# Adult Manifestations of Adrenoleukodystrophy
# Externally Led Patient-Focused Drug Development
# Voice of the Patient Report

Meeting Date: 22 July 2022

**Meeting hosted by**: ALD Connect

**Submitted to**: The U.S. Food and Drug Administration (FDA)

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**Adult Manifestations of Adrenoleukodystrophy Voice of the Patient Report**

The mission of ALD Connect is to improve health outcomes for patients with adrenoleukodystrophy (ALD) by empowering patients, raising awareness, and accelerating the translation of scientific advances into better clinical care. This *Voice of the Patient* report was prepared by ALD Connect as a summary of the input shared by people and families living with Adrenoleukodystrophy (ALD) during an Externally-Led Patient Focused Drug Development Meeting (EL-PFDD). This meeting was hosted virtually on July 22, 2022.

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James Valentine, Esq. and Larry Bauer, RN, MA are employed by Hyman, Phelps & McNamara, P.C., a law firm that represents patient advocacy organizations and companies that are developing therapeutics and technologies to advance health.

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## Executive Summary and Key Meeting Insights

ALD Connect hosted the Adult Manifestations of Adrenoleukodystrophy Externally-Led Patient Focused Drug Development (EL-PFDD) meeting on July 22, 2022. This meeting was held to gather patient and caregiver perspectives of the symptoms and burdens associated with ALD in daily life, and to document the massive unmet treatment needs experienced by those who live with ALD every day.

This EL-PFDD meeting focused specifically on adults with ALD, adrenomyeloneuropathy (AMN) and cerebral ALD. The information gathered at the meeting is presented in this *Voice of the Patient* report, a high-level summary of the perspectives generously shared by the patients and caregivers of individuals living with ALD, who participated in the July 22, 2022, EL-PFDD meeting. The report includes selected comments that were submitted by email, through ALD Connect and through an online portal.

The information in the *Voice of the Patient* report may be used to guide therapeutic development and inform the FDA's benefit-risk evaluations when assessing therapies to address ALD. The hope is that this information will catalyze better treatments and ultimately a cure for those affected by ALD. ALD Connect has provided this report to the FDA, government agencies, regulatory authorities, medical products developers, academics, and clinicians, and it is publicly available for the many stakeholders in the ALD community, including ALD Connect's partners and advocacy organizations. Note that the input received from the July 22, 2022, EL-PFDD meeting reflects a wide range of ALD experiences, however not all symptoms and impacts may be captured in this report.

### Key meeting themes and insights

1. **Adult patients with ALD struggle to obtain an accurate diagnosis**. Early symptoms are often dismissed or misattributed. Until very recently, women with ALD were mistakenly believed to be asymptomatic; they often feel invisible and excluded from drug trials.

2. **ALD is a complex disease that affects multiple body systems and has a heavy disease burden.** Symptoms are unpredictable and life changing. Mobility challenges, including balance and gait issues and spasticity, fatigue, as well as bladder and bowel unpredictability have enormous quality of life impacts. Many individuals living with ALD must concentrate hard when walking so that they don't lose their balance and fall. Often, they must plan every aspect of every day and many of them are unable to even leave the house because they fear accidents.

3. **ALD is a progressive disease**. ALD increasingly impacts the lives of those living with the disease as well as their families. Some individuals are severely affected. Cerebral ALD robs people of their cognition and the ability to care for themselves and leads to death.

4. **The impact of ALD on families is particularly severe**. One family described the disease as "*ALD, the destroyer of life. ALD, the destroyer of families"*. Many patients who are living

with symptoms of ALD are also caregivers for children or other family members with the disease. Patients and caregivers often experience psychosocial impacts, including burnout.

5. **People living with ALD and their families are burdened with many worries**. Their top worries are that symptoms will get worse, that they will lose the ability to walk, that they will develop cerebral ALD and that they will fall.

6. **There are no FDA approved treatments for adult manifestations of ALD**. Instead, individuals living with ALD have tried any available approach to mitigate health effects, including vitamins and supplements and treatments approved for other indications, most of which are only palliative.

7. **Most treatments are not very effective and only help address disease symptoms "somewhat".** Some individuals living with ALD reported some success with specific treatments. However, these therapies or approaches do not address the underlying disease causes or stop disease progression.

8. **Despite engaging in regular exercise to maintain function, individuals living with ALD experience decline and increasing disability**. They use numerous other tools, adaptations, supports and strategies including canes, walkers and leg braces to manage symptoms**.** Many have modified their homes and vehicles.

9. **Adult individuals living with ALD urgently and desperately need better treatments**. Many expressed a willingness to try experimental therapies or to participate in clinical trials – even in the control arm – just to advance treatments for this community. Short of a complete cure, they wish for treatments to help maintain their quality of life. They want a therapy to increase their ability to walk, to slow or halt disease progression and prevent the development of cerebral ALD. Women need to be included in research and clinical trials.

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# Introduction and Meeting Overview

## Clinical Overview of X-Linked Adrenoleukodystrophy[1]

X-linked adrenoleukodystrophy (ALD) is a single gene disorder caused by a gene defect in *ABCD1*. The *ABCD1* gene encodes a peroxisomal half-transporter and the resulting faulty protein leads to accumulation of very long-chain fatty acids in all tissues. This leads to progressive inflammatory demyelination of the brain in some patients but more commonly affects the adrenal gland, spinal cord and nerves.

ALD is a rare disease, with less than 10,000 people affected in the United States. Based on newborn screening, which often identifies children in a presymptomatic state, the estimated minimum frequency is one in 14,700 people. True estimates of prevalence in the US are not yet determined.

The most common phenotypes of ALD include childhood cerebral ALD, adult cerebral ALD, adrenal insufficiency, adrenomyeloneuropathy (AMN), and ALD in women. While each phenotype has a distinct pathophysiology, symptoms can overlap. The July 22nd EL-PFDD meeting focused on adults with ALD, AMN and cerebral ALD.

**Adrenomyeloneuropathy or AMN** is typically experienced by males. Myeloneuropathy affects the spinal cord, impairing motor signals and sensory information such as proprioception (the sense of joint perception), pain and balance. AMN is characterized by progressive stiffness and weakness of the legs, leading to balance problems and falls. The bowel and bladder are affected by abnormal sphincter control, neurogenic bladder, and sexual dysfunction. Polyneuropathy leads to numbness and pain. Men with AMN are also often affected by adrenal insufficiency.

