FALL 2024

INSIDE

FSIG Connection

News from the Fabry Support & Information Group

Study: ERT safe while pregnant

By Patricia Inácio, PhD
FabryDiseaseNews.com

(April 12, 2024) A woman in her 20s with Fabry disease was safely treated with agalsidase alfa—a commonly used enzyme replacement therapy (ERT)—during her two pregnancies with no resulting complications, a case study reported.

During the first pregnancy, "we did not observe any adverse event on administration of ERT," the authors wrote, noting that agalsidase alfa "was continued during her second pregnancy."

The patient also did not experience any problems for several years after the birth of her second child.

According to the authors, this case confirms previous reports supporting the use of ERT during pregnancy.

The case, "Two successful pregnancies in a woman with Fabry continuing enzyme replacement therapy," was published as a letter to the editor in the journal *Therapeutic Apheresis and Dialysis*.

Whether ERT can be safely used during pregnancy in women with Fabry is still a matter of debate. Now, two clinicians at the University Faculty of Medicine, Turkey, described the case of a woman prescribed agalsidase alfa during both of her pregnancies.

This ERT is not approved in the U.S. but has won approval in the European Union and other countries worldwide under the brand name Replagal. The woman, whose age was given as 28,

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Pregnancy worsens pre-existing Fabry pain

Austrian study finds preeclampsia, preterm birth also more likely

By Steve Bryson, PhD
FabryDiseaseNews.com

(May 10, 2024) Pregnancy increased the severity and frequency of pain among women with Fabry disease who lived with moderate pain before becoming pregnant, a study from Austria reported.

Further, preeclampsia, or dangerously high blood pressure during pregnancy, occurred three times more often in Fabry women than in the general population, according to the study. Babies born to mothers with Fabry also were more likely to be born preterm, smaller, and have a lower birth weight.

Overall, however, "despite a substantial number of high-risk pregnancies, neonatal outcomes were acceptable in this study on Fabry disease," the researchers wrote.

Still, "our data provides valuable information for pregnancy counseling in patients with Fabry disease," the team wrote.

The study, "Pregnancy outcomes of Fabry disease in Austria (PROFABIA)—a retrospective cohort-study," was published in the *Orphanet Journal of Rare Diseases.*

Studies suggest that Fabry-related symptoms may worsen during pregnancy, with a greater likelihood of patients experiencing digestive problems, numbness and tingling, elevated urinary protein, known

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WELCOME

Dear Friends,

In April, we increased awareness of Fabry by hosting two fundraisers and running social media campaigns. Between both events, over $40,000 was raised for the newborn screening and the assistance programs. We are extremely thankful for those who participated and donated to these important programs. You can see their names listed on the Acknowledgements page.

This Fall 2024 issue of FSIG Connection features stories of hope, clinical challenges and promising new therapies. As always, there's plenty of information to share.

If you have a Fabry story to contribute, we'd be thrilled to include it in our next issue. Don't worry if you're not a writer—our editor can help pull your story together. To submit or to ask questions, please email: support@fabry.org

Jack

Jack Johnson, Executive Director

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experienced intermittent abdominal pain that gradually worsened for four years. Her mother, a 49-year-old woman, also was diagnosed with Fabry and treated with agalsidase alfa.

According to the clinicians, the patient had the same GLA mutation as her mother, and also started treatment with agalsidase alfa—at a dose of 0.2 mg/kg every 14 days—for abdominal pain. The treatment resolved her symptoms.

About 10 months after starting on enzyme replacement therapy, the woman became pregnant and her pregnancy developed normally. The patient gave birth to a baby boy by vaginal delivery at 37 weeks. During gestation, a prenatal test confirmed the baby was negative for the GLA mutation. No adverse events linked to the ERT during her pregnancy or lactation were reported.

Standard tests on the baby, conducted immediately after birth. also showed no abnormalities. The baby was breastfed and developed normally.

Two years later, the woman once again was pregnant. Routine ultrasound checks confirmed the fetus was normal. Agalsidase alfa at the same dosing was continued throughout the pregnancy, which occurred without complications.

The woman delivered a healthy baby at 37 weeks. No prenatal genetic tests were conducted due to the parents' refusal. The baby developed normally and also was breastfed.

Read full story: bit.ly/ERT-Pregnancy

PREGNANCY: continued from page 1

as proteinuria, and headaches. Complications such as gestational diabetes and high blood pressure also may occur more frequently in pregnant Fabry women as compared with those in the general population.

Now, a team led by researchers at the Medical University of Vienna sought to further examine symptoms related to Fabry, focusing on pain, in women with the disease with a history of pregnancy.

"For the first-time we have analyzed the delivery outcomes of these women in detail," the team wrote.

