2023 ALD Connect Annual Meeting & Patient Learning Academy
November 3-4, 2023
Houston, Texas
Houston Marriott Medical Center

Friday, November 3rd - Scientific Session

7:30 AM **Registration and Breakfast**

8:00 AM **Welcome & Overview of Annual Meeting**

Kathleen O'Sullivan-Fortin and Kelly Miettunen will welcome everyone to the 2023 Annual Meeting and Patient Learning Academy. Kathleen is an ALD Connect Founding Board Member and patient advocate, and Kelly is the Executive Director.

8:15 AM **Bearing Witness: New Technologies and Old Trauma** **Florian Eichler, MD**

8:45 AM **Breakout Room for Patients and Caregivers** **Catherine Becker, NP**

At this time, for in person attendees only, we will offer a Breakout Room for Patients and Caregivers who are recently diagnosed or who have never attended an ALD Connect Annual Meeting and Patient Learning Academy before. We encourage new patients and caregivers to break out for a warm welcome to our community with Catherine Becker, NP. The presentations are recorded, so you will not miss out on any content. This is a great opportunity to ask questions and make connections.

8:45 AM **An Update on Vitamin D Trials for ALD** **Keith Van Haren, MD**

This session will review new clinical & preclinical data and future plans for vitamin D studies.

9:15 AM **Brain Engraftment, Biomarkers, and Transplant** **Troy Lund, PhD, MD**

Active cerebral adrenoleukodystrophy (cALD) is attenuated through the engraftment of donor-derived or gene-corrected myeloid cells. This process is poorly understood. Using mouse models, we can describe the conditions that promote brain engraftment: higher levels of radiation, higher levels of busulfan, and the removal of host microglia. The search for useful cALD biomarkers before and after transplant is ongoing. We analyzed several key blood and CSF based biomarkers associated with the extent of cALD disease observed on MRI.

Biomarkers provide information about disease status. We can utilize a biomarker called neurofilament light chain to measure neuronal damage before and after transplant (both allogeneic BMT and gene therapy).

BREAK

10:00 AM **Morbidities and Mortality in Adults with AMN** **Joshua L. Bonkowsky, MD, PhD**

Adrenomyeloneuropathy (AMN) is a neurodegenerative disease phenotype of ALD, resulting in progressive myeloneuropathy causing paraparesis, ataxia, and bowel/bladder symptoms. We conducted a retrospective study using two administrative databases to characterize mortality and the burden of illness in adult men with AMN in the US. We identified 303 commercially insured men with AMN. Compared with non-AMN, individuals with AMN had significantly more inpatient hospital admissions and outpatient clinic visits. Rates of comorbidities were significantly more common in AMN, including peripheral vascular disease, chronic pulmonary disease, and liver disease. Among individuals age <65, mortality rates were 5.3x higher for adult AMN males and the age at death significantly younger. Among Medicare beneficiaries ages ≥65 mortality rates were 2.2x higher for men with AMN. AMN imposes a substantial and underrecognized health burden on men, with higher healthcare utilization, greater medical comorbidity, higher mortality rates, and younger age at death.

Adrenomyeloneuropathy (AMN) is a neurodegenerative disease phenotype of adults with ALD, resulting in progressive symptoms. We conducted a study to understand the mortality and the burden of illness in adult men with AMN in the U.S. We found that AMN imposes a substantial and underrecognized health burden on men, with higher healthcare utilization, greater medical comorbidity, higher mortality rates, and younger age at death.

10:30 AM **Multiple Cases of Mosaic X-ALD Identified Through Newborn Screening** **Alexandra C. Keefe, MD, PhD**

We identified a male with mosaic X-linked adrenoleukodystrophy (X-ALD) diagnosed through newborn screening (NBS). ABCD1 sequencing by next-generation sequencing (NGS) showed a likely pathogenic variant present in ~82% of reads, suggesting mosaicism. Testing of genomic and cell-free DNA in 7 other tissues found that the level of mosaicism ranged from 66%-82% within this individual. We then identified multiple other cases of de novo mosaic X-ALD males, with mosaicism ranging from 32-82% suggesting our case was not an isolated phenomenon. Analysis of newborn screening data suggests that these mosaic X-ALD cases represent >1% of all males with X-ALD. While gonadal mosaicism in females is an established phenomenon, X-linked mosaicism in males is more rarely reported. It is an open question whether mosaicism could decrease the likelihood of developing cerebral X-ALD. These findings have implications for identification of X-ALD through newborn screening, as well as for the general reporting of mosaic variants in human disease.

X-ALD is an X-linked condition which may be inherited within families, or may occur "de novo", meaning an individual may be the first in their family to be diagnosed. My research has found that some individuals (both males and females) who are "de novo" are actually mosaic - which means that only some, but not all cells in the body have the genetic change and the other cells do not. I am interested in learning exactly how many mosaic individuals exist in the world, looking to see whether these individuals are less likely to develop symptoms (or even remain asymptomatic), and also exploring whether these individuals may be able to teach us about factors that are protective from developing disease.

11:00 AM **Patient Experience Panel** **Moderator: Greg Benton**

During this panel, Jana Hale, Morgan Bullard, Janelle Zavodnik, and Aaron Gardner will share their experiences with ALD. As patients and parents, they are experts in ALD and their stories make up a crucial part of our meeting. We particularly encourage our academic and industry colleagues to attend and utilize this valuable panel.

12:15 PM **LUNCH**

2:00 PM **2022 Emerging Investigators**

ALD Connect funded our first round of Emerging Investigator grants in 2022. The goal of this program is to introduce graduate students, medical students, and post-doctoral fellows to our field and foster their continued learning and interest in ALD. We awarded three grants in 2022 with the condition that each awardee present at our 2023 Annual Meeting. We are now thrilled to welcome Chenxu Li, MS, Hemmo Yska, MD, and April Rickle, and to hear the updates of their exciting research projects.

Developing Nervonic Acid, a Dietary Fatty Acid, as Therapy for Adrenoleukodystrophy by Targeting Mitochondrial Dysfunction and Cellular Oxidative Stress **Chenxu Li**

X-linked Adrenoleukodystrophy (ALD) is caused by mutations in the ABCD1 gene, which encodes a peroxisomal ATP-binding cassette transporter protein (ALDP). Deficiency in ALDP results in the accumulation of saturated very long-chain fatty acids (VLCFA), mainly hexacosanoic acid (C26:0), in plasma, brain, spinal cord, and adrenal cortex. Oxidative stress and mitochondrial dysfunction induced by C26:0 are considered leading factors in disease progression and, therefore, promising therapeutic targets for ALD. Monounsaturated fatty acids have been demonstrated to reduce VLCFA accumulation in ALD patient-derived fibroblasts, suggesting their potential to lower the toxic C26:0 levels and delay disease onset or progression. We investigated nervonic acid (NA, C24:1), a naturally occurring monounsaturated fatty acid, as a potential therapy for ALD given its biochemical benefits in reducing C26:0 levels. Our study demonstrates that NA can significantly attenuate cellular oxidative stress and improve mitochondrial function in AMN-derived fibroblasts.