**Women experience an AMN-like phenotype with peripheral neuropathy and myelopathy symptoms**. Symptoms of women with ALD were first systematically described in 2014. Women generally experience ALD symptom onset 10-15 years later than men, and do not suffer from adrenal insufficiency or experience brain demyelination. Women with ALD experience gait and balance difficulties with leg weakness and spasticity, and experience more fecal incontinence and numbness and pain than men. Women also experience a higher incidence of small fiber neuropathy and pain and more frequent movement disorders, such as restless leg syndrome and tremors.

**Cerebral ALD** is caused by rapid, progressive brain demyelination resulting most commonly in cognitive decline and behavioral abnormalities but can also impact motor performance. Among other frequent symptoms are impaired visual processing and auditory discrimination as well as seizures. In general, cerebral ALD affects only males.

Even in the absence of brain disease, the ALD disease burden is high. ALD has a complex clinical spectrum, gait and sensory impairments in men usually appear in the late 20s or early 30s, and bowel and bladder symptoms manifest later. Women generally experience ALD symptom onset

[1] Summary from the presentation of Dr. Florian Eichler, "*Clinical features of ALD & AMN and therapeutic approaches*", presented on July 22nd, 2022.

10-15 years later than men. These significantly impact activities of daily living with complications including disability, death, depression, fatigue and psychosocial impacts. These can lead to substance abuse, economic consequences, hospitalizations, and surgeries.

There are still no disease altering treatments for adults with ALD/AMN or cerebral ALD. Rehabilitation, antispasmodics and pain medications can only provide limited relief and do not halt disease progression. However, numerous opportunities around biological pathways and new genetic therapies are currently being explored.

## Meeting summary

The Adult Manifestations of Adrenoleukodystrophy (ALD) Externally-Led Patient Focused Drug Development (EL-PFDD) meeting was held virtually on July 22, 2022. The meeting represented an important opportunity - for adults living with ALD, AMN, and cerebral ALD -to share their experiences with FDA staff and other key stakeholders about patient and caregiver perspectives on the challenges and unmet treatment needs of those living with ALD. The meeting was co-moderated by Kathleen O'Sullivan-Fortin, a founding board member of ALD Connect, a caregiver and a patient living with ALD, as well as by James Valentine, JD, MHS, from Hyman, Phelps and McNamara. The ALD EL-PFDD meeting was structured around two sessions. Session 1 was *ALD symptoms and daily impacts,* and Session 2 was *Approaches to Treatments for ALD*: Men with adrenomyeloneuropathy, cerebral ALD, symptomatic women with ALD. The meeting agenda is in **Appendix 1,** the names of all panelists and callers are listed in **Appendix 2** and the meeting discussion questions are in **Appendix 3.** The meeting was livestreamed in both English and Spanish.

Kathleen O'Sullivan-Fortin welcomed all meeting attendees and participants and briefly described her own ALD journey. Dr. Wilson Bryan, Director of the Office of Tissues and Advanced Therapies in the Center for Biologics, Evaluation and Research, CBER, at the FDA provided some opening comments from the FDA perspective. He emphasized that because ALD is a very heterogeneous disease, the FDA needs to hear from individual voices as well as the community as a whole. Dr. Florian Eichler, an Associate Professor of neurology at Massachusetts General Hospital, MGH, and Harvard Medical School provided a clinical overview of ALD and AMN.

James Valentine provided an overview of the meeting structure and encouraged individuals living with ALD to contribute to the dialogue via online polling, calling in by phone, and contributing written comments using the online portal. Online polling was used to determine the demographics of the meeting attendees, with results shown in **Appendix 4**. Meeting attendees included those living with ALD (57%), caregivers of someone living with ALD (28%), and those who were both living with ALD and a caregiver (15%). Most attendees were located the Eastern US, with strong representation from the US Central and Pacific time zones, as well as attendees from Europe, the US mountain time zone, other and Canada. Half of attendees were female, just less than half were male and a small proportion identified as "other". This meeting focused on adult manifestations, so most attendees were 31-70 years old, with smaller numbers in the 19-30 and over 71 age categories.

The live meeting was attended by 254 individuals who attended the English and Spanish livestreams, including 91 people living with ALD, 62 caregivers, family members and friends as well as 11 health care practitioners. There were 41 attendees from the FDA, in addition to 27 individuals representing industry, 16 from non-profit entities, five scientists, and two consultants.

The morning session continued with pre-recorded patients selected to represent a range of individuals living with different adult manifestations of ALD. James Valentine moderated a discussion between several people who served on a live Zoom panel as well as people who dialed in by phone. Additional comments entered through an online submission form were read by Kathleen O'Sullivan-Fortin.

The afternoon session opened with a pre-recorded panel of patients who described different medical therapies and other approaches they have used to address the symptoms of ALD. Individuals living with ALD and their caregivers described their wishes and hopes for future therapies. Again, meeting attendees participated in online polling, called in and submitted written comments which were added to the moderated discussion by James Valentine and Kathleen O'Sullivan-Fortin. At the end of the meeting, Larry Bauer, RN, MA provided a reflective summary of the key meeting messages. Kathleen O'Sullivan-Fortin concluded the meeting by thanking all the participants and attendees.

The online polling results from Topic 1 and Topic 2 are included in **Appendices 5** and **6**, respectively. To include as many voices as possible, the online comment submission portal was open for four weeks after the meeting. Selected comments are included in the body of this report, and all submitted comments as well as additional content from emails and social media are included in **Appendix 7**.

This *Voice of the Patient* report is provided to all ALD stakeholders including the US FDA, other government agencies, regulatory authorities, medical products developers, academics, clinicians, healthcare providers and any other interested individuals. The final report, the meeting transcript, and both the English and Spanish meeting videos can be found at https://aldconnect.org/pfdd/. According to YouTube statistics, the English meeting recording was streamed over 870 times, and the Spanish meeting recording was streamed over 129 times as of 13 April 2023.

## Session 1: Living with ALD: Men with adrenomyeloneuropathy, cerebral ALD, symptomatic women with ALD

### Top ALD-related health concerns: balance issues, incontinence, altered gait and spasticity

Meeting attendees used online polling to select all of the ALD-related health concerns that they or their loved ones had ever experienced, and to select their three most troublesome. Most individuals living with ALD experience many ALD-related health concerns, with balance issues, altered gait, incontinence, and spasticity topping both polls. Some patients experienced every symptom.

