that a single injection of a new gene therapy treatment, called rAAV.sFLT-1, could possibly stop blood vessel growth and leakage in wet AMD for several years. A single injection of a drug could create a kind of biofactory that continuously secretes a therapeutic protein over an extended period. This would avoid the need for frequent injections, as is now the practice, and the therapeutic effect was hoped to last from18 months to as long as several years.

Since that time, trials through phase IIa have demonstrated that rAAV.sFLT-1 has been safe and well tolerated for a period of three years. The drug has been used in combination with Lucentis injections as needed. Using gene therapy in this way is different than usual, in that, rather than targeting a specific genetic disease, it is being used to treat the more complex wet form of AMD.

XI. BIONIC IMPLANTS

Alongside research to find ways of restoring vision through stem cell therapy and gene therapy, attempts are also being made to restore vision electronically by means of bionic implants. In past reports, we have described the ARGUS-2, which has shown success in providing a basic pixelated sense of sight to the totally blind.

Now, Pixium Vision has presented information about their newest bionic device called PRIMA. Along with the expected approval of their IRIS®II system over the summer for patients affected by Retinitis Pigmentosa, PRIMA aims at providing a less invasive and higher performance system suitable for AMD patients. PRIMA is a tiny wireless sub-retinal implant that can provide prosthetic vision at video rate, thereby suggesting advanced performance in humans. The Vision Institute in Paris confirmed these modeling results on an animal model, showing light response to electrical subretinal stimulation. With these results, PRIMA is advancing toward clinical trials in patients with macular degeneration. Pixium Vision is refining the less invasive subretinal surgical technique ahead of the first human implant by the end of 2016.

Resources:

Implications of low prosthetic contrast sensitivity for delivery of visual information (Poster board #: D0184; Abstract Number: 3723 - D0184)
Spatio-temporal characteristics of retinal responses to subretinal photovoltaic stimulation (Poster board #: D0182; Abstract Number: 3721 - D0182)
Retinal safety of near infrared radiation in photovoltaic restoration of sight (Poster board #: D0187; Abstract Number: 3726 - D0187)
Ex-vivo characterization of photovoltaic subretinal implants using non-human primate retinas (Poster board #: B0076; Abstract Number: 603 – B0076)
Photovoltaic restoration of sight in rodents with retinal degeneration (Daniel Palanker, Podos Colloquium (Alcon Research Institute meeting at ARVO)

XII. SURGICAL PROCEDURES

A novel biosynthetic RPE-BrM (Retinal Pigment Epithelium-Bruch's Membrane) assembly suitable for retinal transplantation therapy
Abstract Number: 3767
Authors: Andrew J. Lotery, et al

Since some clinical trial data suggests that anti-VEGF injections for wet AMD may accelerate geographic atrophy, researchers are looking for ways to repair and/or replace the damaged tissue. One group has shown that a fully-functional synthetic assembly of the underlying retinal membrane, called Bruch’s membrane, can be made that is suitable for transplantation. It is essentially a scaffold on which transplanted cells could readily attach and proliferate.This approach has the potential to bring rapid long-lasting benefits to patients with retinal diseases such as AMD or Retinitis Pigmentosa, and could also be adapted for other regenerative treatments.

Studies of Structure and Function in Whole Eye Transplantation
Abstract Number: 3770
Authors:Kia M. Washington, et al

Transplantation of a whole human eye is still well into the future, but science is making strides toward that goal. This study evaluated the structure and function of a whole eye transplant animal model. The experiment succeeded in maintenance of vitreous gel dynamics, intraocular pressure, and integrity of the blood-ocular barriers of the transplanted eye. There was lack of electrical response to light stimuli in the transplanted eye, but the progress achieved so far is promising.

XIII. NEW TECHNOLOGY

New Device Helps Blind People See With Their Tongues
lowvision.preventblindness.org/latest-news/new-device-helps-blind-people-see-with-their-tongues/

The Food and Drug Administration has announced marketing approval of a new device that can help orient people who are blind by helping them process visual images with their tongues.

The BrainPort V100 is a battery-powered device that includes a video camera mounted on a pair of glasses and a small, flat intra-oral device containing a series of electrodes that the user holds against their tongue. Software converts the image captured by the video camera in to electrical signals that are then sent to the intra-oral device and perceived as vibrations or tingling on the user's tongue. With training and experience, the user learns to interpret the signals to determine the location, position, size, and shape of objects, and to determine if objects are moving or stationary.

Studies showed that 69 percent of the 74 subjects who completed one year of training with the device were successful at the object recognition test. Some patients reported burning, stinging or metallic taste associated with the intra-oral device. There were no serious device-related adverse events.

The device is intended to augment, rather than replace, other assistive technologies such as a white cane or dog guide.

LowViz Guide Completes Successful Pilot Program
lowvision.preventblindness.org/latest-news/lowviz-guide-completes-successful-pilot-program/

LowViz Guide, an indoor navigation app for the visually impaired, was tested last summer by MD Support at six national and state conventions around the U.S. The purpose of the ambitious pilot project was to test the operation of, and public response to, the organization's new wayfinding technology.

With an iPhone or iPad, a visually impaired user can call up audible navigation information delivered via VoiceOver and/or a routing tone. The application is similar to portable Geographic Positioning Systems (GPS) already in wide use for outdoor wayfinding. But new technology is now making it possible for a union of smart phones and Bluetooth beacons to serve that same purpose indoors, where satellites are unable to reach.

A team from MD Support mapped, set up portable beacon systems, and provided individual support at no cost to the participating organizations. The app received 1,330 views on the App Store and was downloaded a total of 678 times. Virtually all feedback has been enthusiastic.

