August 30, 2023

Dear Friends,

Thank you so much for continually believing in and supporting me. I deeply appreciate it! Your encouragement has been such a driving force in our journey. Excitingly, we're making significant strides in our therapeutic development for Wolfram syndrome. I can't wait to fill you in on all the details. Let's dive right into an update about our current clinical trial.

Ongoing clinical trial

We're genuinely excited about the positive strides being made in Wolfram syndrome treatments. In collaboration with our partners at Amylyx Pharmaceuticals, we're actively advancing the development of AMX0035, an innovative oral medication designed to halt the progression of Wolfram syndrome. Interested in understanding how AMX0035 addresses endoplasmic reticulum stress and mitochondrial dysfunction? We invite you to explore our latest article here: https://insight.jci.org/articles/view/156549.

In 2020, the US FDA granted AMX0035 orphan drug status for Wolfram syndrome. Using previous study data, we developed a safety and effectiveness protocol for AMX0035, which has been approved by the US FDA and the Institutional Review Board at Washington University Medical Center:

We've started a phase 2 clinical trial for adult Wolfram syndrome patients: https://wolframsyndrome.wustl.edu/items/a-phase-ii-study-of-safety-and-efficacy-of-amx0035-in-adult-patients-with-wolfram-syndrome/.

Our first participant was dosed in April 2023: https://www.amylyx.com/news/amylyx-pharmaceuticals-announces-first-participant-dosed-in-phase-2-study-of-amx0035-for-the-treatment-of-wolfram-syndrome.

Our trial is progressing smoothly and more patients have been dosed, and we are already mapping out our subsequent steps. Stay tuned for updates.

Gene Editing Therapy

As you are all aware, Wolfram syndrome is a medical condition caused by issues in a gene named WFS1. When this gene isn't functioning right, it can lead to multiple health problems, including optic nerve atrophy, diabetes mellitus, and neurodegeneration. Our current focus and priority is to safeguard the retinal ganglion cells. Why? Because these cells play a crucial role in preventing damage to the optic nerve and maintaining vision.

To address this, we've joined hands with distinguished scientists: Dr. Catherine Verfaillie, Dr. Lies De Groef, and Dr. Lieve Moons from Katholieke Universiteit Leuven in Belgium. Together, we're applying a pioneering technique named "Base Editing" to make corrections in the problematic gene changes. Using iPS cells derived from Wolfram syndrome patients, we've seen promising results with this method. Our next step is to test this approach on a mouse model that simulates the human condition of Wolfram syndrome.

Besides "Base Editing," we're diving deep into an even newer method called "Prime Editing." This is cutting-edge technology in gene correction. For this endeavor, we're collaborating with Dr. David Liu and his team from Harvard/MIT, who are at the forefront of this field.

Ultimately, our heartfelt goal is to harness these innovative techniques to bring relief to those living with Wolfram syndrome.

Regenerative Therapy for Optic Nerve Atrophy – Gene Therapy and Mesenchymal Stem Cell Transplantation

We're looking into new ways to heal and even reverse damage to the optic nerve, which is the nerve in our eyes that helps us see. We've come up with two main ideas.

First, we're trying to introduce a special regenerative factor, called MANF, into the eyes of patients with Wolfram syndrome. We use a virus (a safe one!) to help deliver this factor. MANF helps protect retinal ganglion cells and encourages them to grow.

Secondly, we're testing the use of special cells, called mesenchymal stem cells, which we can get from fat tissues or bone marrow. In previous tests with animals, these cells have been shown to help eye nerve cells survive and grow back after damage.

Right now, we're doing more tests using MANF in rodent models of Wolfram syndrome developed in our lab. If everything goes well, we hope to test these methods on actual patients in the next 3-7 years.

Clinical service

At the Washington University Medical Center's Center for Advanced Medicine, we have established the Wolfram Syndrome and Related Disorders Clinic program, aimed at improving clinical care for patients with Wolfram syndrome and related disorders, including WFS1-related deafness and optic nerve atrophy.

Our program provides genetic evaluations, education, and counseling services to patients and family members of all ages who have either been diagnosed with Wolfram syndrome, are suspected of having it, or have WFS1-related disorders.

Our team collaborates with other specialists, including neurologists, neuro-ophthalmologists, urologists, medical geneticists, and endocrinologists at our medical center, to provide personalized management plans. We strive to see patients either on the same day or within two consecutive days. Our services are available to both pediatric and adult patients.

Patients in the US

If you're in the US, please call Christine Manning, RN, Nurse Coordinator, at 314-747-7055 or 314-362-3500. Let her know that you or your family member has Wolfram syndrome or WFS1-related medical conditions and need to make an appointment. Once we review your medical records, Dr. Urano or his staff will contact you to discuss which specialists you may need to see.

Sending Medical Records via Fax
Please fax your medical records to 314-747-7065.

Referrals via Fax for both Missouri patients and out-of-state patients
Please fax your referral request to 314-747-7065.

International Patients
International patients are welcome to contact our international patient care office to schedule an appointment by calling +1-314-273-3780 or sending an email to Internationalpatients@wustl.edu.

Conclusion
So many things are happening in the world of Wolfram syndrome. Let's keep the momentum going! Our team's dedication to therapeutic development for Wolfram syndrome shines bright, and it's deeply inspired by the resilience of patients and families facing this condition. The positive results we're seeing are truly uplifting and fuel our hope for the future. While challenges remain, rest assured, we're wholeheartedly committed to driving breakthroughs that could transform the lives of those with Wolfram syndrome. Stay tuned for more updates, and a huge thank you for being our rock-solid support!

With grace and gratitude,
Fumi

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