Rare Disease Newsletter

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THE CENTER FOR RARE DISEASES

Welcome to the sixteenth edition of the rare disease newsletter.

This quarterly publication strives to keep you up to date on initiatives and activities driven by PRA's Center for Rare Diseases. Interested in learning more about any of the rare diseases mentioned here, or have a suggestion for a specific rare disease you would like to learn more about? Email us – we take requests!

To learn more or to obtain support for a specific clinical study or project, please contact us. You can reach the entire team by emailing us at PRACenterForRareDiseases@prahs.com.

Edition Highlights

Disease Spotlight: GM1 Gangliosidosis

GM1 gangliosidosis is one of over 50 genetically inherited disorders that result from defects in lysosomal storage function. Lysosomes are sacs of enzymes within cells that digest large molecules and pass the fragments on to other parts of the cell for recycling, sort of like the "stomach" of the cell. All forms of GM1 gangliosidosis are caused by a mutation in the GLB1 gene, which encodes for the enzyme beta-galactosidase (ß-galactosidase), which plays an important role in the brain. Reduction or loss of ß-galactosidase activity results in damage to nerve cells in the brain and spinal cord. This is a progressive and degenerative condition with a broad and debilitating array of symptoms and complications. This rare disease is estimated to occur in 1 per 100,000 to 200,000 newborns.

GM1 gangliosidosis is inherited in an autosomal recessive fashion – individuals who carry a mutated gene are healthy, and any two carriers of this gene defect have a 25% chance of having an affected child. There are three major types of GM1, depending on the age the symptoms start appearing, but likely representing a continuous disease spectrum: Infantile (Type I), late infantile/juvenile (Type II), and adult/chronic (Type III). Type I is the most severe and most frequent type of GM1. Children with Type I usually do not survive past early childhood due to infection and cardiopulmonary failure. Type II, which includes the late-infantile and juvenile forms, is an intermediate form of the condition. People with Type II GM1 who have late-infantile onset usually survive into mid-childhood, while those with juvenile onset may live into early adulthood. Type III, known as the adult or chronic form of GM1, is the mildest form of the condition. The age of onset and life expectancy for people with Type III varies, but life expectancy is usually shortened.

Where Are We Today?

Like 95% of rare diseases, there are currently no approved treatments for GM1 gangliosidosis. There is, however, hope on the horizon with active research programs including enzyme replacement therapy, chaperone therapy, substrate reduction therapy, and gene replacement and gene editing programs. There are currently more than one gene therapy being developed in simultaneous clinical trials!

Disease Spotlight: Raynaud's and Scleroderma by Nicola Haycock

Raynaud's disease affects the blood flow to the fingers, toes, and other areas such as the ears or nose. Around 10% of the UK population are thought to have Raynaud's disease, most frequently affecting young women. Approximately 90% of Raynaud's patients have primary Raynaud's, which is less severe than secondary Raynaud's. Secondary Raynaud's is caused by an underlying disease such as scleroderma (or other conditions, such as lupus, rheumatoid arthritis, or Sjogren's syndrome). Scleroderma is a rare, chronic disease of the immune system, blood vessels, and connective tissue. 2.5 million people worldwide have scleroderma and it affects 4 times more women more than men.

In Raynaud's disease, arteries to the fingers and toes suddenly narrow when exposed to cold or stress, which temporarily reduces the blood supply. As a result, affected areas appear bloodless and white or grey appearance and have the sensation of "pins and needles," or throbbing. When normal blood flow resumes, the affected area may become painful. If severe, the tips of fingers or toes may ulcerate. Scleroderma is caused by the immune system attacking the connective tissue under the skin and around internal organs and blood vessels. This causes scarring and thickening of the tissue in these areas. Symptoms include hardening of the skin, swelling of the hands and feet, joint pain and stiffness, and blood vessel damage leading to Raynaud's disease.

The cause of Raynaud's disease is unknown, but it is believed that the nervous system's control of the blood vessels contributes, plus it may be inherited. Scleroderma is thought to be caused by immune system problems, genetic factors, and environmental triggers.