Mutations in Adrenoleukodystrophy (ALD) protein result in the accumulation of very long chain fatty acids (VLCFAs), which in turn causes the elevation of harmful substances including reactive oxygen species in the body. This can further damage other cellular components such as the mitochondria, the energy source of the cells.

Attitudes of Patients with Adrenoleukodystrophy towards Sex-specific Newborn Screening — **Hemmo Yska, MD**

Newborn screening (NBS) for X-linked adrenoleukodystrophy (ALD) can identify individuals before the onset of life-threatening manifestations. This study investigates the attitudes of persons with ALD towards sex-specific NBS for ALD. A questionnaire was sent to all patients in the Dutch ALD cohort. Invitees were asked who they thought should be screened for ALD: only boys, both boys and girls or neither. Motives and background characteristics of respondents were compared between screening preferences. Sixty-six of 108 invitees (61%) participated in this study. The majority of respondents (n=53, 80%) were in favor of screening both newborn boys and girls for ALD, while 20% preferred boys only. There were no differences in the background characteristics of the respondents between screening preferences. A variety of motives why respondents preferred a type of screening were identified. The results of this study can inform parties involved in the implementation of NBS programs.

We investigated the opinion of people with ALD towards the addition of ALD to newborn screening (NBS). We found that all participants had a positive attitude towards the addition of ALD to NBS and that most preferred to screen both newborn boys and girls. Many different reasons for this preference were identified and background did not influence preference.

Testing the impact of the drug leriglitazone in a fruit fly model of ALD — **April Rickle**

There is a dire need for a pharmaceutical treatment for ALD. Leriglitazone, an experimental drug that is currently in clinical trials, has been shown to protect neurons from damage in cell culture models of ALD and improve motor function in ABCD1 mutant mice. Thus far, metabolomic studies of leriglitazone in brain tissue have been limited to cell culture. While promising, these studies have not included brain tissue from an ALD model organism. Using a Drosophila model of ALD, we study how lifelong leriglitazone treatment affects brain metabolism on a molecular scale and neurodegeneration on a behavioral and histological scale. These results aid in understanding the effects of leriglitazone treatment on the brain as well as understanding ALD as a whole.

In this study, we use a fruit fly model of ALD to look at how the experimental drug leriglitazone affects the brain's metabolism. We also assess the effect of the drug on the ALD model flies' movement, sleep, and brain pathology.

3:00 PM **bluebird bio – Gene Therapy Update** **Vinod Prasad, MD**

Dr. Vinod Prasad will present an update on bluebird bio's commercial gene therapy product, SKYSONA®.

3:30 PM **Update on Continued Efficacy and Occurrence of Myelodysplastic Syndrome in the CALD Gene Therapy Trial** **David Williams, MD**

The abstract for this presentation can be found in the Appendix.

In this presentation we will review the combined results of two multi-center clinical gene therapy trials for CALD sponsored by bluebird bio (ALD-102, ALD-104). We will discuss both effects of treatment on disease and the safety issues, especially related to the occurrence of myelodysplasia in several patients who participated in these trials. We will discuss how gene therapy vectors are chosen for use in trials and how they can sometimes cause leukemia.

4:00 PM **Minoryx** **Arun Mistry, MD**
Patricia Musolino, MD, PhD

Dr. Arun Mistry will provide an update on leriglitazone (MIN-102).

Dr. Patricia Musolino will present an overview of the NEXUS trial. Dr. Musolino will be presenting the results of a study that look into the ability of a drug called leriglitazone to decelerate or halt cerebral lesion progression in children and adults with cerebral ALD. This drug has been developed by a company called Minoryx and tested in kids and adults. For the children with early cerebral ALD the study was called NEXUS and for the adults the data comes from the AMN study called ADVANCE and 13 patients treated outside the study as compassionate use. Briefly, leriglitazone was able to decelerate lesion growth in most patients and completion of the studies will tell if the effect is sufficient to halt cerebral ALD.

4:30 PM **SwanBio** **Cristobal (Chris) Passalacqua, MD**
Lawrence Hayward, MD, PhD

Chris will provide an update on Propel: A Phase 1/2 Study of Gene Therapy for Adult Patients with Adrenomyeloneuropathy. The objective of this gene therapy trial is to evaluate the safety and efficacy of delivering the normal *ABCD1* gene to the nervous system in individuals with adrenomyeloneuropathy (AMN). The experience to date of the trial at UMass Medical School will be discussed.

Dr. Lawrence Hayward will present an overview of the ongoing Propel Clinical Trial and the experience at UMass Medical School.

5:00 PM **International validation of meaningfulness of postural sway and gait to assess myeloneuropathy in ALD** **Amena Smith Fine, MD, PhD, Bela Turk, MD, Hemmo Yska, MD**

The most common manifestation of X-linked adrenoleukodystrophy (ALD) is a slowly progressive myelopathy in adults. The variable progression of the disease complicates evaluation of the rate of its progression. Wearable sensors allow for readily-accessible, easy and more frequent balance and gait variable collection. We report data on the quantitative assessment of balance and gait with wearable sensors, and association of these variables with falls, assistive device use, and quality of life.

We show clinically meaningful relationships between sway and gait with falling frequency, use of a device, and patient-reported quality of life. Wearable device measures of sway and gait show consistent results compared with prior studies using lab-based measures. Select variables of sway allow identification of individuals who require an assistive device. These measures may be well suited as primary outcomes for clinical trial design to assess myeloneuropathy in ALD and to monitor disease progression in individual patients.

5:30 PM **ALD Connect Birthday Party and ALD Connect Awards Presentation**

ALD Connect is 10 years old in 2023! Help us celebrate with cake and champagne while our founding board members reflect on the impact of ALD Connect as an organization and the changing landscape of ALD.

Welcome Remarks **Dr. Ali Fatemi**

ALD Connect Awards **Kathleen O'Sullivan-Fortin and Greg Benton**

Each year, ALD Connect gives out awards for community members who have made an outstanding contribution to the field of ALD or to the ALD community. The ALD Connect Ambassador of the Year Award goes to a member or members of the ALD Connect community who, through example and accomplishment, have provided outstanding volunteer service to ALD Connect over the last year with the goal of advancing our organization's central mission. The purpose is to recognize the dedication, commitment, enthusiasm, initiative, or innovation of ALD Connect community members in helping the organization further its goals. The Ann B. Moser Award is an honor presented by ALD Connect to an individual or group to recognize an unusually impactful contribution to the ALD community at large. This recognizes major milestones in the history of our disease. The award is named in honor of Ann B. Moser, who has been instrumental in pushing forward both scientific and advocacy efforts for ALD patients for decades.