Data were collected using a study-designed questionnaire, and from the Austrian Mother-Child Health Passport, a program in the country that tracks pregnancy-related health data of the mother and child from pregnancy until the child's 5th year of life.

A total of 44 women with Fabry, with a median age of 44, enrolled in the study. In all, 32 had a history of 70 pregnancies, with 61 pregnancies resulting in 64 live births between 1971 and 2021. Among the babies born, half were girls and half boys.

During the 61 pregnancies with successful outcomes, 24 women (39.3%) smoked. Four women (6.6%) developed gestational diabetes, 10 (16.4%) had high blood pressure, and 17 (27.9%) had proteinuria.

Preeclampsia occurred three times more often during a Fabry pregnancy than in the general population (11.5% vs. 3.8%), the researchers noted.

Nearly all participants (86%) reported symptoms likely related to Fabry disease, with pain, burning and tingling, and gastrointestinal symptoms as the most common. There were no differences noted between women with and without a history of pregnancy.

Fabry women with a history of pregnancy were older (median 48 vs. 24 years) and more frequently experienced other symptoms related to the heart, kidney, lungs, and nervous system. The women with Fabry also experienced more psychiatric problems.

Fabry disease pain can manifest in a variety of ways. Importantly, Fabry women with low levels of pain before pregnancy did not experience worse pain during pregnancy. In contrast, however, those with moderate pain before pregnancy reported an increase in pain intensity or frequency during the gestational period.

When compared with the Austrian birth registry, children born to mothers with Fabry were significantly more likely to be preterm, meaning they were born before 37 weeks gestation. These babies also had a lower birth weight and were smaller more than twice as often. Inpatient hospital stays for a newborn also occurred more frequently in those born to mothers with Fabry.

Read full story: bit.ly/Fabry-Pregnancy

Continuing partnership will aid getting Fabry diagnosis

By Steve Bryson, PhD
FabryDiseaseNews.com

(March 29, 2024) Centogene has extended a collaboration deal with Takeda in which the two companies will continue to provide diagnostic services to patients with lysosomal storage disorders—which may help people with Fabry disease to get a correct diagnosis.

The partnership was initially established to improve patient access to fast and dependable diagnostic services for people with Fabry and other forms of lysosomal storage disorders, such as Gaucher disease and Hunter syndrome.

"Extending our longstanding partnership with Takeda highlights the continuing need to accelerate diagnoses for [lysosomal storage disorder] patients globally and the ability of Centogene to fulfill this vital service," Ian Rentsch, Centogene's chief commercial officer and general manager for pharma, said in a company press release.

Fabry is marked by an abnormal buildup of toxic materials in lysosomes, the cell's recycling centers, that's caused by inherited deficiencies in certain enzymes. Given its progressive nature, it's important for clinicians to make a Fabry disease diagnosis as early as possible, so as to get treatment started.

Research shows that conditions like Fabry, Gaucher, and Hunter syndrome are often misdiagnosed or underdiagnosed. Because people with these conditions often face considerable diagnostic delays, an earlier diagnosis that allows patients to begin treatment as soon as possible may help to ultimately improve health and quality of life.

Read full story: bit.ly/Fabry-Partnership

RELATED STORIES

Fighting Fabry one newborn blood sample at a time
Feature on Brian and Tia Jones, founders of Testing for Tots:
bit.ly/Fabry-Newborn

Korea expands screening for lysosomal storage disorders
Starting this past January, all newborns in South Korea are screened for LSDs within 28 days of birth. Learn more:
bit.ly/NB-Screening

Study: Early diagnosis, ERT prevent worse symptoms

By Margarida Maia, PhD
FabryDiseaseNews.com

(May 17, 2024) Early diagnosis and a quick start to enzyme replacement therapy (ERT) with agalsidase alfa eased a patient's Fabry disease symptoms, preventing them from getting worse for at least six months.

That's according to a new report from China that detailed the case of a man in his 30s, who was diagnosed with Fabry after various tests and quickly started on treatment.

"Commencing ERT at an early stage may be more efficacious than [among] patients with more advanced stages of the disease," the researchers wrote, noting that Fabry "is a progressive disorder, so early initiation of ERT has the potential to eliminate major organ damage, and yield enhanced long-term benefits."

The diagnosis and treatment of the patient were described in "Case report: enzyme replacement therapy for Fabry disease presenting with proteinuria and ventricular septal thickening," which was published in *BMC Nephrology*.

In this case, a 37-year-old man was admitted to the First Navy Hospital of Southern Theater Command in Zhanjiang. He was experiencing recurrent proteinuria, or excess proteins in the urine, and thickening of the heart's ventricular septum, the wall that separates the ventricles—two lower chambers of the heart—from one another.