CURE GM1 FOUNDATION

The CURE GM1 FOUNDATION's mission is to fund research for the benefit of all those who suffer from GM1 gangliosidosis. This nonprofit organization was founded by parents of children who suffer from GM1 who seek to save the lives of all those who suffer from this wretched condition. The Cure GM1 Foundation is dedicated to directly funding research for a cure for GM1 gangliosidosis.

Where Are We Today?

Both without cures, Raynaud's disease and scleroderma require long-term management with lifestyle changes and medication. Lifestyle changes to prevent symptoms of Raynaud's disease include includes avoiding triggers such as exposure to cold, stimulants, smoking, emotional stress. If lifestyle changes are insufficient, therapy with a vasodilating mechanism of action can be used such as amlodipine or nifedipine. Additionally, for scleroderma, treatment may involve physiotherapy, and medication to improve circulation, reduce the activity of the immune system, and treat other symptoms such as joint and muscle problems, pain, and/or blood pressure issues. In some cases, scleroderma patients may also need surgery to remove areas of thickened skin and relieve tightness.

SCLERODERMA & RAYNAUD'S UK

February was Raynaud's Awareness Month! The Scleroderma & Raynaud's UK charity is dedicated to improving the lives of people affected by scleroderma and Raynaud's.

PRA Rare Disease Day

On February 28, 2020, PRA collaborated with the University of Pennsylvania Orphan Disease Center to celebrate Rare Disease Day at the Blue Bell, PA office with 70+ employees, patients, advocates, and sponsors. This is an annual gathering for all stakeholders in rare disease research to share experiences and strategies. The theme for 2020 was "Re-framing Rare," and lectures and round table discussions focused on the perspectives of researchers, treating clinicians, patient advocates, and regulators.

Participants at this year's event could 'frame' themselves with a self-portrait and helped to build personal care packages for use by caregivers who travel with family members for medical treatment. By the end of the day, 200 packages were prepared and donated to the Ronald McDonald House in Center City Philadelphia!

Scott Schliebner, Senior Vice President of PRA's Center for Rare Diseases, kicked off the event by sharing the mission and vision for the Center with attendees. In his remarks, Scott acknowledged the daily challenges faced by the rare community and invited participants to share their perspectives on how clinical research can be accomplished within those challenges.

The following experts shared their perspectives and videos of these great presentations can be viewed here.

Photo above: (L to R) Kendall James-Davis (PRA Patient Advocacy Manager), James Valentine (Hyman, Phelps & McNamara), and Lisa Schill (RASopathies Network)

Photo right: Rare Disease Day: (L to R) Ronald McDonald House Managers Laisa Turano and Linda Pusatere accepting personal care packages prepared by attendees at Rare Disease Day 2020

Dr Eric Marsh

Associate Professor of Neurology & Pediatrics, Children's Hospital of Philadelphia

Dr. Marsh is an attending pediatric neurologist in the Division of Neurology at Children's Hospital of Philadelphia (CHOP), specializing in diagnosing and treating children with developmental epilepsies, epilepsy, infantile spasm, and malformations of cortical development. Dr. Marsh gave a presentation on "Reframing Patient Standard of Careto Include Clinical Trials." To illustrate the challenges in incorporating clinical trials into traditional care, he shared research from a study done by Center Watch in Washington, DC that showed 75% of patients weren't aware clinical trials could be a care option.

James E. Valentine

Associate Attorney, Hyman, Phelps & McNamara, P.C.

To close the day, James spoke about "reframing" how regulators use the patient voice in their decision-making. James described the evolution of FDA's engagement with patients through the addition of policies for patient listening and collaboration but emphasized this evolution must continue. Patient voice and input can be product-specific and context-setting when it comes to their contribution to the FDA.

Pam Gavin

Chief Strategy Office, National Organization for Rare Disorders

In her presentation, Pamela emphasized to her audience the importance of empowering patients to sign up for patient advocacy organizations. Together, patients and advocacy organizations can unite to reframe drug development by putting the patient voices in trial design, highlighting that both these groups bring valuable first-hand experience and preferences to the drug development industry, as well as a strong understanding of risks in trial design.