Group Photo **All**

Toast with Champagne and Cake **Dr. Florian Eichler**

Reflections **Founding Board Members**

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Saturday, November 4th – Patient Learning Academy

7:30 AM **BREAKFAST**

8:00 AM **Overview of ALD Connect** **Kathleen O'Sullivan-Fortin**

Kathleen O'Sullivan-Fortin, ALD Connect Founding Board Member and patient advocate, will introduce programming and resources offered by ALD Connect to community members. These resources include our Community Calls, Peer Mentor Program, webinars, and financial assistance.

8:15 AM **International Partners**

ALD Connect is proud to partner with leukodystrophy organizations around the world to better serve ALD patients internationally. In this panel, three of our international partners will highlight the important work they are doing to provide resources for the ALD community across the world. Featured will be Bob Wyborn, who runs the Leukodystrophy Resource Research Organization (LRRO) out of Australia; Verónica de Pablo, who runs Fundación Lautaro te Necesita out of Argentina, and Karen Harrison, who runs Alex TLC out of England.

9:00 AM **The Grey Zone: My Genetic Test Comes Back 'Variant of Uncertain Significance' – Now What?** **Stephan Kemp, PhD**

The advancements in population screening, including newborn screening, enables the identification of disease-causing variants and timely initiation of treatment. However, screening may also identify mild variants, non-disease variants, and variants of uncertain significance (VUS). The identification of a VUS poses a challenge in terms of diagnostic uncertainty and confusion. X-linked adrenoleukodystrophy (ALD) serves as an illustrative example of this complex issue. ALD is a monogenic neurometabolic disease with a complex clinical presentation and a lack of predictive tests for clinical severity. Despite the success of ALD newborn screening, a significant proportion (62%) of missense variants identified through newborn screening exhibit uncertainty regarding their pathogenicity. Resolving this issue requires ongoing efforts to accurately classify variants and refine screening protocols. While it is indisputable that ALD newborn screening greatly benefits boys with the disease, the identification of VUS underscores the need for continuous research and collaboration in improving screening practices.

ALD newborn screening is a proven way to help boys with the disease and save lives. But when the test results show a "variant of uncertain significance," it can lead to confusion and uncertainty. It's incredibly important to figure out how to solve this problem, so families and doctors can have clear answers about the test results and know the best course of action. The goal of the Grey Zone project is to develop new tests that can provide more definite answers and reduce the confusion caused by uncertain results, ultimately improving the care and support for those affected by ALD.

9:30 AM **ALD Below the Belt** **Cristina Sadowsky, MD and Jennifer Keller, MS**

Many adult ALD and AMN patients experience symptoms associated with bladder and/or bowel incontinence and sexual dysfunction. These symptoms have a significant impact on quality of life, but tend to be discussed less frequently than symptoms associated with gait. Join Jen Keller and Dr. Cristina Sadowsky as they answer your questions about ALD "below the belt".

10:00 AM **Voice of the Patient – Reflections**

ALD Connect hosted an Externally-Led Patient-Focused Drug Development (EL-PFDD) meeting on July 22, 2022, with the goal of educating the FDA about adult manifestations of ALD. We cannot extend enough thanks to the patients who joined us live or as recorded panelists, and to those patients who called in or submitted comments online. Your testimony to the FDA was extremely powerful. The key themes from the EL-PFDD meeting were captured in our Voice of the Patient (VOP) report which is now published on our website. To continue the conversation sparked by patient testimony at the EL-PFDD, this panel will feature ALD experts, Dr. Florian Eichler, Dr. Ali Fatemi, and Dr. Amena Fine, who will reflect on the key themes identified from the meeting in our Voice of the Patient Report from a provider point of view.

10:30 AM **BREAKOUT SESSION**

Join us either in-person or online for breakout sessions, similar to our monthly community calls. These sessions are not recorded and serve as an opportunity for community members to come together, get to know each other, and share their experiences. Unlike our community calls, these breakout sessions will be open to all attending the meeting, including doctors, researchers, and industry members.

Noon **LUNCH**

1:00 PM **Academic Studies and Clinical Trials**

Dr. Yedda Li, Jennifer Weinstein, and Dr. Troy Lund will discuss ongoing studies involving ALD patients.

Clinical Trials for Women with Adrenoleukodystrophy **Yedda Li, MD, PhD**

Many women with adrenoleukodystrophy (ALD) experience neurologic symptoms that negatively impact their quality of life. We present a summary of ongoing clinical trials for women with ALD at Mass General Hospital, and we focus specifically on a large intercontinental clinical trial that assesses restless legs syndrome (RLS) and other lower extremity symptoms in the context of ALD. RLS is a common condition ALD patients experience that disproportionately affects more women than men. It is characterized by an irresistible urge to move the legs that often worsens at night, causing insomnia. Pramipexole is an FDA-approved treatment for RLS; however, this medication has not been studied in women with ALD. This clinical trial will assess the efficacy of pramipexole in treating RLS for women with ALD. We hope that the data gathered from this study will help to improve the quality of life for women ALD patients with these debilitating symptoms. (continued on next page)

Restless legs syndrome (RLS) is a condition that disproportionately affects more women with adrenoleukodystrophy than men. We present a large intercontinental clinical trial that assesses the efficacy of the medication pramipexole in treating the symptoms associated with RLS. We hope that the data gathered from this study will help to improve the quality of life for women ALD patients who experience this debilitating condition.

The Development & Validation of the Adrenoleukodystrophy-Health Index (ALD-HI) **Jennifer Weinstein, MS**

The abstract for this presentation can be found in the Appendix.

In preparation for Adrenoleukodystrophy (ALD) therapeutic trials and to optimize the clinical care of patients with ALD, it is critical for the ALD research community to have access to valid, disease-specific, and responsive patient-reported outcome measures (PROs) that are accepted by patients. We have developed and validated the ALD-HI, an instrument that consists of 20 subscales which comprehensively measure patient-reported disease burden in the areas of health that are most important to individuals with ALD. This research provides initial evidence that the ALD-HI is a valid mechanism to quantify multifaceted patient-reported disease burden in ALD.

Intravenous Administration of Mesenchymal Stem Cells (IV-MSC) for the Treatment of Cerebral Adrenoleukodystrophy (cALD) **Troy Lund, PhD, MD**

Mesenchymal stem cells (MSC) are a highly immunosuppressive form of cellular therapy. This is a single-institution study to evaluate the use of intravenously administered allogeneic, off-the-shelf mesenchymal stem cells (IV-MSC) in patients with active, cerebral adrenoleukodystrophy. Our goal is to arrest an active cerebral ALD process.

