SUMMER 2025

INSIDE

FSIG Connection

News from the Fabry Support & Information Group

GENDER & ETHNIC DISPARITY IN FABRY

Attitudes on treatment vary by gender

By Marisa Wexler, MS
FabryDiseaseNews.com

(March 20, 2025) People with different lysosomal storage diseases have varying beliefs about prescribed medicines, which reflect their current medical needs, a study has found. Particularly, attitudes toward treatment in Fabry disease vary according to gender and are different in Fabry and other related disorders.

According to researchers, these beliefs should be considered in personal counseling and when creating new treatments.

The study, "Treatment Beliefs Reflect Unmet Clinical Needs in Lysosomal Storage Diseases: An Opportunity for a Patient-Centered Approach," was published in *JIMD Reports*. In this study, researchers in the Netherlands wanted to explore attitudes toward treatments for people with different types of lysosomal storage disorders.

The researchers conducted a survey of people with Gaucher, Fabry, or caregivers of people with Sanfilippo syndrome.

As part of the survey, participants answered a series of questions that ranked their attitudes toward treatment on two scales: necessity, rating how much they felt they needed treatment, and concern, how worried they were about treatment having side effects or not working well.

In Fabry disease, there was a division based on gender.

See ATTITUDE, Page 2

Fabry underdiagnosed in UK ethnic minorities

By Steve Bryson, PhD
FabryDiseaseNews.com

(Feb. 13, 2025) Fabry disease is underdiagnosed across different minority ethnic groups in the U.K., a study suggests.

Despite making up about one-fifth of the population of England and Wales, less than 10% of those who received a Fabry diagnosis were ethnic minorities, compared with 90% of the white population.

"Further research should be performed to identify why this may be the case and to ensure that any barriers to the diagnosis of [Fabry] in minority ethnic groups can be identified and overcome," the researchers wrote. The study, "Underdiagnosis of Fabry disease in minority ethnic groups," was published in *Molecular Genetics and Metabolism Reports*.

Fabry affects both men and women across different ethnicities. Its estimated prevalence is about 1 in 1,000 to 9,000 people worldwide.

See ETHNIC, Page 2

Sex-specific inflammation points to heart disease

By Lindsey Shapiro, PhD
FabryDiseaseNews.com

(March 27, 2025) Distinct groups of inflammatory proteins may contribute to the progression of heart problems in men and women with Fabry disease, a study suggests.

While men exhibited a profile associated with a strong pro-inflammatory response, women had a profile that could be linked to accumulating scar tissue. The identified markers may be useful for detecting cardiac problems in Fabry patients early and the findings suggest anti-inflammatory treatments may help slow cardiac progression.

Heart disease is a common symptom of Fabry. Hypertrophic cardiomyopathy (HCM), where the heart muscle becomes abnormally thick and the heart has a harder time pumping blood, is particularly common. But there are sex differences in Fabry-related heart disease, with data suggesting women are typically affected at a later age than men.

See HEART, Page 3

WELCOME

Dear Friends,

This month, we're focusing on the gender and ethnic disparities in Fabry disease—issues that continue to delay diagnosis and limit care, especially for women and communities of color. Women are still battling outdated myths about being "just carriers," while people of color face barriers rooted in both access to care and lack of provider awareness. It's a conversation we must keep having, and more importantly, take action on.

We're also excited to introduce a new section: Fabry Provider Spotlight, where we'll highlight the dedicated professionals working to advance care and equity in our community.

Let's keep pushing for awareness, understanding, and change—together.

Jack

Jack Johnson, Executive Director

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ETHNIC: continued from p. 1

This is likely an underestimate of its actual prevalence, however, due to inherited mutations associated with milder and later-onset forms of Fabry.

Minority ethnic groups do face challenges in accessing healthcare, likely the result of a variety of factors, including cultural differences, language barriers, historic abuse in healthcare and research, and fear of discrimination. Such inequalities can lead to poorer health outcomes.

Fabry occurs across all demographic and ethnic groups, but the frequency of ethnicities with Fabry in the U.K. hasn't been assessed, leading scientists at the University of Birmingham to analyze the self-reported ethnicities of patients using two different sources: the University Hospitals Birmingham and the Society for Mucopolysaccharide Diseases (MPS Society).

Because UHB data contained 17 ethnicities and MPS data contained 20, the team grouped them into five categories: white, South Asian, Black, mixed, and other ethnic backgrounds.

Among the 123 cases in the UHB group, 111 (90%) patients described their ethnicity as white, five (4%) as South Asian, one (1%) as Black, two (2%) as mixed, and three (2%) as belonging to another ethnicity. One patient didn't disclose an ethnicity. Overall, 9% of UHB patients were classified as minority ethnic.

Likewise, of the 416 (81.5%) MPS Society members who provided their ethnicity, 387 (93%) identified as white, 17 (4.1%) as South Asian, three (0.7%) as Black, four (1%) as mixed, and five (1.2%) as other. Here, 7% were classified as minority ethnic.

However, 18.3% of the population in England and Wales are minority ethnic, and that figure rises to 23% in the West Midlands, where most of the UHB group lives. Birmingham is a diverse city where citizens from minority ethnic backgrounds make up more than half (51.4%) the population.

