February, 2024

Dear Friends,

Spring is just around the corner, and our dedicated team continues to work tirelessly on advancing safe and effective treatments for Wolfram syndrome. Here's the latest update:

Rare Disease Day at National Institutes of Health 2024

I'm excited to share some fantastic news with you. I've received an invitation to present our research on Wolfram Syndrome at the Rare Disease Day event held at the National Institutes of Health on February 29, 2024. This event is widely regarded as one of the most prestigious gatherings for rare diseases, offering an excellent platform for us to raise awareness about Wolfram Syndrome. Even if you can't attend in person, you can still participate by watching my presentation remotely. Here is the link to access it: https://ncats.nih.gov/news-events/events/rdd

Ongoing clinical trials

We have been collaborating with Amylyx Pharmaceuticals to advance the development of AMX0035, a novel oral medication that has been designed to halt or delay the progression of Wolfram syndrome. The US FDA has granted AMX0035 orphan drug status for the treatment of Wolfram syndrome, which is an encouraging milestone. To assess the safety and effectiveness of AMX0035, we have developed a protocol using data from previous clinical studies, which has been approved by both the US FDA and the Institutional Review Board at Washington University Medical Center. Currently, we are conducting a phase 2 clinical trial for adult patients with Wolfram syndrome at Washington University Medical Center. Our first patient commenced taking AMX0035 in April 2023, and we have recently completed the recruitment of participants for this study as announced. We look forward to the preliminary results from the trial anticipated later this year. Our trial is progressing smoothly, and we are mapping out our subsequent steps. While we cannot disclose any specific information about the preliminary results or future steps, we will release public statements once it is permissible. Please stay tuned.

Regenerative Therapy for Optic Nerve Atrophy

Our current focus is to halt and reverse low vision from optic nerve atrophy in Wolfram syndrome patients using regenerative medicine. We're introducing a neurotrophic factor called MANF into their eyes via a viral vector. MANF, unique for protecting against ER stress, a key mechanism in Wolfram syndrome, also boosts stressed cell proliferation. Preclinical studies on cell and rodent models show promising results, including data from a humanized mouse model. This approach holds potential for treating other causes of low vision. Our aim is to launch a regenerative therapy trial for optic nerve atrophy within 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.

Wolfram Syndrome Clinic

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. Please visit the following website for further information: https://wolframsyndrome.wustl.edu/patient-care/

Conclusion

In closing, our journey towards combating Wolfram syndrome is marked by promising advancements in treatment, innovative research endeavors, and unwavering commitment to patient care. As we press forward, fueled by dedication and collaboration, we remain steadfast in our mission to offer hope and tangible solutions to those affected by this rare disorder. Together, we aspire to pioneer transformative therapies and improve outcomes, heralding a brighter future for individuals and families impacted by Wolfram syndrome.

With grace and gratitude,
Fumi

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