2:00 PM Transitions in ALD **Moderator: Kathleen O'Sullivan-Fortin**

Families with ALD go through many transitions in their journeys. Transitions occur when families receive an ALD diagnosis, when boys begin their monitoring schedules, when symptoms progress, if cerebral involvement is detected, when children become adults and take over their own medical care, etc. This panel will feature panelists, Bill and Kate Groel, Julie Purschke, and Tim Maguire, who will discuss the transitions they have encountered in their experiences with ALD and AMN, along with our moderator Kathleen O'Sullivan-Fortin, who will facilitate the discussion.

2:45 PM ALD Associated Trauma **Moderator: Dr. Amber Salzman**

ALD families experience trauma at many points through their journeys, and the impact of these experiences can be long-lasting. This panel will begin with a presentation by A. Bruce McClary, LCSW-C, CCM, who will introduce the basics of trauma and how medical trauma can present in ALD. The panel will also feature Amber Salzman, PhD, and Jesse Torrey, LAC, who have personal connections to ALD and will add their perspectives as ALD community members.

3:45 PM **BREAKOUT SESSION**

This breakout session will represent a continuation of the trauma panel and will serve as a place for in-person attendees to decompress. Jesse Torrey, LAC, ALD community member and mental health professional, will lead mindfulness exercises, while Kathleen O'Sullivan-Fortin, ALD Connect Board member and yoga instructor, will lead chair yoga. You are welcome to join a group or use the time in the way that will best support your own mental health. These sessions will only be offered in person, and we encourage our virtual attendees to take the time to care for themselves at home.

4:30 PM **Ask an Expert: Clinical Panel** **Moderator: Kelly Miettunen**

Do you have questions about ALD that you can't seem to find an answer to? Now is your chance! Join our panel of ALD experts as they answer your questions about ALD symptoms, treatments, trials, and more.

5:00 PM **Closing Remarks** **Dr. Florian Eichler**

Thank you for participating in our 2023 Annual Meeting and Patient Learning Academy!

SPEAKER BIOS

Catie Becker, NP

Catherine (Catie) Becker is a Pediatric Nurse Practitioner at Massachusetts General Hospital. Catie received her master's degree in Pediatric Acute/Chronic Advanced Practice Nursing from the University of Pennsylvania. Catie joined the MGH Leukodystrophy Clinic in 2011 and has been fortunate to work with a multidisciplinary team of care providers treating both children and adults with leukodystrophy, while participating in multiple ongoing clinical trials.

Greg Benton

Greg's first exposure to the horrors of myelin disease was when his uncle lost his battle to AMN in 2001. His brother Mike was diagnosed seven years later and fought the very same illness for most of his adult life. On February 25th, 2020, Greg's eldest brother Michael lost his battle with AMN. Greg served as the Program Director for the Myelin Project from 2012 – 2017. In 2015, he started the ALD Family Support Program to support low-income families living with ALD, AMN, and other leukodystrophies. He also worked on the campaign to pass California Assembly Bill 1559 enacting ALD newborn screening in California. Greg was elected president of the World Leukodystrophy Alliance (WLA) in 2016. In 2019, Greg joined the ALD Connect Board of Directors.

Josh Bonkowsky, MD, PhD

Dr. Bonkowsky is the Director of the Center for Personalized Medicine at Primary Children's Hospital and Chief of the Division of Pediatric Neurology at the University of Utah.

Patti Chapman

Patti's journey with ALD began in 1960 when her younger brother Bobby passed away from the disease at the age of five. Patti's second brother Richard passed away in 2001 from AMN just ten years after his diagnosis. Herson Michael, fought the very same illness for most of his adult life. On February 25th, 2020, Michael lost his battle with AMN. Patti served on the Board of Directors of The Myelin Project for over 20 years, and became president of the Myelin Project in 2009. She has helped raise well over a million dollars for ALD and AMN disease research through out her days with The Myelin Project dating back to the early 90s. Patti joined the ALD Connect Board of Directors in 2019.

Verónica de Pablo

Co-founder and current President of Fundación Lautaro te Necesita

I was born in Bs As (Buenos Aires) in 1964. I have a Law Degree and I was a Primary School Teacher and Principal of an Elementary School. In 2011 my youngest son was diagnosed with MLD and he was able to receive a bone marrow transplant at Duke Hospital. After that, my husband and I decided to create a foundation to promote research and education in pursuit of early diagnosis that allows access to treatment in all kinds of leukodystrophies. My husband Eduardo Javier passed away last year. His legacy lives on in all of us and gives me the strength to continue the project we started together. Actually my 3 children (Lautaro, Nazareno and Guadalupe) are my support and the engine that drives me to continue supporting all the families that live with leukodystrophies in Argentina and Latin America.

Florian Eichler, MD

Dr. Florian Eichler is a co-founder and president of ALD Connect. He is a Professor of Neurology at Massachusetts General Hospital (MGH) and Harvard Medical School. His career has been dedicated to advancing the care and treatment for devastating neurogenetic conditions. Following neurogenetics training at Johns Hopkins with the late Dr. Hugo Moser and residency in pediatric neurology at MGH, he became the Director of the Leukodystrophy Service that cares for patients with an increasing variety of neurogenetic conditions. Dr. Eichler runs a laboratory at MGH that explores the relationship of mutant genes to specific biochemical defects and their contribution to neurodegeneration. In 2015, he became Director of the Center for Rare Neurological Diseases at MGH. The Center aims to eradicate rare disorders of the nervous system by leveraging the power of biological insights towards design and implementation of clinical trials. Dr. Eichler is the Principal Investigator of several NIH-funded studies on neurogenetic disorders as well as a gene therapy trial of adrenoleukodystrophy. For this work, he received the Martin Research Prize from MGH and the Herbert Pardes Clinical Excellence Award from the Clinical Research Forum. Dr. Eichler also serves as Chair of the Rare Disease Think Tank at MGH.

Felicity Emerson, PhD

Felicity joined ALD Connect as a Volunteer in 2020 and was hired as a Project Manager in 2021. She has a PhD in Biomedical and Biological Sciences from Cornell University and is a genetic counseling student at Rutgers University. She values every opportunity she has to learn from the ALD community about the experiences of families with ALD.