The man had a history of Hashimoto's, an autoimmune disease that causes inflammation of the thyroid gland located in the neck, and preexcitation syndrome, a heart disease in which the heart's ventricles are activated too early.

However, he had no history of reddish or dark-blue spots on the skin, known as angiokeratomas, numbness or tingling sensations in the hands or feet, blurry vision, or excessive sweating, called hyperhidrosis. All are typical symptoms of Fabry disease.

Urine tests revealed an excess of proteins and the presence of red blood cells. The kidneys appeared normal in size, but a kidney biopsy revealed the presence of foamy podocytes, a type of cells in the kidneys that wrap around blood vessels to help filter waste and fluid from the blood.

The podocytes also contained myelin bodies, known as zebra bodies, a hallmark of Gb3 buildup in cells. These findings were consistent with nephropathy, or damage to the kidneys, caused by Fabry disease.

Further testing revealed low alpha-Gal A activity in white blood cells, and high levels of Gb3. Genetic testing revealed a mutation in the GLA gene, c.902G>A (Arg301Gln), that has been linked to late-onset Fabry disease, which generally manifests after the age of 30. Based on this information, a Fabry diagnosis was made.

Read full story: bit.ly/Early-ERT

Fabry can take a hike

Brothers get rare opportunity to complete 17-mile Half Dome trail

By Cameron Zahn
FSIG Contributor

My name is Cameron, age 39, and my brother Cory is 35. We're from Lubbock, TX. My brother and I have lived with Fabry disease our whole lives. Several family members also have it—our mother and aunt, our Granny, and several others who are not with us anymore due to Fabry.

We grew up managing the symptoms and challenges that come with this disease, and through the challenges, we have learned to cope with Fabry and find the good in it. By God's grace we have been fortunate to receive the infusion therapy since we were young children. Prior to the treatment getting FDA approval, Cory and I were sent to the National Institutes of Health for annual testing so doctors could learn more about the disease.

Our parents also took us there several summers to get looked at, in hopes we could get more help and not have to suffer as much as other family members did. We're fortunate that, outside of taking medication, we've been able to live somewhat normal lives and manage the symptoms.

It's because of this I would like to share an experience Cory and I completed together, to encourage Fabry patients. Cory and I have an annual tradition of going to a different national park together every summer to vacation with our families. This summer we planned to go to Yosemite National Park in California. and Cory got the idea to do something difficult while we were there.

We both love to hike, so we decided to enter the lottery

system for a permit to do the park's renowned Half Dome hike. This is not your average day-hike, but it's a hike that can be done in a day. When the time for our vacation arrived, we learned we had been chosen for the Half Dome!

This opportunity is somewhat rare, and we got to complete the hike on our last day of vacation... finishing out our already amazing experience with a bang!!

To start the day, we got up at 2:45 a.m. and drove an hour and a half into the park. We started the trailhead at 5 a.m., hiked to the top and made it back down at 6 p.m. This 13-hour hike took us 17 miles and 5,000 feet in elevation (ascending from 4,000 to 9,000 feet above sea level)! It was absolutely amazing and one of the greatest experiences of our lives, which I got to share with my best friend.

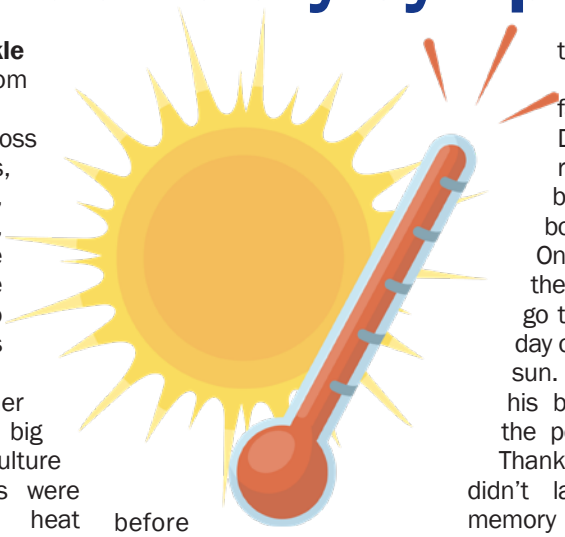
Afterward, Cory and I discussed how cool it would be to share this experience with the Fabry community—to let people know that even with this awful disease, life can still be good. We're grateful to God for providing us with great doctors and medicine to make an adventure like this possible.

Our uncle and three great-uncles did not get to benefit from these things, as no doctor even knew what was wrong with them or how to treat them. Even with Fabry being better known today, I still today have to educate doctors and people about it.

But moving forward, Fabry will no longer exist for our family—my wife and I have 2 boys, and my brother is about to have a new baby boy, which means we won't be passing our "X" chromosomes to the next generation. They will all be disease free.