Brett Brackett

General Manager and Director of Sports Impact, Uplifting Athletes

Brett spoke at the event about his involvement in the rare disease community. In 2006, when he was a Wide Receiver at Penn State University, Brett's teammate's dad was diagnosed with a rare disease. This inspired Brett to serve the rare disease community by volunteering with the Penn State Chapter of Uplifting Athletes. Uplifting Athletes hosts a variety of programs to drive this awareness, such as the Young Investigator Draft, which recognizes scientific advancements in rare cancers, rare autoimmune and immunological disorders, rare blood disorders, rare genetic disorders, and rare muscular and neurological disorders.

Meeting Highlights

Young Investigators Draft 2020

PRA sponsored the 3rd Annual Uplifting Athletes Young Investigator Draft at Lincoln Financial Field in Philadelphia, PA on March 7, 2020. Uplifting Athletes is a fundraising organization that aims to inspire patients with rare diseases through the power of sport. Throughout the year, Uplifting Athletes works with rare disease advocacy groups to solicit nominations for scientific researchers who have contributed to the understanding of rare diseases. At the Young Investigators Draft (so called because it imitates the National Football League draft), these groups award a Young Investigator Draft Grant to a selected scientist thereby funding their research and continuing the pursuit of cures for rare diseases.

The event was emceed by Cameron Lynch, a former football athlete for Syracuse University, Los Angeles Rams, and Tampa Bay Buccaneers. This year's patient advocacy partners (and Young Investigator grant recipient) included Team Telomere (Dr. Abhishek Mangaonkar), Oxalosis & Hyperoxaluria Foundation (Dr. Jonathan Whittamore), Malan Syndrome Foundation (Dr. Kathryn Hixson), Castleman's Disease Collaborative Network (Dr. Joshua Brandstadter), Cure VCP Disease (Dr. Cheng Cheng), and Emily's Entourage. Dr. Benjamin Chan was awarded the Collaborative Leadership Award for mentoring young scientists in their pursuit of treatments and novel delivery mechanisms.

Biotech Showcase

Biotech Showcase™, held January 13–15th in San Francisco, CA adjacent to JP Morgan, is one of the industry's leading investment conferences. With more than $400 billion in capital represented, more than 3,500 attendees, 2,220 companies, and over 1,000 investors, Biotech Showcase™ provides a key platform where companies can showcase their innovative assets and build their profile with potential investors, strategic partners, and drug development experts.

2020 was the first time PRA Health Sciences sent a team to attend Biotech Showcase™ and it was an incredibly productive opportunity for us to meet with several current and potential target clients. Colleagues from Account Development, Business Development, Center for Drug Development, Project Management, Scientific Affairs, and the Center for Rare Diseases attended the 3-day event.

Young Investigator Draft: (Front L to R) Stacey Flattery (PRA VP & General Partner), Rob Long (Uplifting Athletes Executive Director), Scott Schliebner (PRA SVP Center for Rare Diseases), Sue Capizzi (PRA Account Development Manager), Juliane Mills (PRA Director, Center for Rare Diseases); (Back L to R) Candice Kent (PRA, Executive Director, Marketing), Leyla Honar (PRA Director, Medical Informatics), Simon Rogers (PRA Executive Director, Marketing)

We held several dozen face-to-face meetings with early-stage biotechnology companies and discussed early engagement opportunities and clinical development planning of their assets. The opportunity to meet with so many start-up organizations, early in their clinical development planning, will help to fill PRA's pipeline of new clients who need early engagement support. The awareness, tangible business leads, near-term RFPs, and great contacts assured a fantastic ROI from this event.

In addition to hosting a well-attended client event, we also took a break from client meetings and raced go-karts one evening. A link to a video of Scott Schliebner and Sol Babani describing PRA's approach to working with small biotechnology clients can be found here.

