RRC
RETINA RESEARCH CENTER

Winter 2016

Sustained delivery therapy for neovascular age-related macular degeneration

Genentech
A Member of the Roche Group

Retina Research Center (RRC) is currently enrolling in a Phase II study evaluating the efficacy and safety of a ranibizumab port delivery system (RPDS) for sustained delivery of ranibizumab compared to intravitreal injections of ranibizumab in patients with subfoveal wet AMD. The study is sponsored by Genentech and expected to enroll a total of 220 patients across 60 sites. The patients enrolled will be randomized to four treatment arms in a 3:3:3:2 ratio (Figure 1).

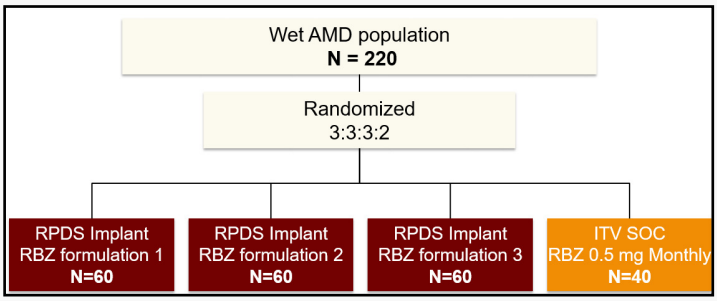

Figure 1: LADDER study design

For patients randomized to the implant arms, the RPDS will be surgically implanted by Dr. Jhaveri or Dr. Berger at the Oakwood Surgery Center. The patients will receive an initial fill with a specific formulation of ranibizumab based on their randomization assignment on the day of surgery. The patients will then be seen monthly in our research office and drug will be replenished as needed per protocol defined refill criteria. The implant is intended to stay in the eye permanently and the patient will continue to get additional drug as needed unless explantation is indicated. The patients randomized to the standard of care arm will be treated with monthly 0.5 mg ranibizumab during study enrollment. The primary objective is to determine the time until a participant first requires a RPDS implant refill according to protocol defined criteria.

Through clinical trial participation, we are able to offer our patients cutting-edge pharmaceutical treatments for a variety of retinal diseases and can now also offer alternative drug delivery methods for neovascular AMD. Sustained drug release via the RPDS implant could potentially result in more effective, consistent, treatment for neovascular AMD with a prolonged therapeutic effect than current standard of care anti-VEGF therapy via intravitreal injection. If effective, this treatment approach could significantly reduce the treatment burden on the patient, physician and family members that accompany patients to their appointments.

Main inclusion criteria include:

- newly diagnosed with neovascular AMD within 6 months prior to screening
- best-correct visual acuity 20/25-20/200 in the study eye

To refer a potential patient, please contact Ivana Gunderson at 512-279-1251 or igunderson@e-retina.net

Optical Coherence Tomography angiography, OCTa

While OCT angiography has been carefully studied since 2006, it has only recently made its way into the clinical setting. OCT angiography is a new, non-invasive technology that creates angiographic images without the use of fluorescein dye in a matter of seconds. OCT angiography compares motion of erythrocytes to the static nature of surrounding tissue, thus creating an angiographic image. By contrast, fluorescein angiography and indocyanine angiography are invasive tests that require administration of intravenous dye with a much longer acquisition time. FA and ICG testing investigate blood flow in a dynamic setting. The quick nature of OCTa combined with the non-invasive method to create a volumetric angiographic image adds to the appeal of OCT angiography. Clinical applications for this technology are still being studied.

RRC is evaluating OCT angiography in several DRCR (Diabetic Retinopathy Clinical Research Network) protocols. In protocols W and AA, OCTa is being compared to current imaging modalities to detect progression of diabetic retinopathy, identify biomarkers that may indicate progression of retinopathy, and to compare different OCTa systems at different sites. We are happy to have the latest cutting-edge OCT technology available to our clinic and research patients to enhance and optimize their treatment.

Genetic Testing for Retinitis Pigmentosa

RRC is working with Sparks Therapeutics to offer genetic testing and counseling for your retinitis pigmentosa patients at no charge to the patient. The genetic testing is conducted at our research office, RRC, located adjacent to our central clinic location. We are the only office offering this unique service in central Texas. The test will check for the 30 most common mutations in RP, but there are over 120 mutations, therefore, a negative result does not necessarily mean that a patient does not have RP. Test results are expected within 4 weeks of testing. Sparks Therapeutics is offering this service to generate a database of patients with RP organized by type of genetic mutation. The data collected will be used to potentially conduct clinical trials using genetic therapy. If a clinical trial arises as a result of this effort, the patients that participated in the genetic testing may be contacted and offered to participate if they meet inclusion criteria.