When summer temperatures rise, so do Fabry symptoms

By Susanna VanVickle
FabryDiseaseNews.com



(May 28, 2024) Across America, ballparks, amusement parks, zoos, lakes, forests, and beaches come alive as people brave the beating sun to make memories outdoors.

These iconic summer pastimes were a big part of our family culture when my kids' lives were unencumbered by heat intolerance. However, gone are the days of being around a campfire on a warm summer night, stringing a clover chain that could encircle our house, taking long bike rides, or enduring blistering hours of coaster-riding at Six Flags Over Texas.

"Beating the heat" isn't possible for those with classic Fabry disease. As temperatures rise, so do headaches, stomach pains, and burning sensations in the hands and feet.

RELATED STORIES

Same mutation, different outcomes
Susanna shares part 3 of her family's Fabry story:
bit.ly/Fabry-Part3

Family connected through Fabry gene
Patti Phelps' husband died of Fabry before her daughter and grandson tested positive.
bit.ly/RHD-Connect

My oldest sons, twins Michael and Anthony, lived with Fabry symptoms long before being diagnosed, but thankfully the slow progression of the disease gave them the freedom to experience fun in the sun before it became intolerable.

As children, my boys spent long summer days on family land, wandering the swamp in knee-high waders. They loved playing at golf camps, selling lemonade, biking, and gathering throngs of neighbor kids to play football in the yard. For money, they could mow up to 25 lawns in a day, and for fun, they could stand for hours in the sun awaiting the high-speed twists and turns of the Batman or the Texas Giant roller coasters.

The joy of adventure outweighed the foot pains, the vomiting, the lightheadedness, and the other ailments for which we had no explanation.

As the twins entered their teen years, we were still clueless about the source of many of their "sicknesses," but Fabry was progressing and their symptoms were intensifying, especially in the summer.

Hypohidrosis, or an inability to sweat, makes heat unbearable for those with Fabry disease. Eventually, the boys' diagnosis shed light on the heat intolerance they were experiencing, but along the way there were a few clear markers that my sons were unable to handle summer temperatures.

An all-time favorite family trip was to San Diego in 2016. We relished time on the beach, and the older boys learned to surf. On our last evening there, we decided to go to church after a full day of riding waves in the sun. Michael passed out, his body crumpling over the pew in front of him. Thankfully, his blackout didn't last long, but the memory stuck with us. He was certainly beaten by the heat.

When Michael and Anthony turned 16 and got their driver's licenses, they were so eager to play chauffeur or run errands for their mama. With the power to drive also came the power to expand their business. They were excited to take on more and more lawns.

When the summer months came, however, they began to struggle with their landscape work. Dominic, their brother who does not have Fabry, worked like the Energizer bunny compared with the twins, who would get lightheaded regularly and need frequent breaks. My enthusiastic new drivers also started to wince when I asked one of them to run to the store. "How big is the parking lot?" was their common and unsettling question. They explained that walking across hot asphalt was torture.

Now, years into our Fabry journey, we're well aware of the correlation between sweltering temperatures and the misery they bring. My kids with Fabry have thus had to find ways not to "beat the heat," but to escape it.

Read full story:
bit.ly/Fabry-Temp

Patients report ongoing symptoms, treatments affect their quality of life

By Marisa Wexler, MS
FabryDiseaseNews.com

(May 24, 2024) Despite available treatments, many people with Fabry disease still experience symptoms that can affect their quality of life, a new study highlights.

The findings "may be helpful for healthcare providers and drug developers seeking to improve the care of patients with [Fabry disease] by addressing unmet needs," researchers wrote in the study "Patient-reported experience with Fabry disease and its management in the real-world setting: results from a double-blind, cross-sectional survey of 280 respondents," which was published in the *Orphanet Journal of Rare Diseases.*

The work was funded by Chiesi, which markets Elfabrio (pegunigalsidase alfa-iwxj), an enzyme replacement therapy (ERT) for Fabry that was approved in the U.S. in 2023, after this study was conducted.

The survey respondents ranged in age from 18 to 77 years, about two-thirds were female, and more than 80% were actively on treatment. Among patients on treatment, the vast majority were specifically taking the ERT Fabrazyme (agalsidase beta), while the rest were either taking the oral chaperone therapy Galafold (migalastat) or another ERT called agalsidase alfa which isn't available in the U.S. but is sold in Canada under the name Replagal.

The scientists noted that patients not on treatment were more likely to be female than male. This highlights "a need to address potential gender disparities to ensure equitable access to recommended treatment for all patients," the researchers said.

Read full story:
bit.ly/Fabry-QOL

Rare disease patients appeal to India PM for funding inclusion

By Melissa James
FSIG Contributor

In April, India's rare disease patient advocacy groups began publicly petitioning the prime minister and defense minister for sustainable funding inclusion the Bharatiya Janata Party's election manifesto.