"The results demonstrate a lack of diversity within both cohorts, which suggests [Fabry] is potentially underdiagnosed in minority ethnic groups," wrote the researchers, who offered the explanation that common and well-characterized disease-causing mutations seen in white populations may not be found in minority ethnic populations. Moreover, the limited data regarding the manifestations of Fabry in minority ethnic populations may complicate interpreting any genetic test results. Also, certain ethnic communities may be more reluctant to join patient organizations and registries.

"Underdiagnosis poses a risk to patients, therefore overcoming barriers to diagnosis in minority ethnic groups is necessary," the researchers wrote.

Read full story: bit.ly/Fabry-Minorities

ATTITUDE: continued from p. 1

In female Fabry patients, the scores for necessity were more evenly spread out compared to other groups, with most leaning toward high scores. Most had low concern about the medicine, but more of them had concerns compared to those with Gaucher disease.

In male Fabry patients, the high necessity and low concern scores were similar to those in Gaucher disease, but 27% had high concern scores—meaning patients felt they needed treatment but also had substantial worries about treatment.

Fabry disease is generally more severe in males because the mutation causing it affects a gene on the X chromosome. Biological males have only one X chromosome whereas biological females have two, so females usually have a second healthy copy of the gene that can compensate somewhat.

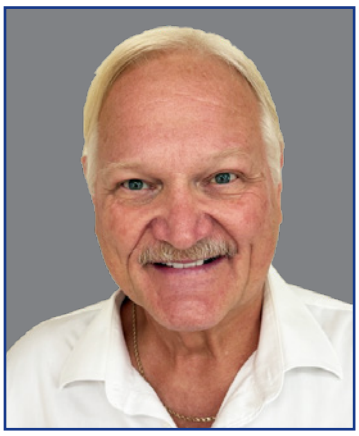
Overall, the attitudes of people with different types of lysosomal storage disorders lined up with the availability of effective treatments, with Gaucher on one extreme, Sanfilippo on the other, and Fabry falling in between. As such, the researchers said the questionnaire used in their survey, called the Beliefs about Medicines Questionnaire (BMQ), "realistically represented the differences in how well medical needs are currently met for different" lysosomal storage disorders.

"We argue that tools such as the BMQ can and should be used to take an individual's preexisting beliefs into consideration during counseling on therapeutic options and to align novel therapy development with a nuanced view of patients' perspectives," the scientists wrote.

Read full story: bit.ly/Fabry-Gender

Q&A with Myrl Holida, retiring Fabry specialist

Myrl Holiday is a physician assistant who initiated the Fabry disease research program at University of Iowa. He retired in March from the university's Medical Genetics, Lysosomal Storage Disorders, division.



Q: What inspired you to pursue a career in healthcare, and what drew you to Fabry? My career choice was simply random. I joined the Army National Guard to help pay for college and was an EMT trained medic. I attended the Military Physician Assistant School and subsequently accepted a position in pediatric bone marrow transplant at the University of Iowa, where I worked for 15 years. I later moved to general pediatric oncology, which included hematology and sickle cell disease management.

A pediatric hematologist/oncologist who I worked for brought in the phase III Fabrazyme trial in 1998, and I was recruited to assist. After FDA medication approval in 2003, I started patients on enzyme replacement therapy.

In 2009, the Fabrazyme drug shortage occurred at about the same time that the physician I worked for left the university. We were the only treaters for Fabry disease, so it fell on me to take it on, which I gladly did. I found Fabry disease to be intriguing and felt I could have an impact. I found satisfaction in treating families and helping patients find the answers to their symptoms. Helping them solve the problem was rewarding.

Q: Can you describe a particularly challenging case that shaped your approach to Fabry? Some patients said they "felt fine" and didn't want therapy, even with evidence showing that they had organ damage that would later cause problems. Despite my recommendations, I was not able to convince them to begin therapy, and they either suffered heart issues or stroke, which may have been preventable. Unfortunately, this is still an ongoing problem of disease denial.

Q: What advancement in Fabry research/treatment got you most excited? I think gene therapy is appearing to be safe and effective, although the jury's still out. This is like implanting a constant infusion enzyme replacement pump. Other forms of gene therapy, which incorporate a mini transplant and induce cells throughout the body to produce enzyme mimicking a more "normal" production of enzyme with minimal risk, may be more physiologic.

Q: How do you handle conversations about treatment options with Fabry patients? I try to be objective and describe the general progression of Fabry disease if left untreated, compared with those who undergo treatment. My favorite part of the job has been interacting with the patients and seeing comfort and knowing that they were being cared for.

Q: Why is there such a need for young doctors to get involved in programs like yours? Fabry disease remains relatively unknown. There should be more emphasis on including Fabry disease in the various symptoms that occur. A lot of young doctors are aware of the disease, but they have never seen a patient with Fabry or treated one.

Q: If you could get Fabry patients to follow one piece of advice, what would it be? Choose a primary doctor not for their knowledge of Fabry disease, but for your perception that they care about you. If that is true, they will learn about Fabry disease and give you better care. Also, always take a list of questions with you to your appointments.