> "*My earliest symptom, that I probably developed in my late teens or early 20s, are balance issues. But then things just kept being added on, neuropathic pain, bladder and bowel issues, fatigue. I basically selected every single symptom that was offered in the first polling question. Every single one of those affects me to varying degrees*." – Aaron, age 36, man living with AMN

ALD-related health symptoms are described in descending order below with patient quotes. Poll results are presented in **Appendix 5, Q1** and **Q2**.

#### *Balance Issues & Altered Gait*

Balance issues were both the most commonly experienced health concern, selected by 81% of those with ALD represented by the polls and selected as most troublesome by 70% of those with ALD represented by the poll results. Altered gait is experienced by 67% and selected as a top three most troublesome health concern by 37% of those living with ALD represented by the poll results. Individuals living with ALD described how balance issues and altered gait both profoundly impact walking and leads to falls.

> *"My top challenges right now are gait and balance. And really, it starts first thing in the morning when I wake up, my legs are so spastic I can't even put any weight on them*." - Jana, age 51, symptomatic woman living with ALD

> "*In my mid-thirties and onwards, my walking gait started getting progressively worse to now, where my balance is horrible, with me swaying to one side over the other and being a wall walker to gain stability. I'm so very cautious about my walking*." – Allen, man living with AMN

> *"My early symptoms were tight calves, falling and tripping, and some balance issues. These were sporadic and I was not symptomatic until around 2017 when my gait and walking speed affected my daily routine, I walked as if I were in pea soup. My gait was uneven and I began to walk as if I were drunk. I was not yet using a walking aid, but clearly everyone around me would get ticked off as to why a seemingly healthy person*

*was walking so slowly and tipping over for no reason*." - Julie, symptomatic woman living with ALD

### *Incontinence (bowel and bladder)*

Bowel and/or bladder incontinence is experienced by 65% of those represented by the poll results and was the second most troublesome health concern, selected by 57% of poll respondents. Many described experiencing frequent accidents and how the fear of this happening kept them at home.

> "*This is the area that is really not fun for anyone to experience, as you feel that you will wet your pants if you don't get to a restroom quickly. And when you get to the restroom, it is challenging to fully drain urine, as the bladder is not working correctly with a neurogenic bladder. And when you cannot walk fast, getting to the bathroom in time sometimes doesn't always happen*." - Eric, age 43, man living with AMN

> "*Uncontrolled bowel frequency is the issue that most effects my current daily life. In my 30's, I started soiling myself while out in public. It's something I have to manage constantly and that severely limits my daily activities***."** - Emily, symptomatic woman living with ALD

> "*I'm worried about walking outside with an accident about to happen, urinating, or solid waste on myself. It really makes me take a second thought on when I'm eating or drinking.*" - Allen, man living with AMN

### *Spasticity*

Spasticity is experienced by 67% of those living with ALD represented by the poll results and selected as a top three most troublesome health concern by 26%. Spasticity profoundly affects mobility and also sleep.

> "*I began to develop symptoms of ALD such as spasticity, my running began to decline, and I started to notice some beginning stages of coordination and sensation issues with my feet and legs. … Spasticity can be described as a constant feeling of tightness in the muscles and sometimes uncontrolled spasms. It really never goes away*." - Eric, age 43, man living with AMN

> "*Over time, he no longer could walk on his own as his muscles frequently froze up and spasmed in place. He continued to develop more nerve issues and needed at least one person to help him transfer from his wheelchair to a chair or a bed. He could not walk up and down the stairs anymore, which further complicated his life and the demands on our family*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

> Emma's mom stands up from her wheelchair and braces herself against the counter to cook. "*Her legs will start spasming so much that she'll knock her legs into the kitchen counter and start getting bruises and cuts all down her legs*." - Emma, caregiver for her mom, age 53, symptomatic woman living with ALD

### *Foot Drop*

Foot drop is experienced by 59% and selected as a top three most troublesome health concern by 9% of those living with ALD represented by the poll results, and like some of the other health concerns, impacts the ability to walk.

> "*I couldn't get from my car to the classroom without tripping over my feet with foot drop and loss of coordination. The challenge of being embarrassed that you are tripping and having to walk in front of people is taxing on the mind*." - Eric, age 43, man living with AMN

> "*I experienced a lot of drop foot, which also caused the tripping and the falling*." – Ken, age 38, man living with AMN

> "*My walking is horrible. My therapist was concerned about my crooked walking and how it would change my alignment, walking the way I did. My spinal cord would be crooked or worse. My legs weren't straight when I was walking and there was no heel to toe proper form. I'm really more of a drag with my right leg specifically*." - Allen, man living with AMN

### *Tingling, numbness, or impaired sensation*

Tingling, numbness or impaired sensation are experienced by 57% and selected as a top three most troublesome health concern by 13% of those living with ALD. Some described this as "pins and needles", others described burning and pain, and some reported having no sensation at all.

> "*My symptoms have increased over the years, always impacting my life. Symptoms started when I was 22 with pins and needles in my feet, hip pain, gait disturbance, balance trouble, extremely cold hands and feet, and legs giving out suddenly leaving me on floor*." – Barbara, symptomatic woman living with ALD

> "*I have severe burning neuropathy in my feet and legs and numbness in my toes. … Neuropathy symptoms started last fall and I was experiencing severe numbness in my feet and stinging in my legs*." - Shari, symptomatic woman with ALD

> "*I don't have any feeling in either one of my feet or from the knee down on both legs. Thank goodness I have the neuropathy bad enough to where I can still feel my feet when I have pressure on them. If I have my feet up in the air and there's no pressure on, no socks, I couldn't tell you where my feet are*." – Jamie, age 56, symptomatic woman living with ALD

### *Pain*

Pain is experienced by 54% and selected as a top three most troublesome health concern by 23% of those living with ALD represented by the poll results. They described chronic pain, neuropathic pain, and pain in their feet, legs, back, and sciatic regions.