Biotech showcase: (L to R) Sol Babani (PRA SVP, Drug Development & Therapeutic Expertise), Scott Schliebner (PRA SVP, Center for Rare Diseases) speaking with Biotech Showcase reporter

Foundation Spotlights:

The Chan Zuckerberg Initiative

On February 3rd, 2020 The Chan Zuckerberg Initiative (CZI) announced 30 Rare Disease Patient Organizations who have been selected to receive a Rare as One Grant. The Rare as One grant program is providing funding, totaling 13.5 million dollars, to support patient-led organizations who are working to accelerate research and treatments in the rare disease space. Originally the project set out to fund 10 Rare Disease Organizations but due to the volume of grant applications, CZI expanded the funding to 30 organizations.

Among the 30 incredible awardee organizations, are KIF1A.org and Lennox-Gastaut Syndrome (LGS) Foundation. PRA is proud to have representatives (Luke Rosen and Tracy Dixon-Salazar, respectively) from both organizations as members of The PRA Rare Disease Advisory Committee. Another member of the RDAC, Andra Stratton, has also joined CZI as a Lead Trainer for the Rare as One Project! This grant program is incredibly exciting for the awardee organizations and for rare disease research!

Born A Hero

Born a Hero is a remarkable patient-focused research organization that believes we can confront the world with hope, courage, and love. David and Carolina Sommer's daughter, Mariana Haydee, was diagnosed at the age of 2 with Pfeiffer Syndrome. Frustrated by the surprises they encountered on their unexpected diagnostic journey, Born a Hero was created to bring together information, resources, experiences, and families suddenly thrust into the world of Pfeiffer Syndrome. Based in the greater Seattle-area, Born a Hero is here to fight for change and they lead with a calm, positive, and loving approach to anything and everything they do.

Pfeiffer Syndrome is a rare genetic disorder which causes bones to fuse prematurely or extra bones to grow in different parts of the body, including the skull. Symptoms and severity can vary on a spectrum from very mild all the way to life-threatening. If not corrected, fusions in the skull can form and can affect growth of the brain. As Mariana Haydee grew older, David and Carolina also became more aware of the social impacts related to her condition. To address what they were seeing, they created and developed a curriculum for children from Pre-K through 2nd grade aimed at showing children how to "treat others with kindness." As they attended conferences and learned more about the rare disease space, David and Carolina recognized a lack of research, coordination, and programs within Pfeiffer Syndrome. In order to fill this void, they have shifted the focus of Born a Hero to one emphasizing research, and have developed relationships with researchers, patients, and industry, including a close collaboration with Mount Sinai Hospital.

Born a Hero has also been the drivers behind the creation of the Seattle Rare Disease Fair, started in 2017. As David and Carolina fund raise in support of the Pfeiffer Syndrome patient registry, they also have learned that there are an additional 15 syndromes that have a genetic component similar to Pfeiffer Syndrome. Their hope is that by making research progress within Pfeiffer Syndrome, that their findings can also have a broad application to several other disease areas.

Born a Hero will continue to focus on "how we can be most impactful" by continuing to partner with industry and researchers with a community-focused, authentic, and collaborative vision and approach. Visit their website here.

Rare Disease Indications – High Activity

- Amyotrophic Lateral Sclerosis
- Nephrotic syndromes
- Sickle Cell Disease
- Angelman's Syndrome
- Netherton's Syndrome
- Krabbe Disease
- Hereditary Hemochromatosis
- Refractory Gout
- Primary & Secondary Hemophagocytic Lymphohistiocytosis
- Macrophage Activated Syndrome
- Myotonic Dystrophy
- Lennox-Gastaut Syndrome

Newly Awarded Rare Disease Studies

- Hypoparathyroidism – Phase I hybrid SAD/MAD
- Hypoparathyroidism – Feasibility
- Complex lymphatic malformations – Phase Ib
- Adult Onset Still's Disease – Phase Ib
- Chronic proteinuric glomerulonephritis including focal segmental glomerulosclerosis – Phase II
- Duchenne Muscular Dystrophy – Phase III
- Angelman Syndrome – Phase 0/Natural History
- Alexander Disease – Phase I-III
- Netherton's syndrome – Phase II
- Phenylketonuria (PKU) – Phase II

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