The group sent a letter stating that rare diseases present a unique set of challenges, and cited chronic and ultra-rare diagnoses including LDSs like Fabry, Gaucher disease, Pompe disease and Neiman Pick disease.

The two-page letter noted that India's National Policy for Rare Diseases 2021 has been essential in providing a framework for support, which has created life-saving interventions and better outcomes for patients.

"These efforts have not only helped patients start their life-saving therapies but also provided hope and reassurance to countless families across the nation. However, the journey toward sustainable treatment support for chronic rare diseases remains a crucial next step,'' stated the letter. "The current budgetary provision of up to 50 lakh is only one-time, thereby hindering the process of saving lives for patients diagnosed with these conditions. Several patients across the Centres of Excellence have once again been put off life-saving therapies after the one-time support was exhausted,''

"Any delay in treatment poses serious risk to (rare disease) patient lives,'' said Manjit Singh, president of Lysosomal Storage Disorders Society of India, in an article from The Hindu news website.

Read full story: bit.ly/BJP-Funding

U.S. won't enforce copay aid, but may reclass drugs as 'essential'

Press Release
HIV+HEP Policy Institute

(April 2, 2024) As part of the final 2025 Notice of Benefits and Payment Parameters rule issued today, the federal government completely ignored the D.C. District Court decision that struck down the rule allowing insurers not to count copay assistance for prescription drugs as part of patient cost-sharing.

However, they do move to stop a new scheme that insurers and employers are engaged in: classifying certain drugs as "non-essential health benefits." In the final rule, CMS states that all covered drugs in excess of a state benchmark are essential health benefits.

The federal government has stated that it will issue a new rule pertaining to copay assistance and will not enforce the court ruling until then.

Meanwhile, in a positive note, the final rule ends the practice of "non-EHB" drugs in the individual and small group markets, and states that the Departments of Labor, Treasury, and HHS will issue a new rule to end this practice for large group and self-funded plans.

In the proposed rule, CMS stated that the practice of designating "non-EHB" drugs in these markets was not that widespread, but asked for input on how often this practice is being used.

Read full story: bit.ly/CopayAssist

Ruling increases patient access to meds

Press Release
HIV+HEP Policy Institute

(April 26, 2024) The Biden administration has issued a final rule that strengthens the implementation of the Affordable Care Act's nondiscrimination provisions, that when properly enforced, should increase patient access and affordability of prescription drugs.

In the final rule, the application of the law has been reinstated and even strengthened from the previous regulation to include health insurers and all HHS programs and activities, including Medicaid. For the first time, the regulation calls out PBMs, and states that their activities are subject to the rule as they relate to "their role of administering prescription drug benefits on behalf of payers, pharmacy benefit managers develop drug formularies and related policies, create pharmacy networks, reimburse pharmacies for patients' prescriptions, negotiate rebates and fees with drug manufacturers, process enrollees' claims and appeals, and review drug utilization, among other things."

The final rule also stresses that insurance marketing practices and benefit design are subject to the rule and describes certain practices that can be potentially discriminatory.

Read full story: bit.ly/Rx-Access

One third of Fabbers suffer lung ailments

(April 26, 2024) Nearly one-third of Danish patients in Fabry disease registries were found to have poor lung function, with obstructive airflow limitation most common among those with severe disease and smokers, a study found.

People with Fabry "frequently develop an obstructive airflow limitation," which is found "not only in smokers, but also in never smokers," researchers wrote. They urged caregivers to "be aware of the development of respiratory illness as part of the disease."

The study, "Respiratory impairments in patients suffering from Fabry disease–A cross-sectional study," was published in *Chronic Respiratory Disease*. Of patients in the study (54 women and 32 men), half were on ERT at the time, while the other half were not, either by indication or their own choice.

Read full story: bit.ly/Fabry-Lung

Study: Ozempic cuts kidney-disease risks

(May 25, 2024) New research has determined that he diabetes drug Ozempic reduces the risk of kidney failure and death in patients who have both Type 2 diabetes and chronic kidney disease. These findings were published Friday in the *New England Journal of Medicine.*

Compared with the placebo, patients taking Ozempic had a 24% lower risk of severe kidney outcomes and death from cardiovascular or kidney causes. The study was sponsored by Ozempic maker Novo Nordisk and presented at a European Renal Association conference in Stockholm.

The study also found that people taking Ozempic had a slower rate of kidney-function decline and an 18% lower risk of heart attack and other major cardiovascular events.

Read full story: bit.ly/Ozempic-KD

Heart disease still progresses on ERT

(June 21, 2024) More than a third of Fabry disease patients show signs of cardiac disease progression despite use of enzyme replacement therapy (ERT), according to a recent study.