HEART: continued from p. 1

Moreover, while men characteristically develop progressive HCM with eventual fibrosis, women sometimes develop early fibrosis before overt HCM develops. It's been proposed that inflammation in response to the buildup of fatty molecules may play a key role in Fabry disease progression, including contributing to cardiac damage. This raises the possibility that circulating inflammatory biomarkers could have potential in early screening for cardiac involvement in Fabry patients, said the scientists, who measured blood levels of inflammatory molecules called cytokines in adult Fabry patients and healthy people as part of an observational clinical study (NCT04724083). They also looked at certain growth factors that can drive remodeling of cardiac tissue that contributes to HCM.

The analysis included 45 Fabry patients (21 men, 24 women), of whom 28 had HCM. Twenty healthy people, 10 men and 10 women, served as controls. While heart disease is generally considered to affect women at a later age, early-onset HCM was not uncommon in the study group. The youngest female with a mild form of HCM was 22 and the youngest male was 21.

"Thus, the early detection of HCM in females with [Fabry disease] is crucial for effective disease management," the researchers wrote. Biomarker analyses suggested that Fabry patients had differences in inflammatory markers from healthy controls, with distinct profiles in male and female patients. Various biomarkers were also specifically associated with HCM, again with sex-specific differences.

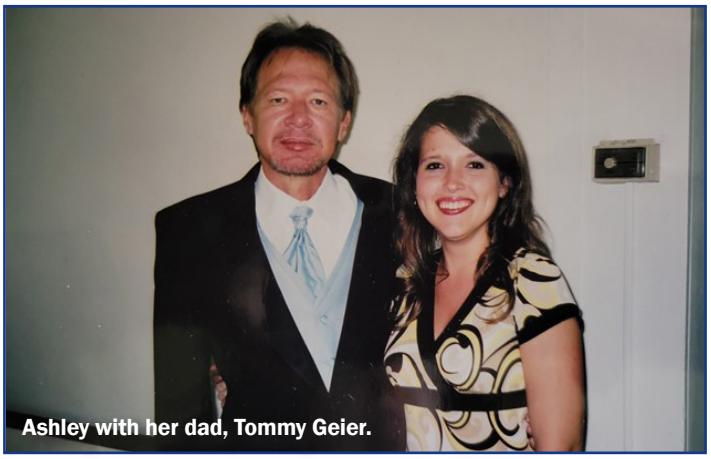
Overall, the biomarker profile in men with HCM suggested activation of the inflammatory NFkB signaling pathway, with markers such as IL-10, IL-2, GM-CSF, and VEGF-A being implicated. This reflects that significant inflammation drives cardiac tissue remodeling that promotes HCM progression in men, said the researchers.

On the other hand, women with HCM showed an inflammatory marker profile consistent with activation of the TNF-alpha, TNFR2, and TGF-beta signaling cluster, which may be related to fibrosis development. This may help explain why women with Fabry often show fibrosis early in the course of cardiac disease.

Read full story: bit.ly/Fabry-Profiles

Diagnosed thanks to a piece of gum

By Ashley Rowland
Fabry Patient


Ashley with her dad, Tommy Geier.

To most people who see me, I probably look like a normal almost-40-year-old woman. In many ways, maybe I am. I love my family, horses, coloring, drawing and writing. Sometimes I say the right thing, and sometimes I don't.

Those who don't know me well are always surprised to learn that I also have Fabry. Of course, that's after I explain what Fabry is. Just like my maiden name, no one has heard of it unless they've known someone with it.

For me, though, Fabry has been a big part of my life for the past 35 years—so it's difficult to sum up my story in one article.

My Fabry journey started when I was five. Thanks to a piece of bubblegum my mom held up from across the room (that I couldn't make out), Mama guessed I'd inherited her near sightedness. She took me to an ophthalmologist. When he used the slit lamp, he saw that I had corneal whirling. Luckily, he knew this was a possible indication of Fabry.

He started asking Mama questions: How many children did she have? What were their genders? How many siblings did Daddy have? He evaluated all of us, and thanks to him, we found Fabry in my family in time to begin treating Daddy and my uncle Rick for kidney failure. Rick also had a daughter, so I wasn't the only female in the family with Fabry.

Much of what I consider part of my story is wrapped up in those years, when the focus wasn't even on me. Back then, many still believed that females were only carriers with possible symptoms. My cousin didn't seem to have any symptoms at the time, but I struggled with neuropathy throughout my childhood. The closer I came to adulthood, the more my gastrointestinal symptoms became prevalent.

By the time I graduated high school, the medical field understood that females were not merely carriers, and that the severity of the disease could range from mild to severe. Also by then, my uncle already had passed away, and my dad had struggled with many symptoms and surgeries and studies. But enzyme replacement therapy (ERT) had been developed, and Daddy started treatment in 2003. I followed the summer of 2004.

I still struggled with some symptoms—neuropathy, stomach upset and pain, tinnitus, fatigue, vertigo, etc.—but my kidneys and heart were doing well. My dad passed away in 2015 from an embolism a few months after heart surgery. He was 58. It may sound odd to some people, but I'm thankful he made it to that age. Before ERT existed, doctors could only treat one problem at a time, and Daddy didn't expect to live past about 48. But he gained another decade because of treatment.

Things changed for me some after Daddy passed. It felt like all eyes turned to me. My family and friends knew why he was gone, and they knew I had the same disease. We were hopeful my road would be much easier, because I'd been on treatment from a young age. But there were still unknowns. Treatment helped many symptoms, but what were the long-term issues, such as impact on the brain? Those things that had not been studied in Fabry patients because they died so young.