Ali Fatemi, MD, MBA

Dr. Ali Fatemi is a founding member of ALD Connect. He is a pediatric neurologist and the Chief Medical Officer at the Kennedy Krieger Institute, and a Professor of Neurology and Pediatrics at Johns Hopkins University. Dr. Fatemi received his medical degree from the Medical University of Vienna, Austria and was recruited by Dr. Hugo W. Moser as a post-doctoral fellow in 2001 and has been conducting research on ALD since. His research encompasses basic laboratory studies in ALD mouse and cell culture models as well as clinical studies and trials in patients with ALD.

Aaron Gardner

I am a 37-year-old man with AMN who was diagnosed eight and a half years ago. I have an extensive family history of virtually every phenotype of ALD/AMN. I live in the Seattle, Washington area with my wife and two young children, one of whom is an asymptomatic female.

Bill and Kate Groel

Bill and Kate Groel have been parent advocates for ALD research and education for over 20 years. Kate learned she was a carrier of ALD after the diagnosis and passing of her brother Robert in 1979. Together, they have three boys named Connor, Carson, and Clancy and given Kate's family history had all three boys screened for ALD at birth using cord blood. Both Connor, 24 and Clancy 17, tested positive for the biochemistry for ALD. They both participated in the Lorenzo's Oil research study for many years and have adrenal insufficiency. As a couple, Bill and Kate have held many fundraising events benefiting ALD support organizations. In 2019, Bill testified before the Texas Senate Finance Committee for the funding and implementation of Newborn Screening in Texas. In 2020, Bill and Kate spoke at the ALD Connect annual meeting on their family's experience with 504 Educational Plans for school age children and currently they participate in the ALD Connect Peer Mentor Program.

Jana Hale

I live in Orange County, California. I started getting symptoms of ALD in my late 30s and was diagnosed at the age of 46. My quest to figure out what was wrong with me took 3 years and countless visits to various specialists. I was finally diagnosed at the UCI Neuromuscular Center, but travel annually to see Dr. Eichler and other specialists at Mass General because I haven't been able to find anyone knowledgeable about ALD in California. I worked as a Registered Dental Hygienist before I was forced to retire because of ALD. I enjoy spending time with family and friends, especially my husband and 21 year old daughter, Olivia.

Karen Harrison

I am the Support Services Manager for Alex, The Leukodystrophy Charity, I am also a carrier of adrenoleukodystrophy and have two affected sons. One of my sons died at age 8 and my other son is now 27 but very severely affected. In my work with the charity, I support families who have been given a diagnosis of leukodystrophy, this has life-changing effects on not just the individual who has been diagnosed but the whole family. We offer emotional and practical support alongside disease information. We also bring families together for mutual support and understanding. I have worked in collaboration with ALD Connect for many years.

Emma Hayes, MS

Emma was ALD Connect's first summer Intern in 2019 and joined ALD Connect again in the spring of 2022. She has a BA in Chemistry from Saint Anselm College and an MS in Science, Technology and Entrepreneurship from the University of Notre Dame. Emma also works for Alexion Pharmaceuticals as a Patient Liaison in Neurology. Emma is a dedicated and fearless advocate for ALD which stems from a family history with the disease.

Lawrence Hayward, MD, PhD

Dr. Hayward is a physician-scientist and board-certified neurologist who directs the Neuromuscular Division at the University of Massachusetts Chan Medical School in Worcester, MA. He participates in basic research using cellular and preclinical disease models of neuromuscular conditions and translational studies to improve outcome measures for clinical trials.

Alexandra Keefe, MD, PhD

Dr. Alexandra Keefe is an Assistant Professor at the University of Washington, where she has established herself as a dedicated physician-scientist. Her academic journey commenced at the University of Utah, where she earned both her PhD in Human Genetics and her MD degree. Driven by a profound fascination with the intricate mechanisms of genetic disorders, she pursued additional clinical training in Pediatrics and Genetic Medicine at the University of Washington. Dr. Keefe's primary research focus centers on gaining a deeper understanding of mosaic conditions, a complex and captivating domain within the realm of genetics. An interesting tidbit worth noting is that Dr. Keefe's partner, Matthew Keefe, received guidance from Dr. Josh Bonkowsky, contributing to the development of the zebrafish model for adrenoleukodystrophy (ALD). Dr. Alexandra Keefe's commitment to advancing medical knowledge is truly commendable, characterized by her unwavering dedication, insatiable curiosity, and genuine care for her patients.

Stephan Kemp, PhD

Stephan Kemp is an associate professor of Inherited Neurometabolic Diseases and Newborn Screening at the Amsterdam University Medical Centers, The Netherlands. He received his training as a translational researcher at Johns Hopkins University/ Kennedy Krieger Institute, Baltimore, Maryland, USA, and earned his Ph.D. from the University of Amsterdam in 1999. With over 25 years of experience in ALD research, he has authored >115 publications and 8 book chapters, with >12.000 citations. Dr Kemp served as the project leader of the SCAN study, a pilot for implementing ALD newborn screening in the Netherlands, which officially commenced on October 1st, 2023. In 1999, he founded the freely accessible worldwide ABCD1 variants database and the www.adrenoleukodystrophy.info platform, a comprehensive resource available in five languages and attracting over 200,000 visitors annually. In 2015, he was honoured with the Amsterdam UMC Societal Impact Award. His research group collaborates with ALD physicians and researchers globally, emphasizing open communication and intensive collaboration. Dr. Kemp also serves on medical and scientific boards in Europe and the USA, and is a board member of ALD Connect (USA).

Ben Lenail

Ben Lenail is an ALD Connect co-founder and Board member. He is based in Palo Alto, California and has consulted with biotech companies such as Minoryx Therapeutics, Autobahn Therapeutics, and Deep Genomics. Ben is an investor in 15 early-stage healthcare companies with HealthTech Capital. He is a mentor with the Chan Zuckerberg Initiative. He is on the Advisory Board of the UCSF Center for Vulnerable Populations. Ben has worked in high-tech in Silicon Valley for 30+ years. He's a graduate of the University of Washington in Seattle, Washington and Sciences-Po in Paris. Ben's wife Laurie Yoler has been his partner for three decades.

Chenxu Li, MS

Chenxu Li is currently a Ph.D. candidate in the Department of Experimental and Clinical Pharmacology at the University of Minnesota Twin Cities. She obtained her B.S. degree in Pharmaceutical Analysis from Shenyang Pharmaceutical University in 2019, followed by a M.S. degree in Pharmaceutics from the University of Minnesota in 2021. Shortly after earning her master's degree, she began her doctoral program, investigating novel therapies for Adrenoleukodystrophy under the supervision of Dr. Reena Kartha.

Yedda Li, MD, PhD

Yedda Li received her MD and PhD degrees from Washington University in St. Louis, where she studied the pathophysiology and treatment for Krabbe leukodystrophy in the lab of Dr. Mark Sands. She is now a resident physician in the Mass General Brigham adult neurology residency program, where she has had the privilege of working with Dr. Florian Eichler. With his mentorship, she hopes to dedicate her life to treating adult patients with leukodystrophies, studying leukodystrophy disease mechanisms, and devising effective treatment strategies for these disorders.