An existing diagnosis of the heart disease, called left ventricular hypertrophy (LVH), was found to be the strongest predictor that a person would see cardiac progression over time. Being male and older were also linked to both cardiac progression and other Fabry disease-related adverse events.

Given the fact that male patients younger than 30 and women younger than 50 remained relatively stable over more than 10 years, researchers believe this might offer "a window of opportunity" to start treatment and effectively prevent the progression of organ damage in Fabry disease.

The study, "Fabry disease: development and progression of left ventricular hypertrophy despite long-term enzyme replacement therapy," was published in *Heart*.

When starting ERT (baseline), 22 patients had LVH. Over a median follow-up of 10.5 years, 22 people (36%) showed signs of an increasing left ventricular mass index (LVMI), which reflects that the left ventricle is starting to enlarge.

Read full story: bit.ly/Fabry-ERT

Higher inflammatory markers for Fabbers

(April 19, 2024) People with Fabry disease have higher-than-normal levels of three inflammatory markers in their blood, according to a recent study. The study, "Serum Neopterin, Biopterin, Tryptophan, and Kynurenine Levels in Patients with Fabry Disease," was published in the *Balkan Medical Journal*.

The first two inflammatory markers assessed were neopterin and biopterin. Neopterin is produced by cells of the immune system when they are activated, while biopterin is involved in the production of neurotransmitters and plays a role in maintaining immune system balance.

Results showed average levels of both these markers were significantly increased in Fabry patients. The ratio of neopterin to biopterin also tended to be higher in Fabry patients—which could indicate increased activity of the immune system or inflammation.

Read full story: bit.ly/Fabry-Markers

Fabry GLA gene mutations found in Parkinson's patients

(May 31, 2024) Researchers detected a mutation in the GLA gene, which is defective in Fabry disease patients, in people with Parkinson's disease, a study revealed.

Parkinson's patients who carried this mutation showed signs of Fabry, particularly affecting the heart and nervous system.The findings follow a previous report that found this same GLA mutation in people with Parkinson's. Unlike patients in this new study, however, patients in the previous study did not show Fabry signs.

The study, "Morbus Fabry and Parkinson's Disease—More Evidence for a Possible Genetic Link," was published in *Movement Disorders.*

GBA gene mutations are the most commonly known genetic risk factor for Parkinson's disease. However, little was previously known about a potential relationship between Fabry and Parkinson's.

Read full story: bit.ly/Fabry-GLA

FSIG

FSIG is a support group dedicated to dispensing information and encouraging mutual self-help as a means of emotional support.

FSIG was formed in 1996 by two Fabry patients and supportive family members with the hope that their particular understanding of this disease, combined with experience gathering information and working with doctors could benefit others.

FSIG is a nonprofit, tax-exempt organization and relies on charitable contributions to provide services to those with Fabry disease, their families and supportive others. Donations may be sent to the address below.

Please feel free to make copies of the FSIG Newsletter to share with your family, friends and others. We encourage anyone interested in FSIG or the newsletter to contact us so we can make sure you receive the next issue.

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Report: Vericiguat improved heart function in Chinese Fabry patient

By Andrea Lobo, PdH
FabryDiseaseNews.com

(May 3, 2024) A 69-year-old man diagnosed with Fabry disease who developed heart failure, high pulmonary arterial pressure, and heart microcirculation dysfunction saw his symptoms ease after treatment with vericiguat, according to a case reported in China.

Vericiguat, which is sold as Verquvo, is an oral medicine that's approved in the U.S. and other countries for adults with chronic heart failure and reduced ejection fraction, which is the amount of blood the heart pumps out to the body in each beat. It's a guanylate cyclase stimulator that relaxes blood vessels to improve heart function.

The case was reported in "Vericiguat improves cardiac function and microcirculation of a male patient with Fabry disease: A case report" in the *Annals of Noninvasive Electrocardiology*. According to the researchers, "[Fabry disease] patients with confirmed coronary microvascular dysfunction might benefit from treatment with vericiguat."

Read full story: bit.ly/Vericiguat

Adeno-associated virus gene therapy revolution faces two major hurdles

(April 5, 2024) In a review from Signal Transduction and Targeted Therapy, researchers presented recombinant adeno-associated virus (rAAV)-based genetic applications to treat human diseases.

News-Medical.Net reported on the review, explaining that adeno-associated virus (AAV) is a crucial component of clinical gene therapy due to its low pathogenicity and capacity to generate long-term gene expression in various tissues. It went on to describe how Recombinant AAV (rAAV) is designed to increase specificity and can cure several illnesses.

However, there are concerns about the safety of high-dose viral therapy, as well as immune responses and side effects. The article said that researchers prefer AAV vectors due to their broad tissue tropism, high safety profile, and adaptability in manufacturing procedures. Further research could assess vector immunogenicity, dosage optimization, and long-term safety.

