RRC RETINA RESEARCH CENTER

NEWS

Fall 2019

Innovations in Geographic Atrophy

Geographic atrophy (GA) is considered the late stage of the dry form of age-related macular degeneration (AMD). GA is less common than neovascular AMD and affects more than 10 million people world wide. Currently there is no approved or effective treatment to prevent either the onset or progression of GA, however, in recent years, there has been progress in understanding the origin and development of this disease, leading to new potential therapies currently undergoing clinical trial evaluation. Retina Research Center is participating in several pivotal trials focusing on new therapeutic targets in geographic atrophy.

NGMBio

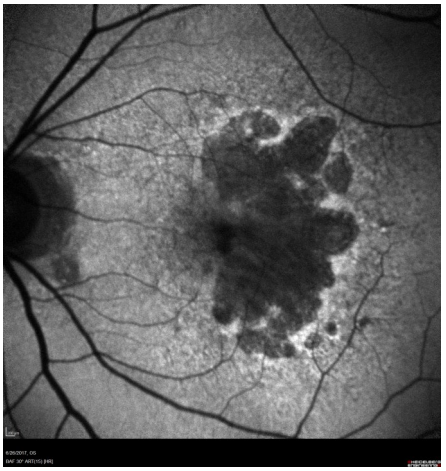
This Phase 1, open label, study aims to investigate humanized monoclonal high affinity antibodies that provide potent inhibition against component 3 (C3.) It will evaluate the safety, tolerability and pharmacokinetics of single intra-vitreal injections of the investigational product in adult patients with GA secondary to AMD.

IONIS

The ISIS 696844-CS5 phase II, 2.5 year long trial, sponsored by **IONIS** Pharmaceuticals is evaluating subcutaneous injections of investigational IONIS-FB-Lrx an antisense inhibitor of complement Factor B (a protein required for initiating the complement system originating in the liver.) By introducing IONIS-FB-Lrx systemically they aim to halt complement activation in the eye that is believed to be the underlying cause of geographic atrophy. Complement inhibition is thought to slow progression of macular degeneration.

Genentech
A Member of the Roche Group

This phase II study will evaluate the safety, tolerability, and efficacy of intravitreal injections of RO7171009. The drug is a monoclonal antibody against a protein, high temperature requirement A1, which has been associated with macular degeneration.



Stealth BIOTHERAPEUTICS

Stealth Biotherapeutic's lead investigational product, elamipretide, is a peptide being evaluated for the potential to increase mitochondrial cell respiration by binding reversibly to cardiolipin in this phase 2 trial. The elamipretide-cardiolipin relationship has been shown to normalize the structure of the inner mitochondrial membrane, thereby improving mitochondrial function. Improved function is shown to have the potential to reverse damaging oxidative stress in a phase one study. The drug is self administered. with a special applicator.

DERBY

The Apellis Derby phase 3 trial evaluating APL-2vs. sham aims to inhibit complement C3 (a portion of the bodies natural immune system.) Through this broad inhibition of C3, APL-2 reduces inflammation which has been associated with progression of macula degeneration. The drug is administered monthly through an intraocular injection.

All trials are open and enrolling, for more information contact Ivana Gunderson at igunderson@e-retina.net

STUDY RESULTS

AERPIO Time-2b Trial

The TIME-2b trial was designed to evaluate the effect of investigative AKB-9778 in patients with moderate-to-severe non-proliferative diabetic retinapathy. The primary endpoint was the percentage of patients who improved by at least two points on the diabetic retinapathy severity scale. Unfortunately, the study did not meet this primary endpoint, showing little difference between investigational medication and placebo. Stephen Hoffman, M.D., Ph.D., Chief Executive Officer of Aerpio.said, "We and our clinical advisors believe that collectively these data support a potentially important role of the Tie2 pathway for the treatment of diabetic complications, as well as for open angle glaucoma. After a full analysis of the study data, we plan to provide an update on the status of the NPDR program. We would like to thank the patients and investigators that participated in this trial."

DRCR Protocol V

Protocol V addressed the unanswered question of whether anti-VEGF injections are the best strategy in the clinical scenario of center-involved DME with good vision. The clinical trial concluded that patients with center-involved diabetic macular edema and good vision can confidently be managed by observation, scheduling anti-VEGF injections only if vision deteriorates. Retina Research Center would like to thank patients who participated in this pivotal trial.

NEW COLLABORATIONS

Stealth Pharma

- An innovative biopharmaceutical company developing therapies to treat the mitochondrial dysfunction associated with genetic mitochondrial diseases and many common age-related diseases.
- Founded 10/22/07, their offices are located in Newton, MD.
- 4 Indications in Phase 2 and 3 Trials evaluating the lead investigational drug, elamipretide.
- 1 drug SBT-272 in the pipeline with designated Orphan drug status to treat rare neurodegenerative disease.
- Working with RRC on Phase 2 study examining elamipretide in geographic atrophy secondary to age related macular degeneration.

