



National Tay-Sachs &  
Allied Diseases Association

**Canavan Disease Research Day Breakout Session  
NTSAD's 47<sup>th</sup> Annual Family Conference in Dallas  
April 25, 2025**

The Canavan Disease Breakout Session featured updates from four groups and was moderated by Orren Alperstein.

**Dominic Gessler, MD, PhD, University of Massachusetts Chan Medical School**

This year Dr. Gessler was unable to attend the conference, but he submitted a video that shares updates on his research studies. His research is aimed at determining the best method to target ASPA gene therapy to treat the entire brain successfully. Using a Canavan mouse model, he presented his data that showed that ASPA gene therapy to all cells by IV delivery resulted in mice that were as good as healthy controls. He also showed that delivering ASPA gene therapy to astrocytes only was as good as healthy controls. Thus, his work indicates that oligodendrocytes don't need to be specifically targeted. IV gene therapy to all brain cells and the entire body is therapeutic. Also, IV gene therapy limited to astrocytes is therapeutic. Both gene therapy delivery methods improve gene expression profiles and metabolism.

**Amanda Nagy, MD, Massachusetts General Hospital**

Dr. Nagy's research is focused on understanding the pathologic and imaging changes in the brain in Canavan disease. The purpose of her work is to develop new prognostic tools and ultimately improve clinical trials. Specifically, her goals were to understand swelling in the brain, examine the relationship between swelling and clinical features and assess whether the amount of swelling predicts the ultimate amount of atrophy. She reviewed MRIs and clinical records of Canavan patients seen in Leukodystrophy Clinics. This work is important because it may be possible to use early imaging to predict the trajectory of disease and head circumference may be a predictive variable. Her data showed that brain structures affected in Canavan disease go through a period of relatively normal size followed by an increase in size (swelling) and then a decrease in size (atrophy), that these changes occur in a predictable sequence over time, and that the location in the brain determines the timing of involvement (areas that are myelinated earliest in typically-developing brains show the earliest signs of injury).

**Robert Lober, MD, PhD, Myrtelle**

Dr. Lober presented updates on the Myrtelle gene therapy clinical trial for Canavan disease. He is a pediatric neurosurgeon at Dayton Children's Hospital and leads the Myrtelle gene therapy clinical

trial. Their protocol involves a one-time administration of the AAV gene therapy, which is targeted to oligodendrocytes. Preliminary data in Phase 1/2 have shown decreases in NAA levels in the CNS starting one month after surgery in over 80% of patients and improved myelination in 40% of patients one year post surgery. This was accompanied by functional improvements based on the MSEL (Mullen Scales of Early Learning) in the majority of patients. The neurosurgical procedure was well-tolerated, and all patients were discharged from the hospital within one week of the procedure. After the initial three patients were dosed, the neurosurgical procedure was modified due to one serious adverse event (vomiting), and since this modification no serious adverse events have occurred. Enrollment for this trial is continuing and clinical trial updates and informative content created specifically for the community is available on the Myrtellegtx.com website.

### **Mitra Tavakkoli, MD, PharmD, Aspa Therapeutics**

Dr. Tavakkoli talked about the CANinform natural history study of patients with Canavan disease. It was designed to help better understand the disease and provide a foundation for Aspa's gene therapy program. This study enrolled 67 participants from 17 countries and showed that urine NAA levels can distinguish between mild and typical Canavan disease phenotypes, and little to no gains in motor function were seen in Canavan patients between the age of 0-60 months (publication: <https://pubmed.ncbi.nlm.nih.gov/39628365/>). Next, Dr. Tavakkoli shared an update on Aspa's CANaspire gene therapy trial of BBP-812. Fourteen patients have been dosed, eight at a low dose and six at a high dose. IV delivery was tolerated well and some adverse events were seen, but in general the safety appears to be consistent with other AAV9 gene therapies delivered via IV. Clinically, urine NAA levels dropped, and the children showed improvements in motor function. More participants will be needed, as well as follow up over a longer time, to determine the both the safety and effectiveness of this gene therapy, yet overall, the results are encouraging.