Late Onset GM2 (Tay-Sachs & Sandhoff Diseases) Research Day Breakout Session
NTSAD's 46th Annual Family Conference in Chicago
April 12, 2024

The Late Onset GM2 breakout session featured updates from six groups of researchers, and it was moderated by Staci Kallish, DO.

IntraBio

IntraBio has a New Drug Application (NDA) for IB1001 for the treatment of Niemann Pick disease Type C which has been accepted for filing by the US Food and Drug Administration (FDA). The application has been given a Prescription Drug User Fee Act ("PDUFA") date of September 24, 2024, and the company anticipates hearing the outcome of the application at this time. As such, a representative from IntraBio did not present, and moderator Staci Kallish read the following company statement:

"As part of the regulatory process and due to very strict compliance laws which limit what can be shared about a drug while it is formally under NDA review, IntraBio is unable to present at external engagements such as our annual conference. While we understand that it may be disappointing to not have an update this year, we want to emphasize the positive implications of this: the acceptance of IntraBio's NDA for NPC underscores the Agency's dedication to advancing treatments for rare diseases with huge, unmet medical need, such as GM2 Gangliosidosis.
The company has continued to keep NTSAD updated on all milestones and will continue to do so."

Michael Przybilla, PhD, University of Minnesota

Dr. Przybilla submitted a brief video about his research at the University of Minnesota, which focuses on gene therapy and gene editing for lysosomal disorders. In mice models of GM2 and GM1, his proprietary system gene editing (PSG) approach resulted in higher levels of enzyme and improvement in both behavioral function and disease pathology. Currently, his lab is focused on getting enough enzyme from the liver into the brain. He has submitted grants for funding and plans to move toward an Investigational New Drug (IND) application with the FDA or (IND-enabling studies).

Daisy Ng-Mak, PhD, Health Economics & Value Assessment, Rare Disease Business Partner, Sanofi

Dr. Ng-Mak from Sanofi discussed results from the company's recent qualitative study of motor function in patients with Late-Onset GM2. Interviews of patients were conducted, and all patients reported challenges in gross motor functions such as walking and climbing stairs, and many had fine motor function loss, such as issues with brushing their teeth and turning doorknobs. The majority of patients used mobility adaptations like wheelchairs and canes to help with motor function loss. Many also used physical, occupational, and speech therapies as supportive measures, with physical therapy being the most frequently reported supportive therapy.

Heather Gray-Edwards, DVM, PhD, University of Massachusetts Chan Medical School

Dr. Gray-Edwards of UMASS Chan Medical School presented updates on her gene therapy work. Dr. Gray-Edwards' laboratory focuses on testing and optimizing novel AAV vectors and delivery routes, and she presented some of her results using sheep with Tay-Sachs disease. She also talked about the progress of the GM2 gene therapy trial. Phase I and Phase II are complete, and long term follow up with patients continues. Dr. Gray-Edwards said they are stopping the use of the monocistronic vector and transitioning to a bicistronic vector. Bicistronic vector preparation is on-going and currently there is enough in production for approximately eight patients.

Julie Kissell, PhD candidate at University of Wisconsin

Julie Kissell, PhD candidate, talked about the development of a disease-specific clinical rating scale for adults with late-onset GM2. This clinical rating scale is intended to capture disease burden and measure disease progression, and provide outcome measures for future natural history studies and clinical trials. A multi-center study, and natural history data is being conducted using the scale to determine which assessments, including neurological exams, observer reported outcome assessments, and/or patient reported outcome assessments, should be used in the final scale. Enrolled adults with late-onset GM2 are asked to complete home-based assessments and questionnaires at least once per year in addition to yearly study visits. NTSAD supported this research project with a two-year grant.

Camilo Toro, MD, NIH Undiagnosed Diseases Program, National Human Genome Institute (NHGRI)/National Institutes of Health (NIH)
Christopher Stephen, MD, Massachusetts General Hospital, Harvard Medical School

As a result of a work group created after NTSAD's 2023 LOTSS Think Tank meeting, Dr. Toro (a member of the Think Tank and NTSAD SAC) and Dr. Stephen (a LOTSS Think Tank and NTSAD SAC member) convened a small group of neurologists and psychiatrists to help develop a resource for the Late Onset GM2 community on the psychiatric impact some individuals with GM2 experience. This resource, which includes information for healthcare providers and Emergency Department physicians, outlines guidelines for providers to help treat patients effectively. The next stages of this project involve producing a survey to be completed by patients/caregivers, followed by a publication that is intended to be a case series and consensus guidelines for the management of psychiatric symptoms in late-onset GM2 directed to the psychiatry community.