The Inozyme Advocate

Your source for news, information and events on Rare Calcification Disorders

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Welcome to The Inozyme Advocate, a semi-annual communication to bring you news, information and events from the Patient Advocacy Team at Inozyme!

Announcing the launch of the ENPP1 and ABCC6 Genetic Testing Program!

Inozyme Pharma is excited to announce the launch of a no-cost genetic testing program for the *ENPP1* and or *ABCC6* genes for individuals with ENPP1 Deficiency and ABCC6 Deficiency, respectively. ENPP1 Deficiency manifests as either GACI Type 1 (Generalized Arterial Calcification of Infancy) or ARHR2 (Autosomal Recessive Hypophosphatemic Rickets Type 2). ABCC6 Deficiency can manifest as GACI Type 2, which is clinically similar to GACI Type 1.

The laboratory performing the genetic testing is PreventionGenetics.

Healthcare Providers, patients and caregivers who suspect GACI or ARHR2 are encouraged to consider this genetic testing program.

Genetic testing can provide many benefits such as:

- Decreasing the time to accurate diagnosis now an average of 7 years for many individuals with a genetic condition.
- Making informed decisions about health management which could lead to a better quality of life through symptom management and treatment options.
- Provide patients and their family the opportunity to connect with and receive support from others living with the same condition.
- Access to education about the condition, current research and treatment options.

The Genetic Testing Process is as follows:

1. The healthcare provider (HCP) will determine if the individual meets eligibility criteria and discuss the test.
2. The HCP will order the test and collect a blood or saliva sample and ship it to the lab.
3. The genetic test will be processed at PreventionGenetics and the results will be sent to the HCP about 14 days after the lab receives the sample and all appropriately completed paperwork.
4. The HCP will meet the patient to discuss the results.

Please visit www.inozyme.com/genetic-testing/ to learn more about the program. To order a test, visit: https://www.preventiongenetics.com/specialOrders?sp=sp051 or call PreventionGenetics at 715-387-0484, option 2 and mention SP-051.

Meet the Team - Dr. Demetrios Braddock

Dr. Braddock is an Associate Professor of Pathology at Yale University, and Scientific Founder of Inozyme and Chairman of the Scientific Advisory Board. And he is much more!

Dr. Braddock is a passionate and driven physician, striving to ensuring possible treatment options are made available to all individuals with these conditions. His 30 years of experience, beginning as a pathologist at the National Institutes of Health, to practicing hematopathology and leading a lab at Yale University, have provided him with the scientific and clinical insight leading to the creation of an enzyme replacement therapy (ERT) for GACI and ARHR2 5 years ago. Knowing he had a possible life changing treatment for these disorders of abnormal calcifications, he embarked to translate this groundbreaking work into a treatment as he continues the work with Inozyme. But it's even deeper for Dr. Braddock. He has experienced first-hand the devastation parents, siblings and extended family live with when a child dies from an untreatable condition. As physician, he said, "these are conditions you want to correct". On the personal side, as a father of 5, Dr. Braddock said, "I would want someone to fight for my children", and therefore he feels passionate about fighting for others. Thus, from a professional and personnel perspective, he is driven to make a life-changing contribution to those for whom there is currently no treatment. Read more about his research in the section below entitled "In the News".

Did you know? - Enzyme Replacement Therapy

Enzyme replacement therapy (ERT) is a medical treatment which replaces an enzyme that is deficient or absent in the body. Inozyme Pharma is developing an ERT for two rare disorders of calcification, GACI and ARHR2, to restore the enzyme to levels that allow to the body working properly. Find out more at www.inozyme.com

Exciting preclinical data shows that an ERT therapy could help in GACI! The proof of concept research was led by Dr. Braddock. To learn more, read the section below entitled "In the News".

Ways to Get Involved – Natural History Studies

Natural history studies are important to our understanding of the natural progression of a condition and disease burden. In the case of studies of rare genetic conditions, these types of studies could also lead to an understanding of the role genes play in the presentation of the condition, that is the genotype/phenotype correlation.