> *"The worst thing is back pain. I sit in a wheelchair and my back pain can never get better because I sit all day. I am 36 and I already take 18 pills a day. My pain doesn't allow me to do daily things. I have to lay down hours a day."* – Steve, man living with AMN

"*I'm 27, and I've had symptoms since elementary school. I wake up in pain, leg pain, back pain, bladder pain, fatigue, and so many other little things*." - Rachael, symptomatic woman living with ALD

*"The sciatic pain was chronic. It became another dimension in ALD because the spinal doctors I saw could not understand why I was in so much pain when the MRI did not show anything significant. It seems that ALD just magnified the pain*." - Julie, symptomatic woman living with ALD

### *Weakness/paraparesis*

Weakness, paraparesis, or the inability to move legs, is experienced by 52% and selected as a top three most troublesome health concern by 19% of those living with ALD represented by the poll results.

"*I can't predict when I'll have a bad day. Without warning, my legs weaken, my knee collapses. My ankle turns or I spill something*." - Mary, symptomatic woman living with ALD

"*She started using a walker when we would go out places, but she can't really walk more than 50 steps with her walker. She gets really tired, her legs get tired and she's not able to physically move them*." - Emma, caregiver for her mom, age 53, symptomatic woman living with ALD

*"I am having severe weakness in my legs, have difficulty walking with my walker and still exhausted and sleeping huge amounts per day."* - Dorothy, symptomatic woman living with ALD

### *Depression and anxiety*

Depression is experienced by 48% and selected as a top three most troublesome health concern by 13% of those living with ALD represented by the poll results. Some are suffering from the losses of friends and family, loss of their identity, social isolation, and living with the knowledge that their disease will continue to progress. Some experience guilt.

"*When my symptomatic nine-year-old son was diagnosed with adrenoleukodystrophy, I was told that I carried the gene as well. When he was on the transplant floor, his doctor explained to me the reason for my symptoms was that I was a female with ALD. Guilt, knowing I had passed ALD to two of my children, and depression revolving around that and knowing my continued loss of abilities would follow me my whole life*." - Barbara, symptomatic woman living with ALD

Ken lost his oldest brother and a close friend to cerebral ALD, both in their 30s. "*That alone has affected me on a mental note. Here I am living the same life they had with some of the same symptoms. I'm here and they are not. Wrapping your head around that isn't easy and has led me to some times of depression and thoughts of throwing in the towel*." - Ken, age 38, man living with AMN

"*I often feel like a failure as a parent, as a wife and as a person. I cannot work due to this and other medical issues and have lost my identity. I used to be a medical professional. I am still struggling to accept that my future is likely only downhill from here*." – Amy, symptomatic woman with ALD

### *Impotence*

Impotence or other sexual dysfunction is experienced by 35% and selected as a top three most troublesome health concern by 17% of those living with ALD represented by the poll results, however, was not mentioned often during the meeting as this is a sensitive issue.

"*There are other challenges that come with AMN that most men would probably not want to talk about, with ED [erectile dysfunction] and other sexual dysfunction issues*." - Eric, age 43, man living with AMN

### *Adrenal Insufficiency*

Adrenal Insufficiency is experienced by 33% and selected as a top three most troublesome health concern by 11% of those living with ALD represented by the poll results.

"*Mark suffered from hypothyroidism and Addison's disease, which require lifelong medications. These conditions made him more susceptible to infections, so we didn't leave the house often*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

"*My urinary issues led to a UTI, but with AMN, it caused adrenal crisis. And I was rushed to the hospital with adrenal crisis, and experienced some life-threatening complications, including heart [rate] dropping to extremely low levels*." - Tim 1, age 56, man living with AMN

### *Other ALD-related health concerns*

Other health concerns are experienced by 28% and selected as a top three most troublesome health concern by 6% of poll respondents. These include traumatic injuries from falling, fatigue, severe and repeated infections, manifestations of cerebral ALD including death. Other health concerns experienced by individuals living with ALD include extremely cold hands and feet, seizures, shortness of breath, short term memory loss, and glaucoma.

**Traumatic injuries from falls.** Many meeting participants have experienced injuries from falls including broken hips, knees, ankles, feet, shoulders, ribs and concussions. Many injuries resulted in surgeries.

"*The balance issues that came with his AMN resulted in many falls, but over time they became more frequent. And two of them resulted in a broken shoulder and broken ribs*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

"*I have fallen several times. One time I fell and hit my head, horrible concussion. Two falls after that is when I fell and broke my ankle*." – Jamie, age 56, symptomatic woman living with ALD

*"I have fallen 3 times with severe injuries: I broke three toes, swollen and painful; I broke both hips (different occasions one year apart) and had to have two total hip replacements. My recovery for each injury was longer than most because of my balance and unstable walking."* - Cynthia, symptomatic woman living with ALD

**Fatigue.** Many individuals living with ALD experience fatigue from pain, the lack of sleep, and from the disease itself.

*"I think fatigue is a huge issue that needs to be addressed. … I got 10 hours of sleep last night after taking a sleep aid because I was up about six hours the previous night. Yet, I did not feel refreshed when I got up this morning. I never feel rested anymore when I wake up. Fatigue is a major symptom that I deal with daily."* – Janis, symptomatic woman living with ALD

*"My capacity to do those things has fallen over time, I get exhausted and clumsy as the day goes by and I find myself pulled away from the things I love doing, so I can rest and treat my pain*." - Rachael, symptomatic woman living with ALD

*"Sleep was a constant struggle and caused the fatigue and made it difficult to work. … I know if he sat down, when he got home, he could fall asleep the minute... He was always tired. Always*." – Connie, widow and caregiver for Rex who passed away from cerebral ALD at age 62

**Severe and recurrent infections.** Individuals with ALD experienced bone infections and recurrent urinary tract infections.

"*Most recently, I had four different hospital stays, 16 days in the hospital. And the first was osteomyelitis caused by my foot drop, which led to an infection to my foot. And they had to amputate my toe to provide further infection spread.* - Tim 1, age 56, man living with AMN

Due to Mark's intermittent/external catheterization, "*He developed urosepsis nine times in his last year of life. Every infection demanded hospitalization and resulted in more muscle decline and cognitive impairment*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

**Symptoms of cerebral ALD.** These can include personality changes, cognitive decline, loss of speech, swallowing issues, extreme migraines, breathing issues, high fevers, seizures, and death.

