August 2025

Dear Friends,

I hope you had a wonderful summer with your family. Each week, I have the privilege of seeing patients with Wolfram syndrome in our clinic, and every day I stay connected with you through phone calls, Zoom, and email. Many of you travel long distances from across the country and even abroad to come to St. Louis. I know how challenging this can be, and I truly appreciate the effort you and your families make. I also want you to know that we are making steady progress, and I'd like to share some of these updates with you today.

Wolfram Syndrome Workshop in Paris

I had the privilege of attending and co-organizing the 10th International Wolfram Syndrome Workshop, held in Paris on June 13–14, 2025. This landmark event brought together clinicians, scientists, and advocates from around the globe to share the latest research and clinical advancements in Wolfram syndrome. The workshop was made possible through a meaningful collaboration between my team at Washington University, University of Birmingham, Wolfram Syndrome UK, the Snow Foundation, and the French Wolfram Syndrome Association, led by the incredible Nolwen Le Floch. I extend my deepest gratitude to Nolwen for her tireless work in organizing such an impactful meeting and for her ongoing dedication to the Wolfram community. Together, we reaffirmed our shared mission: to accelerate research, improve care, and ultimately find a cure for Wolfram syndrome.

Washington Post Article

Thanks to one of my courageous patients, her long journey to a Wolfram syndrome diagnosis, along with my interview, was featured in the Washington Post this month. The article highlights the Ashkenazi Jewish subtype of Wolfram syndrome, which my team has been actively studying. I deeply admire the efforts of our patients to raise awareness of this disease, and I remain committed to doing my best to achieve one of our three pillars toward a cure for Wolfram syndrome: raising awareness.
https://wapo.st/4lMAKub

Consensus Clinical Guidelines

We're in the process of creating international clinical guidelines for Wolfram syndrome, as many patients, families, and doctors have expressed a need for them. We've been making steady progress and hope to share the final version by the end of the year. We truly appreciate the input and support from all the experts who have helped along the way.

Co-Chairs: Timothy Barrett. MBBS, PhD (University of Birmingham, UK), and Fumihiko Urano, MD, PhD (Washington University, USA)
Committee Members: Josephine Elliott MBBS (University of Birmingham, UK), Saumel Ahmadi MD, PhD (Washington University, USA), Patrick Yu Wai Man MBBS PhD (University of Cambridge, UK), Sarah Gladstone MD (Unravel Wolfram syndrome and Snow Foundation, USA)
Patient Advocates: Stephanie Snow Gebel (Snow Foundation), Tracy Lynch (Wolfram syndrome UK)

Ongoing Clinical Trial of AMX0035 in Patients with Wolfram Syndrome

https://clinicaltrials.gov/study/NCT05676034

We continue our close collaboration with Amylyx Pharmaceuticals on the Phase 2 clinical trial of AMX0035. On May 12, 2025, positive long-term data at the 48-week timepoint were announced. The results showed sustained benefits in pancreatic beta cell function, glycemic control, and neurological function. Visual measures also remained stable or improved in several participants. Importantly, AMX0035 has continued to demonstrate a favorable safety profile. We have now completed the analysis of the 48-week timepoint, which is a critical milestone, and are in the process of preparing a formal publication. These encouraging findings reinforce the potential of AMX0035 as a disease-modifying therapy for Wolfram syndrome. We are working closely with Amylyx and other partners to plan the next steps in development, always keeping the best interests of our patients at the center of our efforts.

Gene-Editing Therapy

We are making significant progress in gene-editing strategies targeting the root cause of Wolfram syndrome. In our ongoing work, we have successfully corrected WFS1 pathogenic variants in brain cells derived from patient iPSCs, which has led to improved cell survival. We are also advancing efforts to correct these variants in insulin-producing pancreatic beta cells from patient-derived iPSCs.

In parallel, we are preparing adeno-associated virus (AAV) systems that express both the editing enzyme and a short corrective DNA template for in vivo delivery. These are being designed to target the brain and eyes in mouse models of Wolfram syndrome to prevent neurodegeneration and vision loss. Selecting the best outcome measures for evaluating these therapies in models is a top priority, and ongoing work is focused on optimizing these assessments.

Wolfram Syndrome and Related Disorders Clinic

Our multidisciplinary clinic at Washington University Medical Center in St. Louis continues to thrive, providing comprehensive care for patients with Wolfram syndrome and WFS1-related disorders. We do our best to accommodate international and out-of-state patients by coordinating visits with multiple specialists within the same day or over two days.

For more information, please visit our website: https://wolframsyndrome.wustl.edu/

Thank You

I want to thank you again for your trust, encouragement, and partnership. Each step forward, whether in research, clinical care, or awareness, has been possible because of the resilience and support of this community. I remain inspired by the strength of our patients and families, and I am committed to continuing this journey with you. Together, I believe we will bring new hope and create real change for everyone affected by Wolfram syndrome.

Sincerely,
Fumi

Fumihiko (Fumi) URANO, MD, PhD
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