Read full story: bit.ly/GT-Rev

Before any treatment starts, ensure GLA gene mutation actually Fabry

(July 19, 2024) It's critical to conduct thorough clinical evaluations to determine whether a newly identified mutation in the GLA gene is actually causing Fabry disease—before initiating treatment in patients.

That's the message highlighted in a report from Italy describing the case of a woman now in her early 40s whose GLA mutation, years after starting treatment, was found to likely not be pathogenic, or disease-causing.

The woman was initially treated for Fabry when the GLA gene mutation was identified, even though she had no signs of the rare condition. There also were no symptoms of Fabry found in the patient's father, from whom she inherited the genetic change.

"This case underscores the importance of a comprehensive evaluation of new variants of unknown significance to establish their pathogenicity accurately," researchers wrote.

The report, "No evidence of Fabry disease in a patient with the new p.Met70Val GLA gene variant," was published in the journal *Molecular Genetics & Genomic Medicine*.

Read full story: bit.ly/GLA-confirm

What's so promising about AL01211 oral therapy?

By Lindsey Shapiro, PhD
FabryDiseaseNews.com

(June 5, 2024) AL01211 is an experimental substrate reduction therapy that's being investigated for the treatment of Fabry disease. Developed by AceLink Therapeutics, it's intended to slow or prevent organ damage by reducing the levels of fatty molecules that accumulate to toxic levels inside cells.

Relative to other therapies in its class, AL01211 is designed to be more specific for the tissues affected in Fabry disease, such as the heart and kidneys, while avoiding the brain, where it could cause side effects.

AL01211 has been granted orphan drug status for Fabry disease in the U.S., a designation that's intended to provide incentives to speed its clinical development. The therapy is also being developed for the treatment of type 1 Gaucher disease, another condition where fatty molecules toxically accumulate to cause organ damage.

According to AceLink, relative to other SRTs, AL01211 is more potent and exhibits strong penetration into tissues affected in Fabry, such as the kidneys and heart, but has low penetration in the brain. This should help avoid side effects associated with SRT activity in the brain.

In an ongoing Fabry disease clinical trial, AL01211 is being administered as once daily oral capsules at a dose of 30 or 60 mg. Oral doses ranging from 2 mg to 60 mg have been tested and found safe in healthy adults.

To date, the safety of AL01211 has been established in Phase 1 trials involving healthy adult volunteers. Data from a Phase 1 trial (NCT04908462) showed that single (up to 60 mg) and multiple (up to 30 mg for two weeks) doses of AL01211 were well tolerated with no serious side effects. The treatment also dose-dependently reduced levels of Gb3 and related molecules.

At a 30 mg dose, blood levels of GCS and Gb3 were reduced by 78% and 52%, respectively, compared with the beginning of the study.In another Phase 1 trial (ChiCTR2200061431), the treatment was similarly found to be safe and well tolerated with favorable pharmacological properties in healthy adults.

An ongoing open-label Phase 2 trial (NCT06114329) is testing AL01211 in about 16 men with classic Fabry disease, its most severe form, ages 18-60, who've never before received a Fabry disease-specific treatment.

Participants will receive AL01211 (30 mg) taken orally once per day for an initial period of 26 weeks, or about six months. Should preliminary data show good safety, a higher dose group (60 mg) will also be enrolled. The initial six-month period will be followed by an extension phase, where all will continue treatment for up to two years. While safety is the study's primary outcome measure, disease biomarkers and other measures of Fabry disease symptoms and severity will also be evaluated.

Read full story: bit.ly/Fabry-AL

FDA gives LA-GLA monthly injection orphan drug status

LA-GLA can represent a significant advancement with its once-monthly subcutaneous injection regimen, addressing many of the limitations of first-generation therapies.

Read full story: bit.ly/GC-Bio

Relay Therapeutics plans new Fabry treatment

By Andrea Lobo, PhD
FabryDiseaseNews.com

(June 14, 2024) Relay Therapeutics said it expects to start clinical development of its treatment candidate for Fabry disease in the second half of 2025.

The program in Fabry disease, together with other programs under development for another genetic disease and solid tumors, were disclosed in a June 6 event, "New Program & Platform." A replay of the webcast and supporting materials are available on the company's website.

Using its Dynamo platform, Relay was able to create a non-inhibitory chaperone to stabilize the alpha-Gal A protein without inhibiting its activity, allowing greater clearance of Gb3 from tissues in people with Fabry. Chaperones are proteins that assist in the correct folding of larger proteins such as alpha-Gal A.

According to Relay, the molecule could be a potential chronic treatment for people with Fabry disease, either alone or in combination with enzyme replacement therapy one of the mainstay treatments for the condition.