"*I am unable to do simple tasks. I can no longer type, have double vision, and slurred speech, eat with a spoon, and have some swallowing issues*."- Charles, man living with adult cerebral ALD

"*Our son was changing quickly. Loss of appetite, difficulty swallowing, difficulty breathing, loss of upper body motor skills and loss of communication all took their toll on Justin. Justin died January 22, 2022 at 3:00 AM peacefully at the age of 37. ALD took our*

*second son at this incredibly young age*." – Cheryl and Frank, parents who lost both sons to cerebral ALD

"*Unfortunately, Rex was not diagnosed with ALD until just over two years before he passed."* Connie spoke about changes to personality and behavior, then word-finding difficulties, then forgetting. *"He was a brilliant man… And to watch his cognitive abilities to be taken away was very difficult*." - Connie, widow and caregiver for Rex who passed away from cerebral ALD at age 62

"*The confusion that he suffered completing basic tasks grew. And our interactions with him became simplistic. As if we were talking to a child. The less complicated the task or conversation, the easier it was for him to understand and participate*. … *As his brain failed, Mark lost the ability to speak. He needed help with feeding to avoid aspiration. … He lost his memory and eventually did not even recognize his wife. He gradually withdrew from life until he died."* - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

## Additional ALD insights not captured by the polls

The following themes were mentioned repeatedly during the meeting and in the patient comments yet were not reflected in the poll results.

**Symptoms of adults living with ALD are often dismissed or misattributed.**

"*My internist had sent me to a psychiatrist, not a neurologist. It was traumatic. I couldn't control my body and my internist called me a hypochondriac. I was relieved when I was finally diagnosed with ALD*." – Mary, symptomatic woman living with ALD

*"[My brother] developed an unusual gait that gradually became progressively worse over the next few years. He consulted several neurologists who failed to understand or diagnose his condition."* - Harry, age 63, man living with AMN

*"Primarily, I consider myself a caregiver for ALD, and like a lot of us, my son was diagnosed 15 years ago. I was told that I was just a carrier. And as the years have gone on, I've recognized that's not true, unfortunately. So, on top of taking care of my son, who's fully dependent, my symptoms have increased as the years have gone on*." - Jesse, symptomatic woman living with ALD and caregiver for her son with ALD

**ALD can progress very rapidly after diagnosis, particularly with cerebral ALD.**

*"Within two years I went from doing things as normal to where now I'm using a cane and holding onto walls to get around. I need a wheelchair for anything that requires more than a few steps of walking."* - Alisa, symptomatic woman living with ALD

*"Once the lesions took over his brain, disease progression was very fast. It only took 18 months for AMN to take Mark from the fun loving and athletic man he was to the mostly*

*expressionless quiet man that he became*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

*"The symptoms have worsened, particularly it's gone pretty rapidly over the last two years."* - Tim 1, age 56, man living with AMN

**Individuals living with cerebral ALD will eventually require 24-hour care.**

*"[He was] someone who never had to ask how to do anything, he in the end could not do the simplest things and couldn't be left alone for safety reasons*. … *Those last few months of his life were heartbreaking.*" - Connie, widow and caregiver for Rex who passed away from cerebral ALD at age 62

*"There weren't many options my children and I considered when it came to Mark's care. We promised him and ourselves that we would do whatever it took to help him live a fulfilling life at home, no matter how long that would be*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

*"He died weighing 30 kilos, breathing with the help of the 'bipap' and with oxygen when the saturation dropped. We assisted him to cough and aspirated his saliva and secretions continuously to prevent him from choking. We lifted him up and sat him down in a wheelchair that people lent us, which we adapted according to his needs, because the chair that was requested to the health insurance never arrived."* **-** Alicia, mother of a deceased son with adult cerebral ALD

*His body was failing and so we tended to his needs, shower, eating, cleaning. All the nurses began to see him decline, breathing, chewing, swallowing difficult*y." – Frank and Cheryl, parents who lost both sons to cerebral ALD

## Impacts: Walking is the activity that is most severely impacted by ALD but many other aspects of daily life are also impacted.

Poll respondents used online polling to select their top three activities of daily life that are important to them or their loved one, that they are not able to do due to ALD. ALD is unpredictable, impacting all aspects of life. Walking is the activity that is most severely impacted. Poll results are presented in **Appendix 5, Q3** and illustrated with patient comments below.

### *Walking*

Walking is the activity of daily life that is most impacted by ALD, selected by 69% of poll respondents as one of their top three. Many are walking slower, have to concentrate to walk, and some use the wall as a support and described themselves as "wall walkers" or "wall surfers".

> *"As soon as I stand up, I have to make sure, can I feel my feet? Can I move on? …That's all fine most of the time. But then if something happens, somebody talks to me, or I get ahead of myself in my thought process, I can fall over."* - Patricia, symptomatic woman living with ALD

> "*With ALD, I have to think about walking. If I walk in the dark, I become disoriented. If I turn too quickly, I risk falling. I can't even walk and look at my cell phone, or the person I'm walking with. … I rely on a three-legged cane and I can't walk far. My walking gait looks uncoordinated. I bump things and drop things. And often, I have trouble focusing*." – Mary, symptomatic woman living with ALD

> "*Since the beginning of onset of AMN, approximately 15 years ago, I have gone from being able to run to using a cane and wheelchair to ambulate daily. I have experienced weekly falls because the coordination, muscle atrophy, and spasticity in my legs has gotten progressively worse*." – Eric, age 43, man living with AMN

> "*I can't walk more than 50 feet without the help of a scooter, or a wheelchair. And I use a walker at night just to go to the bathroom, which is frequent sometimes, every hour*." - Tim 1, age 56, man living with AMN

### *Playing sports or biking*

Playing sports or biking was selected by 45% of those with ALD as a top three activity of daily life impacted by ALD.

> *"Our younger son, Jason, an outstanding athlete was no longer able to compete in basketball, volleyball, and track. He began to struggle with walking and balance*." – Cheryl and Frank, parents who lost both sons to cerebral ALD

> *"My symptoms were life changing. I went from actively running and playing tennis, to having to think about walking. … I used to be athletic and graceful. Now, I drop things and bump into things."* – Mary, symptomatic woman living with ALD

"*Until two years ago, I had a fairly active life. I was able to walk, golf, and travel with some limitations, such as falling down on the golf course and airports due to balance issues. I have been in a wheelchair for the last year because of the lesion on my brain that was found one and a half years ago."* - Charles, man living with adult cerebral ALD

"*The disease over the 36 years has taken me from good athlete to just a few walking steps per day. I lost my ability to run in 1990. … I am unable to stand independently and need to hold support to stand up. I am able to swim okay, but loss of strength over the years is making it more difficult*." -Michael, man living with AMN

### *Sleeping*

Sleeping was selected by 41% of those with ALD as a top three activity of daily life impacted by ALD. Spasticity and incontinence both affect sleep.