Healthy and Unhealthy Mitochondria

KODIAK

- Founded in 2008 by Stephen A. Charles, PH.D and Victor Pearlroth, M.D. they maintain their headquarters in New York, NY.
- Kodiak Sciences is a clinical stage company developing innovative therapeutics to treat high prevalence ophthalmic diseases.
- Data from the ongoing KSI-301 1B clinical study, that Retina Research Center is participating in, will be presented at the American Society of Retina Specialists (ASRS) 2019 Annual Meeting in Chicago.

NGM Pharmaceuticals

- In February of 2015 NGM and Merck began a collaboration. In addition to the original investment, Merck committed an additional $250 million to research and development over a 5 year period. In March 2019 Merck officially extended support until 2022.
- NGM Bio was incorporated in December 2007 and commenced operations in 2008. They maintain headquarters in San Francisco, CA.
- Since their founding in 2008, they have uncovered novel biological insights underlying several therapeutic areas including cardio-metabolic, liver, oncologic and ophthalmic diseases.
- Retina Research Center is excited to be participating in the NGM Phase 1 Trial evaluating a new formulary in the treatment of Geographic Atrophy secondary to Age Related Macular Degeneration.

NOVO NORDISK

- Novo Nordisk A/S is a Danish multinational pharmaceutical company headquartered in Bagsværd, Denmark, with production facilities in eight countries, and affiliates or offices in 75 countries.
- Novo Nordisk began with two small Danish companies Nordisk Insulin Laboratorium and Novo Terapeutisk Laboratorium founded in 1923 and 1925, respectively. The two companies made their start by producing the revolutionary new drug insulin that had just been discovered by two Canadian scientists.
- Developing new innovations for diabetes has been a primary focus of Novo Nordisk spanning more than 90 years.

Enrolling Trials at Retina Research Center

Wet Age-Related Macular Degeneration

Roche Bluetail; A Phase I study investigating safety of RO7200394 in patients with neovascular AMD

Genentech GR40844 Lucerne: A Phase III study assessing efficacy and safety of faricimab compared to Eylea in patients with neovascular AMD

Novartis Merlin: A Phase III study to assess safety and efficacy of brolucizumab 6mg q4 weeks compared to aflibercept 2mg q4 weeks in patients with neovascular AMD

Kodiak KSI-CL-102: A Phase II study evaluating efficacy and safety of repeated intravitreal administration of KSI-301 compared to Eylea in patients with treatment naïve neovascular AMD

Graybug GBV-102-002 Altissimo: A Phase IIb study assessing efficacy and safety of long-acting sunitinib malate depot formulation (GB-102) compared to Eylea in patients with neovascular AMD - coming soon

Non-proliferative Diabetic Retinopathy

Boehringer-Ingelheim Protocol 1386.12 ROBIN - A Phase IIa study evaluating safety and efficacy of oral BI 1467335 in patients with moderate to severe diabetic retinopathy

Diabetic Macular Edema

Roche BP40899 Dovetail: A Phase I, open-label, single and multiple dose ascending study investigating safety and tolerability of RO7200220 as monotherapy and combination therapy with ranibizumab in patients with diabetic macular edema

Novartis LKA651x2202: A Phase 2 multiple dose study of intravitreal LKA651 in patients with diabetic macular edema

DRCR AC: A randomized trial comparing intravitreal Eylea versus intravitreal Avastin and deferred Eylea for treatment of center-involved DME

DRCR AE: A Pilot Study Evaluating Photobiomodulation Therapy for Diabetic Macular Edema (protocol AE)

Novartis Kingfisher: A Phase III study assessing efficacy and safety of brolucizumab q4weeks compared to Eylea q4weeks in patients with diabetic macular edema.

Genentech GR40550 Pagoda: A Phase III study evaluating efficacy and safety of a port delivery system with ranibizumab compared to intravitreal injections of ranibizumab in patients with diabetic macular edema - coming soon

Macular Telangiectasia

Mactel NHOR: A natural history observation and registry study of Macular Telangiectasia Type II

Neurotech NTMT-03-B Renexus: A Phase 3 Multicenter, Randomized, Sham-Controlled Study to Determine the Safety and Efficacy of Renexus in Macular Telangiectasia Type 2

Dry AMD - Geographic Atrophy

Genentech GR40973 Gallegos: A Phase II, sham-controlled study, assessing safety and efficacy of intravitreal injections of FHTR2163 in patients with geography atrophy

Ionis 696844-CS5: A Phase II , sham controlled study, evaluating safety and efficacy of multiple doses of IONIS-FB-L_{RX} administered subcutaneously in patients with geography atrophy