Natural history studies benefit patients by empowering them as active participants and contributors to research, drug development and future clinical trials. It also provides them the opportunity to learn more about the condition, current treatments and ways to improve their quality of life.

Currently, two natural history studies for individuals with GACI Type 1 and Type 2, and ARHR2 are in progress. The information gathered from these studies could help in the development of new treatments, such as an ERT, for GACI and ARHR2.

Patients, caregivers and HCPs can make an important contribution and help further the understanding of these conditions by providing patient data to these studies. Two of the key opinion leaders in the field are managing these studies with grants from Inozyme. To get more information or to participate in either study, please reach out to them directly:

- Dr. Frank Rutsch, at the University of Muenster in Germany, by e-mail at frank.rutsch@ukmuenster.de or by phone at +49 251 8346439. **OR**
- Dr. Carlos Ferreira, at the National Institutes of Health in the US, by e-mail at ferreiracr@mail.ig.gov or by phone at +1-240-393-5441.

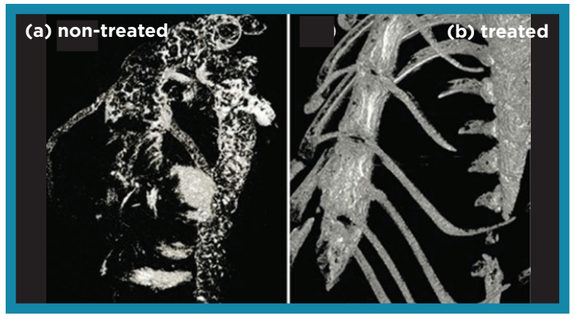
What is the difference between the 2 studies?

The data collected in the studies is nearly identical, but the method of data collection and the types of conditions being studied in each are different. The study performed by Dr. Rutsch involves the HCP collecting data from the patient's medical chart and sending it to him. Individuals with either type of GACI are the focus of his study. The study performed by Dr. Ferreira involves patients providing their medical records to him for data collection. His study focuses on individuals with either type of GACI or ARHR2. Informed consent will be obtained prior to data collection. Results will be published. Therefore, participation in either study is encouraged as it will help inform us about genotype/phenotype correlation, disease progression and disease burden.

In the News – Ground breaking research of an enzyme replacement therapy (ERT) for GACI and ARHR2!

Dr. Braddock published the ground breaking and preclinical proof of concept work of an ERT for GACI in 2015 in Nature Communications (Albright, R. A. *et al.* ENPP1-Fc prevents mortality and vascular calcifications in rodent model of generalized arterial calcification of infancy. *Nat. Commun.* 6:10006 doi: 10.1038/ncomms10006 (2015)). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4686714/.

The study demonstrates a murine enzyme replacement therapy (mERT) that is capable of preventing the lethal vascular calcifications of GACI in murine ENPP1 loss of function models. The dramatic change of this ENPP1 ERT in *enpp1*$^{asj/asj}$ mice is illustrated in the image below. The postmortem high-resolution micro-CT scans revealed extensive calcifications in untreated *enpp1*$^{asj/asj}$ mice in the hearts, coronary arteries, and ascending and descending aortas (a), but absolutely no calcifications in these organs are in the treated *enpp1*$^{asj/asj}$ cohort (b)



Data presented at the 45th European Calcified Tissue Society Congress in Valencia, Spain, May 2018, demonstrated that the same mERT used in the GACI mouse model is also capable of preventing the bone mineralization deficits in the ARHR2 animal model. Full publication of the ARHR2 data is forthcoming.