In January 2019, I began an oral medication for a drug trial. I'm still on that study and wish my dad could have seen it. For years, he and others like him participated in drug studies that were invasive and expensive, with no real hope of the results helping him personally. His hope was that I and any children I might have would benefit.

I wasn't blessed with children of my own, but I have benefited from his sacrifice. Since being on this study, my symptoms have improved drastically. I still get tired and occasionally must run to the bathroom, but it's nothing like it was before. And my kidneys and heart are ticking along just like they should.

I read this newsletter with the new developments happening all the time and remember where we started. I'm so hopeful for the future. I wish Daddy could have seen this, but I'm also thankful for the time my story has spanned.

The heaviness of a shorter life expectancy due to Fabry

By Susanna VanVickle
FabryDiseaseNews.com

(Feb. 4, 2025) For many Fabry patients, the risk of premature death brings with it a sense of heaviness. Not all patients feel the ponderousness of a shorter life expectancy; I know I don't. Still, it's a reality that can be burdensome.

If I could go back to the beginning of our Fabry story, I'd be more attentive and careful not to sow fear of death. My kids must've heard me say over and over that our disease is progressive, irreversible, and can lead to organ failure.

Of course, I couldn't completely shelter them. My sons were in the room when a doctor asked about our family history and eliminated the possibility of my dad having Fabry because he was still alive at 78.

Read full story: bit.ly/Fabry-Heavy

Completing college and living full lives with Fabry

By Susanna VanVickle
FabryDiseaseNews.com

(March 4, 2025) Two friends and I recently left the warmth of Texas to brave the snow and freezing temperatures of Kansas, where the three of us have sons at Benedictine College. The campus hosts a mother-son (and father-daughter) event, with a cocktail hour, a fine dinner, and a dance. It was a fantastic opportunity to spend quality time with my sons Anthony and Dominic, and I loved every minute.

Spending eight hours behind the wheel each way afforded me lots of time for reflection—specifically on my sons and their lives in college. Anthony is a senior business accounting major while Dominic is a junior in business management. Soon they'll be stepping into the world as adults, and as cliché as it sounds, it seems like just yesterday that they were taking their first wobbly steps.

Anthony was the first in my family to be diagnosed with Fabry disease. In many of my columns, I've referenced that fateful day in 2019, when the heavy news of this rare disease landed on his broad, young shoulders.

To free their bodies of Gb3 buildup, Anthony (and his twin, Michael, who also has Fabry and attends another college) needed to begin enzyme replacement therapy as soon as possible. We had no idea what the rest of high school would look like for Anthony. We had no idea how inhibitory his treatment regimen would be. We questioned whether Anthony would be able to live a "normal" life.

Fast-forward five and a half years, and I was driving to spend time in Atchison, Kansas, where Anthony's been thriving for almost four years now. When I arrived, Anthony walked over and joined me in my room for a hot cup of coffee before Dominic picked us up for dinner with a group of college friends and their parents.

After dinner, Anthony insisted on taking us out to a favorite hangout, O'Malley's 1842 Pub. Throughout the night, it seemed that every college kid or parent I met had something wonderful to say about my son Anthony. I delighted in the compliments as well as the live Irish music.

The next day, when Anthony stopped over again for coffee, he invited me to take a walk with him in the snow. As we walked along the river and through the town, Anthony shared about memories he's made, friends that he'll keep for a lifetime, opportunities for the upcoming year, hopes, dreams, big decisions, and hesitations. What a gift!

That heart-to-heart was priceless. Additionally, his words shed light on that question from almost six years ago. Anthony has been able to live a "normal" life.

The restrictions he faced after diagnosis didn't handcuff him because we learned so much more about Fabry. Anthony was free to live his fullest life despite his condition. Today, he looks forward to college graduation and beyond. And while Fabry is intrinsically written into Anthony's future, his is a future ripe with possibility and abundant life.

Read full story:
bit.ly/Fabry-College

From left, Dominic, Anthony, and Susanna VanVickle at O'Malley's 1842 Pub in Weston, Missouri.

How I answer when poeple ask, 'What is Fabry disease?'

By Susanna VanVickle
FabryDiseaseNews.com

(Jan. 28, 2025) When I'm asked for the hundredth time, "What is Fabry?" I might say something like, "We don't sweat." After that, I may or may not go into a longer explanation of the enzyme we lack, the accumulation of Gb3, and the long-term repercussions. Eyes always widen when I mention the big stuff like stroke, heart attack, and kidney failure.

Yet, despite that big stuff, the weight of Fabry for our family is in the small stuff.

The small stuff becomes heavy when my daughter says "I'll pass" to her favorite Christmas cookie because her stomach can't handle it. Or when my son cancels his weekend trip to a friend's wedding because of a Fabry pain flare-up. Or when heat intolerance prevents one of my kids from enjoying a golf game, a beach day, a long walk, or another summer activity. Or when headaches and feeling feverish mean missed school, workouts, parties, and dinners with friends. Or when many an evening finds a kid lying in bed because he feels too sick to do anything else.