*"I know I'm waking my husband up with all my tossing and turning. … I think there's probably going to be a day at some point where we're going to not be able to just share a bed."* Bladder and severe leg spasms only allow Jana to sleep an hour and a half at a stretch. "*I never have a problem falling asleep, because I'm so exhausted from trying to walk all day long. But then a lot of times I'm woken up within about 15, 20 minutes with a severe leg spasm. And it's a big jolt that wakes me up*." – Jana, age 51, symptomatic woman living with ALD

*"His spasticity would shake the bed so much at night that it would wake up both of us or if he got to sleep through the spasms, I would feel them. …The sleep was a constant struggle and caused the fatigue and made it difficult to work. …He was always tired. Always*." – Connie, widow and caregiver for Rex who passed away from cerebral ALD at age 62

"*My spasticity has caused these leg spasms, which make it really difficult to sleep. And generally, every hour on the hour I'm up, which that certainly impacts my day, and my relationship with my wife, my family, my friends, because of my lack of energy*. … *Sleep deprivation and being fatigued all the time does have an impact*." - Tim 1, age 56, man living with AMN

### *Attending social events with family and friends*

Attending social events with family and friends was selected by 35% of those with ALD as a top three activity of daily life impacted by ALD. Some feel socially isolated.

"*I can't play with my nephews like I want to, my freedom of going out is limited and I'm not able to walk. I may not join in sport or some other activity with my family or friends*." - Allen, man living with AMN

"*When I had to stop working people congratulated me on an early retirement. However, unlike others who may finally get to travel and golf, I stay at home unable to go independently. And my friends don't think to ask me along as that means a wheelchair and someone who has difficulty speaking and eating, not the friend they used to know. I*

*want to laugh and have fun too, but I no longer can have fun because of ALD*." – Barbara, symptomatic woman living with ALD

"*Going to a concert, or play, or dance, or any similar event... I have to manage how much I hydrate and when I will able to get to the bathroom*." - Ted, man living with AMN

### *Being intimate with a partner*

Being intimate with a partner was selected by 24% of those with ALD as a top three activity of daily life impacted by ALD.

"*After three to four years of becoming more symptomatic, my wife of nine years filed for divorce. She stated that she had just lost her love for me. Part of this was because of the sexual problems. She wanted more than I could give her. And the loss of income I had once, had some to do with it also.*" – Eric, man living with AMN

"*ALD has impacted my relationships with wife."*- Brett, man living with adult cerebral ALD

### *Working*

Working was selected by 22% of those with ALD as a top three activity of daily life impacted by ALD. For many, ALD symptoms or the time spent caring for a loved one with ALD led them to lose the jobs that they loved. The decision to leave a job is difficult and leads to tremendous financial hardship.

Eric's early ALD symptoms included spasticity, "*This led me to having to leave law enforcement young in my career, and in my late twenties. This was probably one of the most challenging times of my life…. at this point I lost a career that I loved and had to move on.*" - Eric, age 43, man living with AMN

*"I can't work, because some days all I can do is sit, my brain and body will not cooperate. ALD effects every moment of my day*." - Rachael, symptomatic woman living with ALD

"*My hand tremors caused my handwriting to become illegible. I finally agreed with my neurologist. It was time to stop working*." – Barbara, symptomatic woman living with ALD

"*As his brain began to fail, I was forced to step back from my communications career and we lived on savings for the rest of Mark's life. There was no way I could work, as Mark's AMN demanded 24-hour care, plus Massachusetts doesn't pay spouses to care for their spouse, so we suffered tremendous financial distress*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

### *Driving*

Driving was selected by 18% of those with ALD as a top three activity of daily life impacted by ALD.

"*A policeman stopped me for bad driving. I failed the heel-toe walk*." – Mary, symptomatic woman living with ALD

"*I didn't get the opportunity to learn to drive because my doctor told me that my reaction time is slow*."- Allen, man living with AMN

### *Eating independently*

Eating independently was selected by 6% of those with ALD as a top three activity of daily life impacted by ALD.

"*We also learned how to portion Mark's food and safely feed it to him because he could not see, use utensils or effectively chew. Plus, having cerebral ALD and AMN made him a choking and aspiration risk, so he needed supervision when eating and drinking*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

"*I can't eat without coughing and gagging*. … *Now swallowing impacts my living and my ability to get enough nutrition into my body. Dining was one last social thing I could still do. My husband misses us going out and feels badly eating food while I drink my meals using powders to make shakes*." – Barbara, symptomatic woman living with ALD

### *Communicating*

Communicating was selected by 6% of those with ALD as a top three activity of daily life impacted by ALD.

"*My speech became halting and quiet, and in times of stress, nonexistent. … I don't like talking to anyone due to my speech*." - Barbara, symptomatic woman living with ALD

"*He struggled with vision neglect, speech problems, and word recollection. Much of his speech became gibberish. We think he knew what he wanted to say, but his brain was so compromised he couldn't vocalize it. He grew increasingly agitated with aphasia and became more socially reserved*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

### *Other Impacts*

Other activities were selected by 16% of those with ALD as a top three activity of daily life impacted by ALD. These include self care and chores, travel, leaving the house and participating in favorite pastimes.