Troy Lund, PhD, MD

Dr. Troy Lund is an Associate Professor in the Department of Pediatrics at the University of Minnesota. He is an international expert on the use of cell and gene therapy for pediatric and adult patients with adrenoleukodystrophy. His laboratory and clinical interests include mouse models of transplant, peroxisome biology, biomarkers, and outcomes after transplant for rare disease. He has several active research projects focused on improving treatment options and outcomes for patients with ALD at every stage of disease.

Timothy Maguire

Tim is a visionary leader and highly accomplished professional in the financial services industry. As Chairman of Karr Barth Associates, Tim is passionate about helping others achieve greatness and mentoring the next generation of leaders. Tim resides in Wayne, PA with his wife, Colleen, and their four children. He was diagnosed with AMN at the age of 37.

Bruce McClary, LCSW-C, CCM

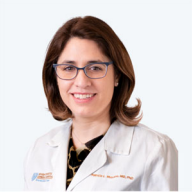
Bruce graduated in 1983 from Linfield College, McMinnville, Oregon with a BA in Sociology and BS in Chemistry. He then attended graduate school at the University of Maryland in Baltimore where he graduated in 1985 with a Masters Degree in Clinical Social Work. He brings 37 years of clinic experience of working with children and adults with various medical conditions, developmental disabilities, and provides counseling services for medical trauma, PTSD, ADHD, and Autism to list a few. Bruce has worked with Liver Transplant Patents at Johns Hopkins Hospital, where he was employed for over 11 years. He provided case management to children in Maryland who had rare and expensive medical diagnosis and lacked appropriate resources. During this time he became a CCM (Certified Case Manager) in 1999. He has worked at Kennedy Krieger Institute for over 16 years. For the last 9 years as a Social Work Manager overseeing social work services the Outpatient Medical Clinics and the Care Coordination Program.

Kelly Miettunen, MHA

Kelly joined ALD Connect as the Executive Director in 2019. She has a Master of Healthcare Administration degree from the University of Minnesota and has worked in administration and with the ALD community for more than 12 years. She enjoys working with such an incredible network of patients, families, advocates, physicians, scientists, and industry partners.

Arun Mistry, MD

Dr. Mistry is the Chief Medical Officer at Minoryx. Arun is an experienced pharmaceutical executive with a background of 10 years in clinical practice and over 20 years in the industry. Involved in strategically developing and launching many NCEs across multiple therapy areas globally, and with a focus on rare diseases in the last 10 years. Recent experience osteogenesis imperfecta programme culminating in a significant partnership deal. Prior to this, Arun worked on the successful development and submission to FDA and EMA for a product in Dravet syndrome and Lennox Gastaut syndrome. Building clinical and medical teams to strategically plan, execute and deliver development programmes globally with a focus on the patient perspective being front and centre. Arun qualified in medicine from the University of Dundee, postgraduate qualifications in paediatrics and is a Member of the Royal College of Physicians (UK) and a Member of the Royal College of Paediatrics and Child Health.



Patricia Musolino, MD, PhD

Patricia Musolino MD, PhD is a critical care and vascular neurologist with expertise in neurogenetics and vascular neurology. She cares for patients in the Intensive Care Unit, the Emergency Department and the Pediatric Stroke Clinic. Dr. Musolino's research focus on understanding how brain inflammation and stroke occurs when patients carry specific genetic mutations. Dr. Musolino is also part of multiple therapeutic clinical trials in stroke and rare disorders.

Kathleen O'Sullivan-Fortin, Esq

Kathleen is a co-founder of ALD Connect. She serves on the Board of Directors as Treasurer and General Counsel. Kathleen is a symptomatic woman with ALD and an ALD mom. Over the past ten years, Kathleen has taken on roles as a patient advocate, industry liaison, developer of programming, and facilitator of many events. Kathleen has served on the ALD Family Weekend planning committee, the NIH RDCRN CPAG committee, the EveryLife Foundation RDLA, the Alliance of Regenerative Medicine Patient Advocacy Committee, the CPSA Analytics Charitable Foundation, and the ALD Connect Industry Advisory Council.

Cristobal (Chris) Passalacqua, MD

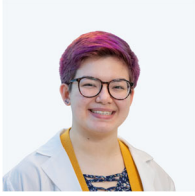
Cristobal (Chris) Passalacqua is a Clinical Geneticist with more than 10 years of experience in Rare Diseases. He is the Head of Clinical Development at SwanBio, working in the natural history and gene therapy program for Adrenomyeloneuropathy (AMN). Before joining Swan, Chris's experience included working in potential treatments for Muscular disorders at PTC Therapeutics and, recently, as Senior Medical Director for Sangamo Therapeutics, developing a potential Gene therapy treatment for Fabry disease.

Julie Purschke

Julie Purschke is a wife, mom of two, teacher, and co-founder/director of Knockout ALD, Inc. Julie's father was a patient of Dr. Hugo Moser and passed away from complications of AMN. Her son Nicholas is an ALD warrior who had a successful umbilical cord blood transplant to treat cerebral ALD in 2016 at the University of Minnesota. She and her husband Dave founded their nonprofit Knockout ALD, Inc. to raise awareness of ALD and funds to further ALD research at the University of Minnesota, as well as support other ALD families. Julie devotes much of her time to and is passionate about the ALD cause and their nonprofit including their main annual event, Run for ALD, Cure the Boys near St. Louis, Missouri. She is a parent advocate for newborn screening and served on the ALD Newborn Screening Task Force in Missouri.

Vinod Prasad, MD

Dr. Prasad joined bluebird bio in July 2023 and is working with various aspects of the eli-cel program for patients with cerebral adrenoleukodystrophy. He continues to work as a professor at Duke University and sees his patients, half a day a week. Prior to joining bluebird, he was the director of the Pediatric Transplant and Cellular Therapy division at Duke University since 2020 where he has been a transplant physician since 2003. For more than a decade he was also the director of the transplant fellowship program. He played critical role in the patient care, research and academic mission of Duke's pioneering stem cell transplant program which is internationally recognized. Prior to Duke, Dr. Prasad was a fellow, chief fellow and a transplant faculty at Memorial Sloan Kettering Cancer Center in New York for almost 10 years. He graduated from University of Delhi with a medical degree and subsequent post-graduate qualification in Pediatrics. He received further training in the United Kingdom before moving to the United States in 1994. He is well known internationally for his expertise in transplantation and genetic diseases and in the last 20 years, he has delivered more than 100 invited lectures at medical institutions and conferences in the United States and around the world. He has been involved in more than 2,000 pediatric transplants for a wide range of diagnosis. His research interests span a number of areas including the use of transplant for inherited metabolic disorders, novel cell therapy approaches, new drug investigation and impact of DNA sequence variation. He has authored and co-authored more than 150 publications for national and international meetings and journals. He was awarded George Santos Award by American Society of Blood and Marrow Transplantation in 2000 for original research and the Fellowship of the Royal college of Physicians (London) in 2014 for his academic success.



