November 24, 2023

Dear Friends,

As we near the end of another remarkable year, I would like to express my gratitude for your unwavering belief in and support of our quest for a cure for Wolfram syndrome. Your continued encouragement has been a guiding light throughout our journey, just like the fading sunlight in these waning days of the year. As we prepare to say goodbye to this year, I am thrilled to share some exciting updates on our progress in the fight against Wolfram syndrome. Our therapeutic development has made significant advances, and I am eager to reveal all the intricate details to you.

Research Progress in Wolfram syndrome this past year includes:

Ongoing clinical trials

In collaboration with our partners at Amylyx Pharmaceuticals, we're actively advancing the development of AMX0035, an innovative oral medication designed to delay/halt the progression of Wolfram syndrome. In 2020, the US FDA granted AMX0035 orphan drug status for Wolfram syndrome. Using previous clinical study data, we developed a protocol to assess the safety and efficacy for AMX0035, which has been approved by the US FDA and the Institutional Review Board at Washington University Medical Center, and we have started a phase 2 clinical trial for adult patients with Wolfram syndrome at Washington University Medical Center. Our first participant started taking AMX0035 in April 2023. Our trial is progressing smoothly, and we are mapping out our subsequent steps. Please stay tuned.

Regenerative Therapy for Optic Nerve Atrophy

Our current main goal is to stop and reverse the progression of low vision caused by optic nerve atrophy in patients with Wolfram syndrome. We aim to achieve this by using regenerative medicine. Our current strategy involves introducing a regenerative factor called MANF into the eyes of individuals with Wolfram syndrome, using a viral vector. As you may already know, our brain produces certain neurotrophic factors, such as BDNF and CDNF, to maintain brain health. MANF is also a neurotrophic factor, but it is unique because it protects against Endoplasmic Reticulum (ER) stress, which is one of the molecular mechanisms of Wolfram syndrome. Additionally, MANF helps to enhance the proliferation of ER-stressed cells. We are currently conducting preclinical studies using cell and rodent models of Wolfram syndrome to assess the effectiveness of MANF in treating optic nerve atrophy. Encouraging preclinical data has been obtained from our humanized mouse model of Wolfram syndrome. This innovative approach has the potential to treat other causes of low vision as well. Our ultimate goal is to launch a regenerative therapy trial for optic nerve atrophy within the next 3-7 years.

Gene Editing Therapy

The root cause of Wolfram syndrome is a pathogenic change in the WFS1 gene. Therefore, correcting these changes in the WFS1 gene is the best way to treat Wolfram syndrome. Instead of CRISPR, we have started using Base Editing (2nd generation) and Prime Editing (3rd generation) to correct WFS1 gene pathogenic changes in Wolfram syndrome because of safety reasons. These are newer versions of gene editing, considered the best gene editing technologies available to date. To test this technology, we have created rodent models that have pathogenic changes in the Wfs1 gene equivalent to changes seen in our patients. Our ultimate goal is to use this therapeutic modality for our patients in the next 5-10 years.

Clinical service

To improve the clinical care for patients with Wolfram syndrome and WFS1-related disorders, including WFS1-related deafness and optic nerve atrophy, we have been running the WFS1 clinic at the Center for Advanced Medicine, Washington University Medical Center. This clinic has been successful, and I see patients from different states and countries almost every week. I appreciate that the Snow Foundation, the Ellie White Foundation, the Unravel Wolfram Syndrome, and the FB groups related to Wolfram syndrome have referred patients to our clinic. We offer genetic evaluations, education, and counseling for patients and family members of all ages with or suspected to have Wolfram syndrome and WFS1-related disorders. We also provide personalized management plans with other specialists at our medical center and beyond. We accept international patients via our international patient care office. We also accept out-of-state 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

The positive results we've seen fuel our hope for the future, and we're committed to pushing forward to create real change. Stay tuned for updates in the coming year, and thank you for being our unwavering support. Together, we'll continue making progress and bringing light to those impacted by Wolfram syndrome. Here's to a brighter future ahead!

With grace and gratitude,
Fumi

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