To qualify for testing, a patient must have a diagnosis of RP based on an eye exam and autofluorescence imaging. Both of these services can be provided by any one of our doctors at any of our three clinic locations at Retina Consultants of Austin, PA. The genetic counseling is a service offered by Sparks Therapeutics and our research staff can provide your patients with additional information on counseling at the time of genetic testing. Please contact our staff at Retina Research Center at 512-454-0138 if you would like to refer a patient for genetic testing. We have tested over 20 patients in the past month.

Students

Lance Lyons, MD grew up in Brooklyn, New York and Edison, New Jersey before attending Vanderbilt University. He received his medical degree from SUNY Downstate Medical Center in Brooklyn. Dr. Lyons is currently an intern completing his transitional year residency at Brackenridge Hospital. He completed his elective rotation in retina with our clinic and RRC in September 2016 and will return to RRC to complete his research rotation in 2017. Dr. Lyons plans to practice ophthalmology upon completion of his residency at UTMB Galveston. Of the many reasons Dr. Lyons chose ophthalmology, one of the strongest was the ability to profoundly impact a patient's quality of life within a short period of time. Outside of work, Lance enjoys the outdoors by hiking, running, and hunting down live music around Austin, TX.

Jihad Harmouche is a 4th year medical student at the University of Texas Medical Branch in Galveston, TX. Jihad is originally from Tripoli, Lebanon and moved to the United States at the age of 13 with his family to fulfill his dream of becoming a physician. He graduated from high school and the University of Houston in 6 years and entered medical school at the age of 18. He plans to practice in Obstetrics & Gynecology after completing his residency. Jihad completed his elective rotation in our office in September/October 2016 and feels that his ophthalmology experience trained him to recognize eye conditions in pregnancy. In his free time, he enjoys watching football, hiking, going to concerts and reading philosophy and psychology related books.

Publications

1. **Lee M. Jampol, MD , Vincent S. Hau, MD, PhD. Making an Impact in Clinical Research Early in Your Carrer With the DRCR.net. Retina Times, Fall 2016, Volume 34 #4, Issue 66.**
   - Dr. Jhaveri is the vice-chair for the DRCR network and was interviewed in this article.

2. **Sarah Mrejen, MD; David Sarraf, MD; Saradha Chexal, MD; Kenneth Wald, MD; K. Bailey Freund, MD. Choroidal Involvement in Acute Posterior Multifocal Placoid Pigment Epitheliopathy. Ophthalmic Surgery, Lasers and Imaging Retina. January 2016 - Volume 47 · Issue 1: 20-26.**

3. **Saradha Chexal, MD, Ivana Gunderson, BS, Brian B. Berger, MD, Chirag Jhaveri, MD. A Novel Compound for Treatment of Wet AMD. Retina Today, May/June 2016 72-78.**

4. **Chirag Jhaveri, MD. 5Q With Chirag Jhaveri, MD. Retina Today, October 2016 82.**

Enrolling Trials

Wet Age-Related Macular Degeneration

Genentech BP29647 AVENUE –A Phase II study evaluating the safety, tolerability, pharmacokinetics and efficacy of RO6867461 compared to Lucentis in subjects with wet ARMD

Daiichi Sankyo Pharma DS7080-A-U101 - A Phase I, dose escalation and expansion study of DS-7080a in subjects with neovascular ARMD

Tyrogenex, Inc. X-82-OPH-201 APEX - A Phase IIb study of oral X-82 plus PRN Eylea compared to PRN Eylea monotherapy in subjects with neovascular ARMD

Regeneron R910-3-AMD-1517 ONYX A Phase II, randomized, double-masked, active controlled, study of the efficacy, safety and tolerability of repeated doses of intravitreal REGN910-3 in patients with wet AMD

Santen Inc. 36-001 PAVE A Phase I/II, open-label, dose escalating, sequential-cohort study assessing the safety, tolerability, immunogenicity and bioactivity of a single intravitreal injection of DE-122 in refractory wet ARMD patients

Genentech GX28228 LADDER–A Phase II, randomized, active treatment-controlled study of the efficacy and safety of the Ranibizumab port delivery system for sustained delivery of Ranibizumab in patients with subfoveal wet ARMD. - New study.