April Rickle

April Rickle is a graduate student at Van Andel Institute Graduate school in Grand Rapids, Michigan under the mentorship of Adelheid (Heidi) Lempradl, PhD. She graduated from Rutgers University with a degree in molecular biology and biochemistry in 2019 and is a fifth year PhD candidate in molecular and cell biology at VAIGS.

Cristina Sadowsky, MD

Dr. Sadowsky, Associate Professor in Physical Medicine and Rehabilitation at Johns Hopkins School of Medicine, is the Clinical Director of the International Center for Spinal Cord Injury at Kennedy Krieger Institute in Baltimore, a program caring for both children and adults with spinal cord related neurologic deficit and built on the philosophy that functional restoration is activity dependent and can be best achieved through structured medico-rehabilitative interventions. She is board certified in Physical Medicine and Rehabilitation and Spinal Cord Injury Medicine. Dr. Sadowsky's research interests center on prevention of complications in children and adults with paralysis related to traumatic and non-traumatic spinal cord dysfunction and the efficacy of activity based restorative therapies (ABRT) in helping individuals with long-term paralysis recover sensation, movement and independence. She is a Fellow of the AAPMR and a Diplomate of the AAP. She thoroughly enjoys mentoring individuals passionate for the care of individuals with disabilities.

Amber Salzman, PhD

Amber Salzman is an experienced Pharmaceutical and Biotech executive who also leads the Stop ALD Foundation and is an ALD Connect Board member. When her family was affected by ALD >20 years ago she began driving therapy development for ALD and better diagnosis for ALD families.

Amena Smith Fine, MD, PhD

Amena Smith Fine, MD PhD. Assistant Professor of Neurology and Developmental Medicine, Kennedy Krieger Institute and Johns Hopkins School of Medicine. Dr. Fine is a physician scientist working in the Moser Center for Leukodystrophies. The focus of Dr. Fine's primary research study is to use advanced MR imaging sequences of the brain and spinal cord in conjunction with quantitative measures of gait and balance obtained with wearable accelerometers to 1) determine the neural substrates of clinical impairment in ALD and LBSL and 2) validate the longitudinal use of wearable technology to identify clinically meaningful quantitative performance measures.

Jesse Torrey, LAC, MA

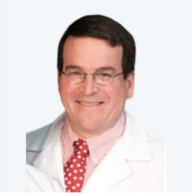
Jesse Torrey is a licensed mental health counselor, writer, and the mother of a son with CALD. She has been sharing her family's ALD story for 16 years on her blog (www.smilesandductttape.com) and in her memoir, Smiles and Duct Tape.

Keith Van Haren, MD

Dr. Van Haren has been dedicated to leukodystrophy care and research for almost 20 years. He is the Director of the ALD & Neuroimmunology Clinics at Stanford Children's Health. He also oversees a clinical and laboratory research program dedicated to ALD and multiple sclerosis where his team works intensively to develop new scientific insights and improved standards of care for ALD. Dr. Van Haren is a founding member of ALD Connect.

Jennifer Weinstein, MS

Jennifer Weinstein is the Lead Clinical Project Manager for the Center for Health + Technology (CHeT) Outcomes team at the University of Rochester whose focus is the development and validation of patient and caregiver-reported, disease-specific outcome instruments for use in clinical monitoring and drug-labeling claims using FDA criteria. Jennifer attended Bryn Mawr College, obtained a master's degree in Public Policy, and an Advanced Certificate in Clinical Research Methods at the University of Rochester. She leads a team of research coordinators at CHeT that has developed and validated over 160 instruments that are used by academic groups, governments, pharmaceutical companies, and foundations worldwide.



David Williams, MD

Dr. Williams is the Chief of the Division of Hematology/Oncology, and the Leland Fikes Professor of Pediatrics at Harvard Medical School. He previously served as Senior and Executive Vice President and Chief Scientific Officer of Boston Children's Hospital and President of the Dana Farber/Boston Children's Cancer and Blood Disorders Center. Williams originally trained in hematology/oncology at Boston Children's Hospital and Dana-Farber Cancer Institute. During his fellowship research at the MIT Cancer Center and the Whitehead Institute, he developed techniques that allowed for the introduction of genes into murine and human hematopoietic cells. Those techniques are still commonly utilized today. He was the inaugural Director of the Herman B Wells Center for Pediatric Research at Indiana University from 1991-2001. Prior to rejoining Children's in December 2007, he was at Cincinnati Children's Hospital Medical Center (CCHMC) where he was founding director of the Division of Experimental Hematology, attending physician in hematology/oncology, and associate chair for Translational Research in the Department of Pediatrics. He was a Howard Hughes Medical Institute Investigator for 16 years and his laboratory has been continuously funded by the NIH since 1986. He has trained over 60 fellows and post-doctoral fellows and numerous residents and medical students in his laboratory, the majority of which are still in academic medicine. He is a member of the National Academy of Medicine and has published over 400 peer-reviewed manuscripts and textbook chapters. He formerly served on the NIH Recombinant DNA Advisory Committee and Gene Therapy Safety Assessment Board. He is actively involved in gene therapy trials for hematologic, immunodeficiency and neurological genetic diseases and has been the investigator, co-investigator or sponsor (IND holder) of multiple previous gene therapy trials and is sponsor or investigator of four current trials. He served as the Editor-In-Chief of Molecular Therapy from 2004-2009 and is co-founder of the Transatlantic Gene Therapy Consortium and the North American Pediatric Aplastic Anemia Consortium (NAPAAC). His basic research has focused on hematopoietic stem cell biology, including genetic diseases of the blood and specifically molecular and biochemical analysis of the interaction between hematopoietic stem cells and the bone marrow supporting environment. His laboratory has significant experience in stem cell biology, hematopoiesis and gene correction and transfer techniques. His basic research has focused on hematopoietic stem cell biology, including genetic diseases of the blood and his laboratory has studied Rho GTPases for over 25 years resulting in his laboratory description of the molecular basis for three rare human diseases due to mutations of GTPases RAC2, RHOH and most recently SEPTIN6. He has multiple patents of which two have been developed into FDA-approved drugs (Neumega™ and Retronectin™) and is co-founder of two biotech companies, Orchard Therapeutics and Alerion Biosciences. (continued on next page)

Dr. Williams has served as an expert consultant for insert site analysis for multiple biotech companies. He served as the coordinating investigator for the pivatol trial for eli-cel™ product, serving from protocol conception through expert testimony at the FDA FDA BLA 125755 Elivaldogene automcel (eli-cel) application Advisory Committee meeting. Dr. Williams is a past President of the International Society of Experimental and the American Society of Hematology. Among other honors he has been awarded the Outstanding Achievement Award and the Founders Award by the American Society of Gene and Cell Therapy.