**Self-care and chores**

"*My husband has to do chores I have always done. I struggle with that as I'm a very independent person and not a person who asks for or accepts help. I have always earned my keep. It is difficult for him to walk the line as he knows how independent I am, but it scares him to know the things I try to do*." – Barbara, symptomatic woman living with ALD

"*It kills me that I am dependent on my family caretakers for everything. I have no privacy. I am never comfortable*." – Ganesh, age 21, living with cerebral ALD

*"I have to get rides to go to medical appointments, have my groceries delivered, depend on others to help me clean the house, have people take care of my yards, have help with*

*the garden. Have help with almost everything*.*"* – Jamie, symptomatic woman living with ALD

Connie's husband took care of his bowel and bladder activities as long as possible. "*The one thing that he hated the most was that I had to do those for him. ... I still remember when I said, 'Okay, it's time for me to help you.' And with tears in his eyes it took away his dignity, that I had to do things to help him that he hoped and wished no one had to do for him*." – Connie, widow and caregiver for Rex who passed away from cerebral ALD at age 62

**Travel**

"*I had visions of spending my retirement traveling, hiking in the mountains, and playing lots of tennis. Now I'm focused on avoiding falls and making sure that I'm never far from the restroom*." – Mary, symptomatic woman living with ALD

"*Can't travel alone easily, need wheelchair to get around. Can't hike, I am only able to walk about 2.5 miles before my legs cramp. I miss tours and activities when we travel. I am unable to walk around museums, so I sit somewhere and wait*." - Cynthia, symptomatic woman living with ALD

**Leaving the house**

"*Many times, I'm unable to leave the house due to a combination of these symptoms, either the spasticity that makes me unable to walk, move my legs, or the fact that I have bowel or bladder issues, I don't want to have an accident either outside the house*." - Tim 1, age 56, man living with AMN

*"[I'm] at home alone because my family is enjoying an adventure that I cannot participate in. My struggles with ALD are absolutely impacting my daily life. My family is dramatically affected by ALD but I am the one with the worst symptoms."* - Laurie, symptomatic woman living with ALD

**Favorite pastimes**

"*I missed out on being an active and participatory grandmother, community volunteer, writing tutor, conductor of workshops, soprano in our seniors choir, hostess and visitor to/with family and friends because of ALD*." - Nancy-Anne, symptomatic woman living with ALD

"*Now I'm home alone all day. I had accepted I would not walk, but decided at least I would be able to do hand work, which I always enjoyed. Now with the tremors in my hands and head, it's difficult to do any of that. So for a person who was always busy, I am no longer myself."* - Barbara, symptomatic woman living with ALD

## Additional ALD insights not captured by the polls

The following themes were mentioned repeatedly during the meeting and in the patient comments yet were not reflected in the poll results.

**Life with ALD is unpredictable and requires a lot of planning.**

> *"With every step that we take and every life event that we want to be a part of, we have to spend so much time strategizing how we can be a part of that without having a life changing accident happen*." - Patrick, man living with AMN

> *"With ALD, you're constantly having to think and predict what's going to happen. Last night, we went to dinner and I was actually walking okay. But I knew I had to take my knee scooter because if I sit while I'm eating dinner for 30, 45 minutes, I'm not going to be able to get up and get out. So that's another thing, just the anxiety and planning."* - Jana, age 51, symptomatic woman living with ALD

> *"There are definitely a lot of things that my mom has missed out on or not been able to do, just because she needs to plan. If we're going to a restaurant, where is the closest table that's going to be next to the bathroom? Or how long could she sit in a car without needing to empty her bladder, things like that. She does take medications for her incontinence issues, but there's definitely a lot of anxiety around planning a day out with us, the rest of her family, and how that's going to work for her*." - Emma, caregiver for her mom, age 53, symptomatic woman living with ALD

**ALD profoundly impacts families and family relationships.**

ALD forces roles within the family to change and individuals with ALD are often unable to participate in family life as much as they want. Some individuals who are living with ALD are also caring for children or siblings with ALD. Patients and caregivers often experience psychosocial impacts, including burnout.

> "*Mark's cerebral ALD ruined his memory. Not just recalling events in his life, but people too. This was the worst part of this experience for me because he forgot who I was more than once. … He was starting to forget me to forget us and forget our life together. This was devastating in the moment that I knew my marriage was over. I cried for hours after this visit. My husband was disappearing and there was nothing I could do but watch it happen*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

> *"He hated that he could no longer take care of his family and we had to take care of him."* - Connie, widow and caregiver for Rex who passed away from cerebral ALD at age 62

*"I no longer walk unassisted because of ALD. I wish I could play on the floor with my grandchildren but I can't because of ALD. ALD has impacted my relationships with my entire family and friends. I missed out on babysitting my grandchildren because of ALD*." - Patti, symptomatic woman with ALD

"*I want to share how challenging and devastating this disease has been for myself and my family. …I have two boys, and while I am very involved and can participate in many activities with them, … there are many times where I have to sit out or stay behind because the activity we are doing is not accessible, so my wife will have to step in*."– Eric, age 43, man living with AMN

## Top worries: worsening symptoms, losing the ability to walk, and developing cerebral ALD

Individuals living with ALD and their loved ones experience many worries. Worsening symptoms, losing the ability to walk, and developing cerebral ALD are at the top of the list. Poll respondents used online polling to select their top three worries about their or their loved ones condition in the future. Their top three were all related to disease progression. Poll results are presented in **Appendix 5, Q4** and illustrated with patient comments below.

### *Symptoms will get worse*

The top worry for the future, selected by 88% of individuals living with ALD represented by the poll results was that symptoms will get worse.

*"I'm constantly on edge worried about what the next symptom will be since none of this is predictable. There's always fear that I will end up paralyzed the way my mother did. She suffered from ALD for 10 years. Watching her go through that was devastating. I don't want my family to experience that."* - Shari, symptomatic woman living with ALD

"*I'm worried about disease progression and cerebral involvement with AMN. It's been a progressive condition for me. And then I have challenging symptoms develop. I learn to adapt to them, but then a new symptom comes or progresses and you have to readjust to the new norm*." - Eric, age 43, man living with AMN

"*As each symptom has been added, I wonder what the next symptom will be and will I be a woman who has cerebral involvement*." - Barbara, symptomatic woman living with ALD

Many especially expressed their worries for how the disease will impact their asymptomatic children.

*"As my daughter gets older, I fear for her future."* – Amy, symptomatic woman with ALD

*"I worry mostly about my 29-year-old daughter who is thus far asymptomatic, but what will her future look like?"* - Janis, age 65, symptomatic woman living with ALD

*"There's always concern that my daughter will also become symptomatic. It's been a never-ending road to travel and my family is still affected*." - Shari, symptomatic woman living with ALD

### *Losing the ability to walk*

Losing the ability to walk was selected as a top worry for the future by 61% of individuals living with ALD represented by the poll results.