It seems easier to say "We don't sweat" than to describe the small stuff. Likewise, it may be less taxing on the mind to accept the inherited malady as a whole than to confront the heaviness of Fabry's daily offenses.

Being a person who wrestles with worry, I understand the fear of being crushed beneath the weight of Fabry. Yet, I know there is hope, even when finding it is a hard-fought battle.

Read full story:
bit.ly/Fabry-Defined

KIDNEYS

Kidney biopsy can confirm, rule out Fabry when gene test inconclusive

By Margarida Maia, PhD
FabryDiseaseNews.com

(Feb. 27, 2025) A kidney biopsy can be important in diagnosing Fabry disease because it can confirm or rule out the condition when other tests like genetic analysis are inconclusive, according to a report detailing the case of a middle-aged woman in Italy.

For this woman, 55, the results helped guide proper treatment, the researchers noted.

However, the team stressed that relying on a kidney biopsy can have both "diagnostic value and potential pitfalls." In a second case described in their report, the researchers noted that, for a man of similar age, the findings of a kidney biopsy partially overlapped with those typical for Fabry disease. Other tests ultimately excluded its diagnosis for that patient, the team noted.

These two cases, the researchers wrote, illustrate kidney biopsy "as both a decisive tool and a potential source of diagnostic confusion." But for individuals suspected of having Fabry disease, a biopsy can in fact play a key role in making a diagnosis, the team noted.

The study, "The importance of a multidisciplinary approach in two tricky cases: the perfect match for Fabry disease," was published in *BMC Nephrology*.

Read full story: bit.ly/Fabry-Biopsy

AL01211 helps kidney function, pain in new trial

By Margarida Maia, PhD
FabryDiseaseNews.com

(Feb. 20 2025) AL01211 may help stabilize symptoms in men with Fabry disease, while easing pain and improving quality of life, according to interim results from a Phase 2 trial.

The trial (NCT06114329), underway at six sites in China, is primarily evaluating the safety of the Acelink Therapeutics treatment. AL01211 is being tested as oral capsules by mouth once daily at a dose of 30 or 60 mg in 18 men with classic Fabry who have never taken any approved medications for the disease. Secondary outcomes include the therapy's efficacy at easing symptoms, as well as its pharmacokinetics (how a drug moves into, through, and out of the body) and pharmacodynamics (its effects in the body).

"The interim results from AL01211 treatment are showing promising safety and efficacy trends, underscoring its potential to address critical gaps in Fabry disease treatment," Nan Chen, MD, the study's principal investigator.

Read full story: bit.ly/Function-Pain

Kidney function stable 5 years after gene therapy

By Steve Bryson, PhD
FabryDiseaseNews.com

(Jan. 30, 2025) Five years after receiving the experimental Fabry disease gene therapy AVR-RD-01, kidney function in all five participants remains relatively stable, according to the final results of the Canadian FACTs study, which tested the treatment candidate in men with the condition.

All five patients had significant and sustained increases in blood alpha-Gal A activity, an enzyme deficient in people with Fabry. At the same time, four of the patients showed a marked drop in blood lyso-Gb3, a biomarker that reflects alpha-Gal A activity.

The team of North American researchers noted that alpha-gal A activity "was observed at day 6-8 in each patient following infusion [of the gene therapy] and has remained durable for 5+ years," with "all 5 patients ... eligible to come off biweekly enzyme therapy." Three of the men did stop enzyme treatment, the researchers noted.

With these results, "we demonstrate that this therapeutic approach has merit, is durable, and should be explored in a larger clinical trial," the team wrote.

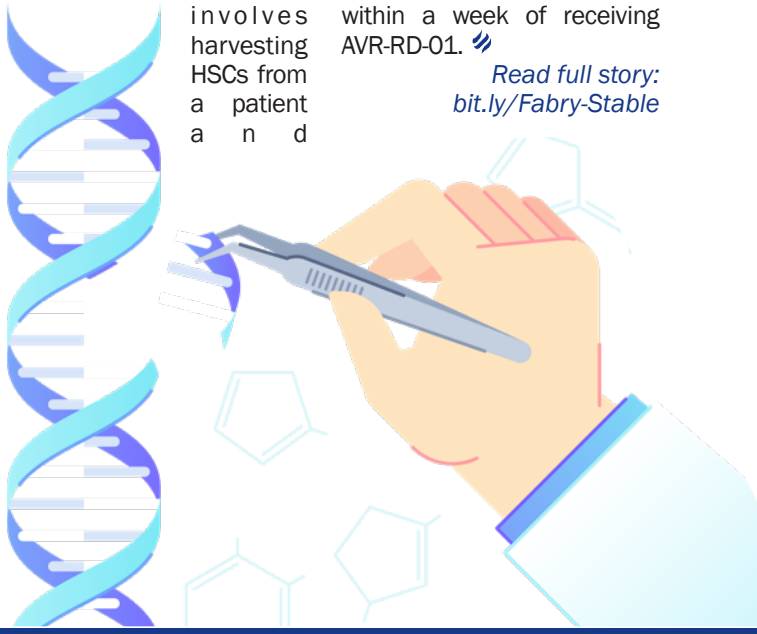
The study, "Lentivirus-mediated gene therapy for Fabry disease: 5-year End-of-Study results from the Canadian FACTs trial," was published in the journal *Clinical and Translational Medicine*.