Hemmo Yska, MD

Hemmo Yska is a PhD-candidate at the Amsterdam University Medical Center in the Netherlands. After becoming a medical doctor, he worked as a resident in pediatrics and developed an interest in scientific research and pediatric neurology. He decided to pursue a PhD and in 2021 joined the ALD research team under the supervision of Dr. Marc Engelen. His main focus is on clinical research in the field of ALD and other leukodystrophies. Currently, together with the other members of the ALD group, he participates in a number of projects that, for example, focus on the addition of ALD to the Dutch newborn screening program and the identification of surrogate outcome markers for spinal cord disease.

Keith Van Haren, MD

Dr. Van Haren is a Child Neurologist and Director of the Neuroimmunology & Leukodystrophy Clinic at Stanford Children's.

Janelle Zavodnik

Janelle Zavodnik is an ALD mom and advocate.

Appendix

Vector design and long-term pooled efficacy and safety data from CALD patients treated with eli-cel

Florian S. Eichler,[1] Christine N. Duncan,[2] Jörn-Sven Kühl,[3] Satiro N. De Oliveira,[4] Adrian J. Thrasher,[5] Jean-Hugues Dalle,[6] Caroline Sevin,[7] Ami J. Shah,[8] Franco Locatelli,[9,10] Hernán M. Amartino,[11] Marc Engelen,[12] Paul J. Orchard,[13] David A. Williams[2,14]

[1]Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; [2]Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, MA, USA; [3]University Hospital Leipzig, Leipzig, Germany; [4]David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA; [5]University College London Great Ormond Street Hospital Institute of Child Health, Great Ormond Street Hospital NHS Trust, London, UK; [6]Robert-Debré Academic Hospital, APHP Nord Université de Paris Cité, Paris, France; [7]University Hospitals of Paris-Sud Bicêtre, Paris, France; [8]Stanford Medicine, Stanford University, Palo Alto, CA, USA; [9]IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy; [10]Catholic University of the Sacred Heart, Rome, Italy; [11]Hospital Universitario Austral, Buenos Aires, Argentina; [12]Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands. [13]University of Minnesota, Minneapolis, MN, USA; [14]Harvard Stem Cell Institute, Harvard University, Cambridge, MA, USA

Autologous hematopoietic stem cell gene therapy with eli-cel (autologous CD34+ cells transduced with *ABCD1* cDNA-encoding Lenti-D lentiviral vector, LVV) showed efficacy in clinical trials ALD-102 (NCT01896102) and ALD-104 (NCT03852498), two 24-month, open-label, single-arm studies in patients with Cerebral Adrenoleukodystrophy (CALD). Following study completion, patients enrolled in long-term follow up study ALD-304. Here, we describe the long-term pooled efficacy and safety of one-time eli-cel gene therapy in patients from these trials up through February of 2023. Patients received busulfan over 4 days, and lymphodepletion over 4 days (cyclophosphamide in ALD-102; fludarabine in ALD-104), followed by eli-cel infusion. At last assessment, 63/67 (94%) patients met the study-defined criteria for stable NFS (maintaining NFS ≤4 with ≤3-point increase from baseline), with 51/63 (81%) maintaining NFS <1. Most changes in NFS were attributed to seizures, incontinence, changes in vision or hearing, or a major functional disability. Loes score remained stable (score ≤9 or <6-point increase from baseline) in 60/67 (90%) patients. Investigator-assessed eli-cel–related serious AEs were reported in 6 patients, with the most serious being myelodysplastic syndrome (MDS) likely due to insertional oncogenesis in 5 (of 67) patients (4 in ALD-104; 1 in ALD-102). MDS was diagnosed with unilineage dysplasia of megakaryocytes (N=4; 14, 26, 28, and 42 months after eli-cel treatment) or with excess blasts (N=1; 92 months after eli-cel treatment). To date three of these patients received a rescue allo-hematopoietic stem cell transplant (HSCT) leading to successful engraftment, however, one patient died following complications from graft-vs-host-disease post allo-HSCT. The other two patients have remained free of MDS with no reactivation of inflammatory brain disease. The choice of vector used and the basis of insertional mutagenesis in lentivirus vector trials will be discussed.

The Development & Validation of the ADRENOLEUKODYSTROPHY-Health Index (ALD-HI)

Jennifer Weinstein, MS,[1] Anika Varma, BS,[1] Jamison Seabury, BS,[1] Spencer Rosero, BS,[1] Nuran Dilek, MS,[2] John Heatwole,[3] Charlotte Engebrecht, BS,[1] Shaweta Khosa, MBBS,[1] Kaitlin Chung,[1] Asif Paker, MD, MPH,[4] Amy Woo, MS,[5] Gregory Brooks, BS,5 Chan Beals, MD, PhD,[5] Rohan Gandhi, PhD,[5] Chad Heatwole, MD, MS-CI[1,2]

[1]Center for Health + Technology, University of Rochester, 265 Crittenden Blvd, CU 420694, Rochester, NY 14642; [2]Department of Neurology, University of Rochester, 601 Elmwood Ave, Box 673, Rochester, NY 14642; [3]Cornell University, Ithaca, NY 14850; [4]SwanBio Therapeutics, 150 Monument Rd, Bala Cynwyd, PA 19004; [5]Autobahn Therapeutics, 9880 Campus Point Drive, San Diego, CA 92121

Background: In preparation for Adrenoleukodystrophy (ALD) therapeutic trials, it is critical for the research community to have access to valid, disease-specific, and responsive patient-reported outcome measures.

Methods: We conducted qualitative interviews and a cross-sectional study of individuals with ALD to identify the most important symptoms. Symptoms with the highest prevalence and relative impact were selected as questions in the ALD-HI. Factor analysis, beta interviews, test-retest reliability, and known groups analysis were performed on the ALD-HI.

Results: Seventeen individuals participated in initial qualitative interviews. One hundred and nine individuals participated in the cross-sectional survey study. During beta testing, the ALD-HI was found to be comprehensive and easy to use. The ALD-HI demonstrated high internal consistency and test-retest reliability. The final ALD-HI consists of 20 subscales which comprehensively measure patient-reported disease burden in the areas of health that are most important to patients.