MD Support is providing LowViz Guide at 12 conventions in 2016, at no cost to the host organizations, thanks to generous grants from MD Foundation and Genentech.

XIV. HEALTH & NUTRITION

Smoking and AMD—Are E-Cigarettes the Answer?
E-cigarettes: an evidence update — A report commissioned by Public Health England. McNeill A, et al. (UK Centre for Tobacco & Alcohol Studies at Institute of Psychiatry, Psychology & Neuroscience, National Addiction Centre, King's College London, and Wolfson Institute of

Preventive Medicine, Barts and The London School of Medicine and Dentistry Queen Mary, University of London.) Published August 2015.

You've heard it before: "Tobacco Smoking Is A Major Cause Of Age Related Macular Degeneration". But what if smokers enjoy their habit so much (or are so addicted that it is too difficult to quit) that they are willing to accept the risks, even if it means hastening vision loss and shortening life? Researchers are finding that such self-destruction may not be imminent after all. Public Health England has undergone an extensive study suggesting that smokers might safely continue satisfying their habit and their need for nicotine by substituting electronic cigarettes for tobacco. Further, a recent Cochrane Review found no significant adverse effects associated with EC use for up to 1.5 years. And electronic cigarettes have been found to be around 95% safer than tobacco cigarettes.

Vaping (they call it) may not be 100% safe, but most of the chemicals causing smoking-related disease are absent, and the chemicals that are present pose limited danger. The authors of the Public Health England report suggest that smokers who switch to electronic cigarettes will significantly reduce their risk of smoking related disease and death. This includes development of age-related macular degeneration. Those who will not or cannot break the habit may find comfort in knowing that there is a seemingly safe alternative.

XV. DAILY LIVING

Prevalence of Visual Hallucinations in a National Low Vision Client Population

Canadian National Institute for the Blind. Keith D. Gordon, PhD (Canadian Journal of Ophthalmology, February 2016, Volume 51, Issue 1, Pages 3–6)

This study has found that one in five Canadians with vision loss who were surveyed experience visual hallucinations known as Charles Bonnet Syndrome (CBS).

Most frequently, according to the data collected, people will see patterns

or simple shapes, however there are many accounts of more complex hallucinations.

The study also showed that:

• There was no higher probability of hallucinations between any of the three major eye diseases (age-related macular degeneration, diabetic retinopathy and glaucoma)

• Respondents who experienced greater levels of vision loss had higher chances of experiencing hallucinations

• Although vision loss occurs more frequently in older people, the risk of developing CBS does not increase as people age.

XVI. LOW VISION DEVICES

Effectiveness and cost-effectiveness of portable electronic vision enhancement systems (p-EVES) compared to optical magnifiers for near vision activities in visual impairment
ARVO Abstract Number: 4337
Authors:Chris Dickinson, et al

These researchers investigated how well individuals with visual impairment performed their everyday activities, and particularly how well they were able to read, using portable electronic magnifiers compared to optical magnifiers. Data was gathered from 82 volunteers, yielding some interesting findings.

- Electronic magnifiers allowed users to read much smaller print comfortably, but they could not read faster than with optical magnifiers.

- The electronic magnifiers were not used as frequently as the optical magnifiers, or for so many tasks. Users reported that for very short reading tasks (such as checking a price label), they preferred the quick and easy use of their optical magnifier. However, with

electronic magnifiers, users reported fewer tasks that they could not do, or that they needed help with.

- The electronic magnifiers allowed users to see more letters of text on screen, and sit in a more comfortable position to read, so it could be used for longer.

- Overall, users reported much less difficulty in performing near tasks using electronic magnifiers.

The researchers noted that electronic magnifiers are more expensive than optical magnifiers, so even with these improvements in performance they are not currently cost-effective. However, it is likely that manufacturers would be able to reduce the costs for a small number of basic models, especially if these were to be supplied in large numbers.

The evidence will be presented to the National Health Service in the U.K. in hopes of initiating a small-scale trial to make electronic magnifiers available in the same way as optical magnifiers.

Hundreds of low vision devices are now available to visually-impaired and blind individuals. Becoming more easily accessible are Braille readers, computer aids, computer speech programs, daily living aids, enhanced lighting, speciality glasses, talking appliances, canes, smart phone applications, magnifiers, electronic readers, global positioning systems, indoor wayfinding applications, and personal digital assistants. Choices are numerous, and prices are gradually coming down as more competitors enter the accessibility market.

Devices can be found, but obtaining the right ones presents two difficulties: 1) How to choose which are most appropriate, and 2) how to pay for those that use high end technology. A good low vision specialist can assist in making the right choices, and for those who qualify, government assistance needs to come to the rescue.

An effort similar to that in the U.K. is underway in the U.S. HR Bill 729 intends to provide data that would assist Congress in making changes to the current Medicare program, which currently does not pay for magnifiers needed by low vision patients. The legislation would make

$12.5 million available for the project over five years, and It would allow reimbursement for certain low-vision devices that are the most function-rich, most powerful, and most expensive.

XVII. CONCLUSION

I usually conclude my annual summaries with a word about the future, but I think we're already there. Science and technology are moving at an amazing pace, even though it may not feel that way to some of us who are waiting for cures and treatments. But when we consider where we were 10 years ago, and how much more we have now, and how close science is getting to curing what ails us, well, it's like riding a fast moving train. We feel like we're sitting still, but we're suddenly at the next station 20 miles down the track.

My hope for you is that our train will will soon reach the station you're looking for. Meanwhile, let's continue to take comfort in one another's company during the ride.