Canavan Disease Research Day Breakout Session
NTSAD's 46th Annual Family Conference in Chicago
April 12, 2024

The Canavan Disease Breakout Session featured updates from 5 groups and was moderated by Orren Alperstein.

Ron Chapleau, United Leukodystrophy Association

Mr. Chapleau is the board president of the United Leukodystrophy Association (ULF), an umbrella organization for the leukodystrophy community. Mr. Chapleau started his video presentation by reflecting on how having a child with leukodystrophy affected his own family and their journey through life. He then described the mission of ULF and their community support programs. The ULF Annual Scientific and Family Conference brings together world experts in leukodystrophy to share their results in the scientific symposium. The families gather to attend educational sessions and workshops, to talk to clinicians in a casual setting and to simply have time together. It also provides the opportunity for smaller Patient Advocacy Groups to organize disease-specific session. In addition, he announced the new Ambassador Program with local mentors for communities who can serve as a resource.

Vanessa Hull, PhD, University of California, Davis

Dr. Hull talked about her work in Dr. Pleasure's laboratory on developing and testing of therapies in preclinical mouse models of Canavan disease. Dr. Hull explained that in Canavan a metabolite called NAA accumulates in the brain, and the hypothesis was that lowering this substance may have beneficial effects. She therefore decided to target the enzyme that produces NAA using antisense oligonucleotide (ASO) therapy. ASO therapies have been approved by the FDA to treat other neurodegenerative disorders. ASO treatment of adult Canavan mice indeed lowered NAA levels in the brain and restored motor function. A second approach was to reduce the amount of NAA accumulating within brain cells by blocking its uptake into the cell. Again, deleting the transporter protein reduced NAA accumulation and improved motor function. These results are very exciting because it appears that in mice the lowering of NAA in brain cells can reverse the disease phenotype to some extent.

Jenny Laforet, MD, PhD, Aspa Therapeutics

Dr. Laforet presented an update of the BBP-812 Gene Therapy Program for Canavan Disease. She started with the CANinform Natural History study which has now enrolled 64 participants from 17 countries. She then provided an overview of the CANaspire clinical trial that is currently in the dose finding phase. Eight participants were so far dosed at the low level, one at the high level. One serious adverse event (SAE) was considered as possibly related to BBP-812 (the gene therapy), but so far the safety profile is consistent with other intravenous AAV9 gene therapies. Improvement of key abilities (head control, grasping, sitting and visual tracking) was observed as compared to the outcomes expected from the natural history. All participants had rapid and sustained decreases in NAA after dosing, although Dr. Laforet cautioned that we do not yet know whether restoring ASPA activity and lowering NAA levels will lead to clinical improvement.

Amanda Nagy, MD, Massachusetts General Hospital

Dr. Nagy talked about her work to understand the brain changes in Canavan disease. By reviewing MRIs and clinical records of Canavan patients she aims to address the question of whether the extent and location of brain swelling correlates with symptom progression and predicts the ultimate amount of atrophy. The purpose is to develop new prognostic tools and ultimately improve clinical trials. Early results show that changes happen in a certain sequence and that brain areas that are myelinated earliest show the earliest signs of injury.

Olga Flamini, MD, PhD, Myrtelle

Dr. Flamini presented a brief overview of the ongoing Phase 1/2 gene therapy clinical trial for Canavan disease. She described the program and walked through the steps of the surgical procedure. So far 8 patients have been dosed with MYR-101 at the single site in Dayton Children's' Hospital, Dayton OH. The preliminary clinical outcome data showed encouraging trends including an overall 70% improvement in brain myelin. With regard to safety, there were 3 serious adverse events (SAEs) assessed as "possibly related" to the surgical procedure, and the neurosurgical procedure was modified after the initial 3 subjects were dosed. These SAEs occurred prior to the changing of the neurological procedure. All subjects were discharged from the hospital within 1-week of MYR-101 administration and tolerated the neurosurgical procedure well. No SAE were assessed as related to MYR-101 (the gene therapy).