Community Insights – Focus on Global Genes

- **Global Genes** is one of the leading rare disease patient advocacy organizations in the world. It is a non-profit organization providing tools, support and promoting the needs of the rare disease community. Visit their website at https://globalgenes.org/
- Global Genes**,** in partnership with the Penn Medicine Orphan Disease Center, held the **2018 RARE Patient Advocacy Symposium** on May 19, 2018 in Philadelphia, PA, USA. The meeting brought together patient, caregivers, and other stakeholders such as physicians, researchers, industry representatives and policy makers, for a full day program. The program focused on rare disease research, drug development, and the patient advocacy organization's role in the process. Highlights include presentations from patient advocates about their involvement with the FDA, whether speaking to an FDA committee about the reason a drug should be approved, to holding patient-focused drug development meetings to educate the FDA about a condition. You can review all the presentations at https://globalgenes.org/2018raresymposium/.
- Global Genes and the Every Day Life Foundation have collaborated to provide free regional events to bring important education and insights to rare disease patients, caregivers and other advocates. The meeting series is called **Rare on the Road**. The goal of these meetings is to build and activate the rare disease community at the local level. Contact Global Genes to find out if travel scholarships are available. Check out the **Upcoming Events** section for dates and locations.
- Global Genes will bring together the patient advocacy community and other stakeholders again in October at the **2018 Rare Patient Advocacy Summit** in Irvine, CA, USA. **Mark your calendars for October 2-5,** with the main events happening on October 3-4, and pre- and post- events on October 2 and 5. More information can be found at https://globalgenes.org/2018summit/. Inozyme is sponsoring a limited number of travel scholarships for GACI/ARHR2 patients and their caregivers that would like to attend the conference. Applications for travel scholarships will be available through Global Genes. **On October 5, Inozyme is planning to meet with members of the GACI and ARHR2 community.** Details will be available soon. Feel free to contact Lori Ann Correia, Director of Patient Advocacy at Inozyme Pharma at lori.correia@Inozyme.com or +1-857-856-5752 if you would like to be included in future updates.

Celebrating You! - Rare Disease Day 2018

Rare Disease Day is observed worldwide annually on last day of February to raise awareness for rare diseases and the daily impact living with a rare disease has on patients and families. Each year the Rare Disease Day organization has a unique campaign. For 2018 it was #ShowYourRare #ShowYouCare, encouraging patient, caregivers and other stakeholders to paint their faces with the organization's brand colors and post pictures on social media with the campaign hashtags. Thousands of people worldwide painted their faces to show their support for those living with rare diseases including members of the Inozyme Team. We added our own hashtag as well: #InozymeCares. We truly do!

Mark your calendars for Rare Disease Day 2019 on Thursday, February 28. Get involved and learn more at https://www.rarediseaseday.org/

Inozyme team participants from left to right: Henric Bjarke, Lori Ann Correia, Steve Jungles, Sean Cullen and Axel Bolte.

Upcoming Events - 2018

The following meetings maybe of interest to patient, caregivers and HCPs. Visit their websites to find the ones of interest to you.

- **June 30: Rare on the Road,** Salt Lake City, UT https://raretour.org/
- **July 21: Rare on the Road,** Nashville, TN https://raretour.org/
- https://www.eurospe.org/meetings/2018/espe2018/
- **September 13: Rare Disease Scientific Workshop,** Washington, DC. https://everylifefoundation.org/10th-annual-rare-disease-scientific-workshop/
- **September 28 – October 1: American Society for Bone and Mineral Research,** Montreal, Canada https://www.asbmr.org/
- **October 2-5: Global Genes 2018 Rare Patient Advocacy Summit** https://globalgenes.org/2018summit/
- **October 5: XLH Network,** Baltimore, MD http://www.xlhnetwork.org/
- **October 15-16: Rare Diseases & Orphan Products Breakthrough Summit**, Washington, D.C. https://rarediseases.org/summit-overview/
- **November 6-8: World Orphan Drug Congress Europe,** Barcelona, Spain https://www.terrapinn.com/conference/world-orphan-drug-congress/index.stm
- **November 14-17: National Society of Genetic Counselors**, Atlanta, GA https://www.nsgc.org/

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