AVR-RD-01 is a one-time gene therapy designed to deliver a working copy of the GLA gene to a patient's hematopoietic stem cells, or HSCs, which give rise to different types of blood cells. Treatment involves harvesting HSCs from a patient and exposing them to the viral vector used to carry the functional GLA gene. After a procedure to eliminate existing bone marrow cells, the modified stem cells are returned to the same patient via a transplant.

Canadian FACTs was a five-year Phase 1 trial (NCT02800070) that tested the gene therapy in five men, ages 29-48, with classic Fabry. All of the participants had been previously treated with enzyme replacement therapy.

Interim results reported in 2021 showed that alpha-Gal A rose to near-normal levels within a week of receiving AVR-RD-01.

Read full story: bit.ly/Fabry-Stable



HEART

Fabry may be underdiagnosed contributor to heart disease

By Lindsey Shapiro, PhD
FabryDiseaseNews.com

(March 13, 2025) The case of a South African man diagnosed with hypertrophic cardiomyopathy (HCM), a disease of the heart muscle, who was later found to also have Fabry disease, suggests the rare inherited condition may be an underdiagnosed contributor to HCM, per a report.

The researchers say this case "demonstrates the importance of screening for [genetic] variants in patients with apparent HCM."

The man's Fabry disease was found nine years after his HCM diagnosis, when genetic testing—not widely available in the region the patient lived—was ultimately done, highlighting "the role of research and humanitarian programs in clinical practice in resource-limited settings," the team wrote.

Reviewing his medical history, doctors found that the man had been experiencing other signs of Fabry disease for decades, but it wasn't until the genetic testing was performed that he was able to get the right diagnosis and treatment.

The case report, "Identification of an Ultra-Rare GLA Frameshift Variant in a South African Family With Hypertrophic Cardiomyopathy: A Case Report," was published in the journal *Cureus*.

Read full story: bit.ly/Fabry-HD

Fabry-related heart failure fixed by transplant

By Margarida Maia, PhD
FabryDiseaseNews.com

(April 17, 2025) A woman with heart failure due to late-onset Fabry disease received a heart transplant in combination with immunosuppressants and Fabrazyme (agalsidase-beta) to resolve her cardiac symptoms, which didn't recur after the transplant.

"Although the risk of disease recurrence in the transplanted organ appears to be relatively low, this observation requires further investigation with extended follow-up and a larger study sample," wrote researchers in Poland.

Their report, "Enzyme Replacement and Immunosuppression in Heart Transplant Recipients with Fabry Cardiomyopathy: A 7-Year Case Study," was published in the *American Journal of Case Reports*. Unlike classic Fabry disease, which manifests during childhood or adolescence, symptoms of late-onset Fabry disease don't start until adulthood, after age 30. They usually involve a major organ, such as the heart, as was the case of a 38-year-old woman with heart failure.

Read full story: bit.ly/Fabry-Transplant

Lomerizine may ease vascular symptoms in Fabry

By Andrea Lobo, PhD
FabryDiseaseNews.com

(April 24, 2025) Lomerizine—used clinically to treat migraines—helped ease vascular-related symptoms in a mouse model of Fabry disease, according to a new study from researchers in South Korea.

The drug, one of a class of medications called calcium channel blockers, which work to lower blood pressure, also improved the health and function of endothelial cells derived from people with Fabry. Endothelial cells line blood vessels, and play a key role in regulating blood flow.

The researchers found that lomerizine treatment improved the ability of endothelial cells to form new blood vessels, and also blocked mechanisms involved in the dysfunction of these cells. In the mice, lomerizine eased heart and kidney issues and improved heat tolerance and sweating.

The study, "Therapeutic effects of lomerizine on vasculopathy in Fabry disease," was published in the journal *Scientific Reports*.

Read full story: bit.ly/Fabry-Mouse

RELATED STORY
Oral RNA splicing drug treats cardiac Fabry
Read story: bit.ly/RNA-Splicing

Fabry commonly impairs blood flow to brain

By Steve Bryson, PhD
FabryDiseaseNews.com

(March 6, 2025) Mild to moderate cerebrovascular disease, which occurs when blood flow in the brain is impaired, is a characteristic brain signature in adults with Fabry, according to a new study.

Nearly half of those examined showed signs of white matter damage, for which impaired kidney function was the sole predictive factor. Also, more than two-thirds had signs of cognitive impairment.

Blood levels of neurofilament light chain a biomarker for nerve damage, may represent a potentially sensitive and easy test to perform for brain involvement in Fabry, according to the researchers. The study, "Prevalence and Clinical Correlates of Cerebrovascular Alterations in Fabry Disease: A Cross-Sectional Study," was published in *Brain Sciences*.

Read full story: bit.ly/Fabry-Flow

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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Sangamo closer to accelerated approval for ST-920 gene therapy

All patients given treatment in trial reach 1-year mark

By Margarida Maia, PhD
FabryDiseaseNews.com

(May 8, 2025) All patients who have so far received the gene therapy candidate ST-920 (isaralgagene civaparvovec)—being developed by Sangamo Therapeutics for Fabry disease—in a Phase 1/2 clinical trial have reached the one-year mark required by the U.S. Food and Drug Administration (FDA) before the company can take the next step toward accelerated approval.