Dynamo works in three steps, the first involving understanding the target protein structure and identifying novel binding sites for new therapeutic agents that could modulate a protein's behavior without affecting its function.

Next, researchers transition to identify a chemical starting point to develop a lead compound, which then is optimized to obtain a molecule that has the most adequate characteristics regarding selectivity, potency, bioavailability, and drug-like properties.

Relay was founded eight years ago.

Read full story: bit.ly/Fabry-Relay

Generic Galafold gets tentative approval

Press Release

(April 1, 2024) Lupin Limited announced that it has received tentative approval from the United States Food and Drug Administration (FDA) for its Abbreviated New Drug Application for migalastat capsules, 123 mg, to market a generic equivalent of Galafold capsules, 123 mg of Amicus Therapeutics US LLC.

This product will be manufactured at Lupin's Goa facility in India. Migalastat capsules are indicated for the treatment of adults with a confirmed diagnosis of Fabry.

Read full story: bit.ly/Lupin-App

Awareness month spotlights Fabry patients, supporters

By Mary Chapman
FabryDiseaseNews.com

(April 5, 2024) Fabry Awareness Month, which is marked every April to draw attention to Fabry disease, is shining a light on the "heroes" who are living with the disease and those who support them.

The month's activities seek to heighten awareness among the general public, as well as among researchers, health professionals, industry representatives, public authorities, and lawmakers.

This year, the nonprofit Fabry International Network (FIN) is reprising its #FabryHeroesMonth campaign to celebrate patients and members of their support systems.

"This April—during Fabry Awareness Month—we want to celebrate the support system of the individuals living with Fabry," the organization states on a webpage. "They might not always be facing the disease themselves, but can also be true superheroes."

Throughout the month, the nonprofit plans to spotlight Fabry's heroes on its social media platforms and asks campaign supporters to follow suit.

To join and promote larger discussions around Fabry, patients are also encouraged to share on social media their own stories of hope and resilience.

"She always goes above and beyond to make me feel welcomed, heard and comfortable during my treatment," Gina, 33, a patient in Japan said of her nurse on a FIN Facebook post. "She's the key person in my medical team and has been with me through all of my good and bad days. I don't feel like a number for a second and I'm so thankful for her."

Elsewhere, the Fabry Support & Information Group will present its 11th Annual Virtual Fun Run & Walk from April 27 to May 4 to coincide with Fabry Awareness Month. The goal is to raise $12,000 to support the nonprofit, which provides a variety of resources for patients and their families.

"The Fabry Fun Run is a one mile jog or stroll in your neighborhood or anywhere safe," notes the organization on the event webpage. "Since the pandemic, the event has been held virtually which has allowed people from all over the United States to participate.

This non-athletic, non-competitive event has helped to raise awareness, honor the families affected by Fabry disease and also remember those we have lost."

Read full story: bit.ly/Fabry-Heroes

Holla Vodka founder raises Fabry profile

(May 28, 2024) Patrick Shorb, co-founder of Holla Vodka, grew up as an active teen. He swam for his high school but always suspected he had a health issue. In an interview with AOL, he described the familiar nerve pain in his hands and feet, as well as temperature intolerance.

But at age 20, while a student at Penn State, he was diagnosed with Fabry. He began receiving ERT infusions hours away each week at Johns Hopkins Hospital in Baltimore, Maryland, but after two years was able to start on an oral therapy.

"Now I take a pill every other night, and that has totally changed my life," he told AOL.

Fighting Fabry for most of his adult life gave Shorb a new perspective on life and a desire to take things less seriously, reported AOL.

He said one of his goals from owning a business was giving back. This summer, Holla Spirits agreed to make a donation to Uplifting Athletes for every bottle of its watermelon lollipop-flavored vodka sold during June, July and August.

Since its inception, Uplifting Athletes has raised more than $9 million by engaging athletes in order to positively impact the rare disease community through driving action, awareness and funding research.

Read full story: aol.it/3Sk4P8q

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AMT-191 Fabry gene therapy maker sells genetics plant in Massachusetts

PRESS RELEASE

(July 1, 2024) -- uniQure N.V., a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today announced that it has entered into an agreement for the sale of its global manufacturing facility in Lexington, Massachusetts, to Genezen, a leading contract development and manufacturing organization specializing in the supply of retroviral vectors, lentiviral vectors, and adeno-associated virus (AAV) technologies.

Genezen agreed to acquire uniQure's commercial-scale gene-therapy manufacturing facility for total consideration of $25 million. Under the proposed transaction, Genezen will be responsible for manufacturing global commercial supply of HEMGENIX® for CSL and providing development and manufacturing services to support uniQure's investigational gene therapies.

Learn more: bit.ly/uniq-sale

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