Stealth SPIAM: A Phase 2 study evaluating safety and efficacy of subcutaneous injections of Elamipretide in patients with geographic atrophy

Apellis Derby: A Phase III study evaluating efficacy and safety of intravitreal injections of APL-2 compared to sham in patients with geographic atrophy

NGM Biopharmaceuticals NGM621: A Phase I, open-label, single and multiple-dose ascending study evaluating NGM621, a complement inhibitor, in patients with geographic atrophy

Gemini Clarity: A genetic screening and registry study to evaluate long-term clinical outcomes and disease progression in subjects with non-central GA who are carriers of high-risk genetic complement variants associated with dry AMD

Retinal Vein Occlusion

Novartis Raptor: A Phase III Study Assessing the Efficacy and Safety of Brolucizumab versus Aflibercept in Adult Patients with Visual Impairment due to Macular Edema secondary to Branch Retinal Vein Occlusion.

Novartis Raven: A Phase 3 Study Assessing the Efficacy and Safety of Brolucizumab versus Aflibercept in Adult Patients with Visual Impairment due to Macular Edema secondary to Central Retinal Vein Occlusion.

Research Dinners

On September 26, 2019 Retina Research Center is hosting a recruitment dinner for the IONIS 696844-CS5 study at Perry's Steakhouse in the Domain at 6:30pm for optometrists. The IONIS study is evaluating the effect of IONIS-FB-LRx on the rate of change of the area of geographic atrophy (GA) secondary to age-related macular degeneration (AMD) measured by fundus autofluorescence (FAF).

Publications & Presentations

1. **Jhaveri C.** Update on DRCR Retina Network Protocols. *Retina Today* 2019 April
2. **Jonna G**, Daniels AB. Enhanced Depth Imaging OCT of Ultrasonographically flat Choroidal Nevi Demonstrates Distinct Patterns. *Ophthalmology Retina 2019; 3:270-7.*
3. **Chexal S**. Interviewed by Bloomberg D. Woman Magazine April 2019 (68) *Into the Blue_Are Tech Devices Harmful to the Eye*
4. Khanani AM, Fineman M, **Berger, BB,** Dugel P, Patel S. *A Phase 1, Open-Label, Dose-Escalation Study of THR 149 for the Treatment of Diabetic Macular Edema (DME)*. Presented at Retina Society, September 15, 2019, Lo don, England. Will be presented at AAO October 2019 , San Francisco.
5. Breazzano MP, **Jonna G,** Nathan NR, Nickols HH, Agarwal A. Endogenous Serratia marcescens panophthalmitis: A case series. American Journal of Ophthalmology Case Reports 2019 Aug 1;16: 10053
6. Nguyen QD, Sepah YJ, **Berger BB,** Brown D, Do DV, Garcia-Hernandez A, Patel S, Rahhal FM, Shildkrot Y, Ren-furm RW. Primary outcomes of the VIDI study: Phase 2 double-masked, randomized, active-controlled study of ASP8232 for diabetic macular edema. International Journal of Retina Vitreous, August 1, 2019, 5:28.
7. Boyer D, Patel S, Kunimoto D, **Berger BB**, Maturi R, Callanan D, Kiernan D, Singer M, Smith V, Semba C. *Primary outcomes of the Graybug Phase 1B-2A ADAGIO study*. Presented at Hawaiian Eye January 2019.
8. **Jhaveri C.** DME and Good Vision: Do We Need to Treat Early? *Retina Today* September 2019.

Teaching and education are an important part of RRC. Our staff doctors, Dr. Berger, Dr. Jhaveri, Dr. Chexal & Dr. Jonna are directly involved with Dell Medical School, Texas A&M College of Medicine, University of Texas Medical Branch at Galveston and the Health Careers Mentorship Program at the University of Texas at Austin. Our physicians devote their valuable time to train and educate current and future medical students in the latest advances in the field of ophthalmology.

INSTITUTE FOR RETINA RESEARCH

If you or your foundation are interested in making a tax-deductible contribution, please visit our website at www.retinaresearchcenter.com or click HERE.

CONTACT US

Brian B Berger, MD—bberger@e-retina.net
Saradha Chexal, MD—schexal@e-retina.net
Ivana Gunderson—igunderson@e-retina.net
Ryan Parmoon—rparmoon@e-retina.net
Daniela Vega — dvega@e-retina.net
Kaitlyn Timmons—ktimmons@e-retina.net
Chirag Jhaveri, MD—cjhaveri@e-retina.net
Gowtham Jonna, MD—gjonna@e-retina.net
Daniela Wilson—dwilson@e-retina.net
Valerie Gatavaski—vgatavaski@e-retina.net
Yong Ren—yren@e-retina.com

www.retinaresearchcenter.com

Phone: 512-279-1251 Fax: 512-600-2882