That's according to a new update from Sangamo, which announced in a company press release that a "pivotal data readout" is expected by the end of June.

The FDA had already said that data from the ongoing Phase 1/2 STAAR trial (NCT04046224) could serve as the main evidence for accelerated approval, eliminating the need for additional clinical testing to confirm the benefit of ST-920 for Faby patients. This could shorten the time it will take for the therapy to enter the market.

In a Type B meeting with the FDA, Sangamo also received clear guidance on how to complete the next steps for manufacturing and quality—known as chemistry, manufacturing, and control plans—keeping the company on track to file a biologics license application (BLA) requesting the therapy's approval in early 2026. If all goes as expected, the gene therapy could become available in the second half of 2026, per Sangamo.

"We have a clear regulatory pathway to a potential approval decision for ST-920 and we continue to advance BLA preparation activities," said Nathalie Dubois-Stringfellow, PhD, Sangamo's chief development officer.

The company said a preliminary analysis of one-year data showed continued positive results with the experimental gene therapy.

Building on early data showing that ST-920 continues to maintain a positive slope in estimated glomerular filtration rate (eGFR)—an indicator that kidney function is improving over time—Sangamo is now planning to file the BLA at the start of next year.

Meanwhile, discussions with European regulators are underway for a similar application, according to the company.

Delivered as a single infusion into the bloodstream, ST-920 is designed to deliver a healthy version of the GLA gene to cells in the liver. This enables liver cells to produce a functional version of alpha-Gal A, which is expected to break down and clear the toxic fatty molecules, thereby easing Fabry disease symptoms.

The STAAR study is testing how safe and well tolerated ST-920 is in more than 30 men and women with a diagnosis of Fabry disease. Patients are being followed for 52 weeks, or one year. Then, they may enter an extension study (NCT05039866) to continue being monitored for up to a total of five years following dosing. The longest-participating patient may have completed more than four years of follow-up.

Read full story: bit.ly/Fabry-ST-920

AMT-191 trial to enroll 2nd patient group

By Patricia Inácio, PhD
FabryDiseaseNews.com

(Feb. 6, 2025) A U.S.-based Phase 1/2a clinical trial testing AMT-191, uniQure's gene therapy treatment for Fabry disease, has completed enrollment of the first patient group, and the company plans to start recruiting for the second group by the end of March.

Dosing in the trial began in August 2024. The trial's independent data monitoring committee (IDMC), a panel of external experts tasked with ensuring the safety of trial participants, reviewed data from the first two patients and didn't find any significant data concerns, uniQure said.

The panel recommended that the study continue enrollment and dosing of the second group, which will receive a higher dose of the therapy. The company expects to initiate recruitment for that second group by end of March at the two trial sites in New York and Fairfax, Virginia.

"We are encouraged by the initial pharmacodynamics [effects on the body], biomarkers and safety profile observed to date for AMT-191 as well as the positive outcome of the IDMC review," Walid Abi-Saab, MD, chief medical officer of uniQure, said in a company press release. "This strengthens our confidence in the potential of AMT-191 to make a meaningful difference in the lives of patients with Fabry disease. We look forward to advancing to the second [group] in this important clinical program."

AMT-191 is a single-dose gene therapy that uses a modified, harmless adeno-associated virus to introduce a working version of the GLA gene into liver cells. This is expected to promote the production of the missing enzyme, normalize levels of fatty substances, and ease Fabry symptoms.

The medication received orphan drug and fast track designation from the U.S. Food and Drug Administration (FDA) for Fabry disease.

The Phase 1/2 study (NCT06270316) is evaluating the safety, tolerability, and preliminary efficacy AMT-191 when administered directly into the bloodstream, in two groups of up to six men with Fabry disease, ranging in age from 18-50.

The first group is receiving a low treatment dose (60 trillion genome copies per kilogram, gc/kg) of AMT-191, while those to be enrolled in the second group will be treated with a high dose (300 trillion gc/kg).

Participants can continue to receive regular enzyme replacement therapy, which delivers a lab-made version of alpha-Gal A directly into the bloodstream, until criteria for withdrawal are met.

Patients will be followed for up to two years, and the therapy's exploratory efficacy will be measured by analyzing alpha-Gal A levels. The trial is expected to end in 2027.

Read full story:
bit.ly/Fabry-AMT-191

RELATED STORIES

Nanoliposomes pave way for new Fabry treatment option

MSN report that an international research team has developed a new therapy based on nanotechnology called nanoGLA for the treatment of Fabry disease. The new therapeutic solution has shown remarkable efficacy in preclinical studies. The study was published this December in *Science Advances*.

Read full story:
bit.ly/Fabry-Nano

AceLink presents Phase 2 trial data

AceLink Therapeutics, Inc., presented interim data from its ongoing Phase 2 clinical study of AL01211 in treatment-naïve, classic male Fabry disease patients. These findings were highlighted in a late-breaking oral platform presentation at the 2025 WORLD Symposium in San Diego, California.

Read full story:
bwnews.pr/4kHOXZe

Study: Galafold may work on newly found mutations

By Steve Bryson, PhD
FabryDiseaseNews.com

(April 10, 2025) Researchers discovered new mutations in the GLA gene, the underlying cause of Fabry, but noted that all of them may be amenable to Galafold (migalastat) chaperone therapy, an approved treatment to slow or prevent organ function decline in Fabry patients, a new study reports.