Dry Age-Related Macular Degeneration

University of Virginia TOGA (Treatment with Oracea for Geographic Atrophy) - A Phase III study to evaluate the efficacy of daily administration of ORACEA®, a tetracycline derivative approved for treatment of inflammatory lesions of rosacea in adults, compared to placebo on the rate of change of GA in dry AMD.

Diabetic Macular Edema

DRCR Protocol U - A short-term evaluation of combination corticosteroid + Anti-VEGF treatment for persistent diabetic macular edema following Anti-VEGF therapy in pseudophakic eyes.

Genentech BP30099 BOULEVARD –A multi-center, multi-dose, randomized, active comparator-controlled , double-masked 28 week study to investigate the safety, tolerability, pharmacokinetics and efficacy of RO6867461 administered intravitreally ion patients with DME.

Alimera Sciences Inc. Paladin - A Phase IV safety study of IOP signals in patients treated with Iluvien 0.19mg

Non-proliferative Diabetic Retinopathy

DRCR Protocol W - Intravitreous Anti-VEGF Treatment for Prevention of Vision Threatening Diabetic Retinopathy in Eyes at High Risk

Proliferative Diabetic Retinopathy

Acucela 4429-203 - Randomized, double-masked, placebo-controlled, pilot study to evaluate the effects of Emixustat Hydrochloride on aqueous humor biomarkers associated with PDR. - New study.

Top Enrollers in the Country

RRC RETINA RESEARCH CENTER

Retina Research Center, RRC, is currently participating in 20 Phase I-IV clinical trials, 12 of which are currently enrolling. RRC is a high enroller in over 75% of trials conducted at the site and has strong, long standing relationships with all of major pharmaceutical and NIH sponsors in the industry. We pride ourselves in quality patient care and precise clinical trial execution.

Retina Research Center Numbers

- 97+ patients currently enrolled in clinical trials
- 5.6 average patients seen per day; range of 1-9
- 99% patient retention rate
- Top 5 enrollers in the country in over 50% of all ongoing clinical trials

RETINA RESEARCH CENTER BABY NEWS!

Dr. Berger is a first time grandfather! On September 27, 2016 Dr. Berger's daughter, Melissa and son-in law, John, welcomed their first child into the world. John Bennett Farleigh is a healthy baby boy weighing 9 lbs, 8 oz at birth and measuring 20.5 inches. Dr. Berger has three daughters and one step-son. The eldest children are twin girls, Melissa and Meredith and the youngest daughter is Amanda. Jesse is the only boy and youngest child in the family.

Melissa and her husband John live in Seattle, Washington and the proud grandfather recently visited to spend time with baby John. Dr. Berger was not only fortunate enough to spend a week with the cutest new family member but was also able to witness his Chicago Cubs pull off a historic win with their smallest fan!

Ivana and her husband, Patrick Gunderson, are proud parents of a healthy boy! William John Gunderson was born on September 15, 2016 at 8 lbs, 6 oz and measured 20.5 inches long. Ivana is the office manager at Retina Research Center and has been with the company for over eight years. Ivana and Patrick's first child, Anabella Jade Gunderson, is 29 months old and is enjoying her new role as a big sister.

Dr. Chexal and husband Nitin are expecting a little bundle of joy just in time for Christmas! Dr. Chexal and Nitin's daughter, Nehali, recently turned three and is looking forward to the addition of their new family member.

Institute for Retina Research

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

RESEARCH DINNERS

On July 19, 2016 RRC hosted a recruitment dinner for ophthalmologists for the Regeneron ONYX clinical trial which is evaluating a new therapy for treatment naïve wet AMD. The dinner took place at Eddie V's Prime Seafood Restaurant at the Arboretum in Austin, TX. Bethany Beazley, PhD, a medical scientific liaison from Regeneron presented the protocol and Phase I experience with the study drug.

On November 16, 2016 RRC hosted a recruitment dinner for the Genentech LADDER clinical trial at Siena Ristorante Toscana in Austin, TX. The LADDER study is testing the efficacy of the ranibizumab port delivery system for sustained delivery of ranibizumab in patients with neovascular AMD. We plan to host additional dinners in the near future. Please contact Ivana Gunderson at igunderson@e-retina.net if you are interested in attending future events.

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