Clinical manifestations of these novel Fabry-causing mutations were detailed in the study. The researchers reported that each patient experienced involvement in multiple organs.

"This study further enriches the Fabry disease GLA mutation database and deepens our understanding of GLA mutations and the structure and function of the [Gal A] protein," the team wrote. Additionally, a model developed by the scientists may predict patients' responses to Galafold treatment, per the study.

The study, "Pathogenicity of novel GLA gene missense mutations in Fabry disease and the therapeutic impact of migalastat," was published in the *Journal of Advanced Research*.

Read full story:
bit.ly/Fabry-Galafold

Study: AI could improve Fabry diagnosis, care

By Lindsey Shapiro, PhD
FabryDiseaseNews.com

(May 1, 2025) Technologies using artificial intelligence (AI) have the ability to facilitate earlier diagnoses and better treatment for people living with rare conditions such as Fabry disease, according to a new review study by researchers in Europe.

In the study, the scientists discussed several ways AI has been applied in recent years to improve Fabry disease care.

Such approaches, the team noted, are also relevant for many other rare diseases, defined in the U.S. as those affecting fewer than 200,000 people, and in the European Union as having a prevalence of 1 in every 2,000 people.

"Patient diagnostic journeys may benefit from AI as these technologies may reduce the rate of misdiagnosis and shorten the period spent without appropriate medical care, thus lessening the psychological and physiological impact of disease," the researchers wrote. The team noted that "the large amounts of data available from [electronic health records], medical imaging (standardized images) and DNA sequencing allow for large-population and patient-centred approaches."

Their study, "Applying artificial intelligence to rare diseases: a literature review highlighting lessons from Fabry disease," was published in the *Orphanet Journal of Rare Diseases*.

"The longer the odyssey, the higher the risk of disease progression and health impairment, especially for the [approximately] 5% of rare diseases for which there is an effective and specific treatment," the researchers wrote.

One example is Fabry, for which there are available treatments—ones that, if initiated promptly, can prevent or slow the progression of organ damage.

Various types of AI are capable of analyzing large amounts of data and recognizing patterns and relationships much more quickly and accurately than the human eye.

In their review study, the scientists discussed some of the ways AI is being applied in rare diseases, focusing particularly on 20 studies related to Fabry disease as an example.

The team pointed out a few main ways AI has been used in Fabry research—including for screening electronic medical records to help identify undiagnosed Fabry patients who may have been overlooked.

The technology also has been used for analyzing large amounts of genetic sequencing data to detect gene mutations and determine if they're likely to cause disease.

Further, the researchers noted, AI-based tools can learn to recognize specific features of a rare disease in clinical tests and distinguish it from other conditions. Such tools may help clinicians to hone in on a diagnosis—and also aid in monitoring disease progression, determining prognosis, and making treatment decisions.

In Fabry, such approaches can be used to identify disease symptoms, such as characteristic facial features, and signs of heart disease and brain changes.

Looking forward, the scientists see several opportunities for using AI in the rare disease space to improve diagnosis and monitoring. These approaches will likely work best when the AI model evaluates and integrates several different disease features, per the team.

Ultimately, the use of these technologies could shorten the amount of time physicians need to look at clinical data, allowing them more time to focus on patient care. It could also make it easier for clinicians without expertise in rare diseases to participate in the diagnostic process and make appropriate referrals.

Read full story: bit.ly/Fabry-AI

FIN celebrating Fabry doctors during awareness month

By Marisa Wexler, MS
FabryDiseaseNews.com

(April 3, 2025) For Fabry Awareness Month this April, the Fabry International Network, or FIN—an alliance of 61 patient organizations in 57 countries—is shining a spotlight on doctors who have focused on caring for people with the rare inherited disease, helping patients better understand the disorder, get accurate diagnoses, and access treatments.

FIN has created a webpage (fabrynetwork.org/fabryheroes2025) highlighting the work of more than a dozen doctors worldwide who care for people with Fabry disease.

"These Fabry heroes have played a critical role in shaping the lives of countless patients and families, offering not just expertise but also compassion and hope," FIN stated on its website. "Through their dedication, they've helped build bridges between science and humanity."

The Fabry Heroes project is just one of the many initiatives marking Fabry Awareness Month, in which the community is aiming to educate others while generating support for people affected by the disease, and funding for research and care.

Read full story: bit.ly/Fabry-FIN

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FSIG would like to express our gratitude to the many physicians, health care professionals, researchers, scientists, and industry working on our behalf. Their efforts make a great difference for us all.

IN MEMORIAM

Former secretary general of U.S. Soccer Federation dies of Fabry

Hank Steinbrecher, who had a profound effect on American soccer as secretary general of the U.S. Soccer Federation for almost a decade, passed away on March 25 in Tucson, Arizona.

Steinbrecher, 77, had suffered from Fabry disease. He played a prominent role during a vital growth period for the federation in three major soccer tournaments the country hosted in the 1990s. He is survived by his wife, Ruth, and sons, Chad and Corey

Read full story: bit.ly/Fabry-RIP

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