> "*My biggest fear is waking up in the morning and I can't walk. That's my fear. I would love to not being into pain. But like I said, I need the pain so that I know where my feet are*." - Jamie, age 56, symptomatic woman living with ALD

> *"I keep exercising as much as I can since there is no treatment for women, and I greatly worry about mobility as I get older (I am 49)."* - Julie, symptomatic woman living with ALD

> *"It would be amazing to be able to continue to walk for the rest of my life, but the reality is, I don't know if I will be that lucky."* - Brandon, man living with AMN

### *Development of cerebral ALD*

Development of cerebral ALD was selected as a top worry by 39% of individuals living with ALD represented by the poll results. Cerebral ALD is a life of profound suffering that leads to death.

> "*It's hard to accept that there are no approved treatments to help the progression of cerebral ALD and that my future could be of that, developing cerebral ALD*." - Ken, age 38, man living with AMN

> *"Every man with AMN deeply fears developing cerebral disease."* Aaron had discussed this possibility with a friend who was also living with ALD. *"We sat across the table from each other and had a very frank conversation looking at each other in the eyes and talking about the potentiality of developing cerebral disease and what that would look like and what we would do if it ever came to that. Two years after that conversation at dinner with him, he had passed away from cerebral ALD. It hits very close to home when you know somebody personally, when you have had a conversation with them, when you've talked about the possibility of this happening and then it's happened. And it's something that is it's always in the background of our lives."* - Aaron, age 36, man living with AMN

> "*The threat of cerebral ALD is always there (even for AMN patients) and the deterioration from AMN can creep up at any age – as early as the second decade of life for some. … This devastates me as a mother."* - Miranda, mother of a son with ALD diagnosed through Newborn Screening

### *Falling*

Falling was selected as a top worry by 29% of individuals living with ALD represented by the poll results and this was reflected by many comments.

> "*My motto is, don't fall. I went from hiking in mountains with very rough terrain, to having trouble walking on soft sand and even grass. … I'm an orthopedic wreck, so that*

*heightens my fear of falling. If I fall, I break. I've got severe osteoporosis*." – Mary, symptomatic woman living with ALD

"*I'm concerned about falling outside and getting up again. And there is nothing around me to raise myself up with my hand. I'm stuck there on the floor. I really make it important to look around at my surroundings, uneven sidewalk and what steps that I take*." - Allen, man living with AMN

"*I'm worried about tripping, … my leg could completely contract, and I could fall to the ground. And at that point, I'm at a much larger risk for a head injury which could be severely detrimental. … Sometimes I feel like I should be walking around with elbow pads and a bicycle helmet."* – Patrick, man living with AMN

### *That my relationships will suffer/Children are going to have to take care of me*

Worries that my relationship will suffer was selected as a top worry by 27% of individuals living with ALD and the worry that children are going to have to take care of me was selected as a top worry by 18% of individuals living with ALD represented by the poll results. During the meeting, Laurie described how her son trained as a personal care aid to care for his declining father. Many expressed gratitude to their spouse and family members for care, but worried about being a burden.

"*I fear I will be a complete burden to him. I am fortunate to have my family and a man who stays true to the 'in sickness' portion of his vows*." – Barbara, symptomatic woman living with ALD

*"I think the biggest challenge - and my fear - is just the burden that I have become to my wife as the caregiver and my family. It's hard on them to see, prior to this, I was an athlete and very active. So it's been really hard on my wife and family.* - Tim 1, age 56, man living with AMN

Holly expressed worry about her husband, *"Basically him being a caregiver of me, having to fall more and more into that role. And he's wonderful and supportive, but also there's the guilt of thinking that he's going to have to do that for me. There is just a constant worry and fear about the future and what that is going to bring."* - Holly, symptomatic woman living with ALD

### *Unable to continue working*

Unable to continue working was selected as a top worry by 16% of individuals living with ALD represented by the poll results. This was reflected in the many comments about having to stop working, discussed in an earlier section.

### *Not being able to get out of bed unassisted*

Not being able to get out of bed unassisted was selected as a top worry by 8% of individuals living with ALD represented by the poll results.

After Mary's husband experiences one of his frequent falls, "*The spasms go up his leg for hours. He's just in excruciating pain. Then he can't get out of bed. He can't do*

*anything else. He can't move. It's just really hard to see and to watch that*." - Mary M., caregiver for her husband who is living with ALD

### *Not being able to have children*

Not being able to have children was selected as a top worry by 6% of individuals living with ALD represented by the poll results.

> *"Another thing that's really impacted our life is we really want kids. We feel that he'll be unable to, sorry, this is a really hard topic… He won't be able to chase kids. It'll be hard for us because it'll just be me. I know that a lot of there are a lot of single parents out there, but just being able to chase after kids, even walk our dogs, simple stuff that people are able to do and he can't do. It's just really, really hard*." - Mary M., caregiver for her husband who is living with ALD

### *Other worries*

Other worries were selected by 8% of individuals living with ALD represented by the poll results and included worries about having to move from their home, worries about having an accident in public, and worries that they will no longer be able to care for themselves or their loved ones.

> *"My concerns are being wheelchair bound and will we have to move from the home that we love so that it will be more accessible to me. What kind of in-home care I'm going to need. And I think a lot of us experience these thoughts of, 'this is not really the life we plan for, or the retirement we plan for.'"* – Holly, symptomatic woman living with ALD

> "*Because [my mother is] so nervous about the incontinence issues, she'll plan her liquid intake for the day. She won't drink water, or tea or anything, but it is variable how long she can last without needing to use the restroom, just based on how much liquid she consumes during the day*." – Emma, caregiver for her mom, age 53, symptomatic woman living with ALD

> "*My biggest concern are my balance issues because I do care for my son. And although he has not lost the ability to work, he does need assistance with everything, including bathing him, getting him dressed, getting him ready for bath, everything. And if my mobility gets severely impacted, I'm really not sure how I can care for him the way he requires."* – Jessie, symptomatic woman living with ALD and caregiver for her son with ALD

> "*I share that fear of not being able to take care of myself and my family."* – Kathleen O'Sullivan-Fortin, founding board member of ALD Connect, a caregiver and a symptomatic woman living with ALD

## Session 2: Approaches to Treatments for ALD and AMN: Men with adrenomyeloneuropathy, cerebral ALD, symptomatic women with ALD

### Currently there are no FDA approved treatments for adult manifestations of ALD

Instead, individuals living with ALD try any approach available to alleviate ALD symptoms, including vitamins and supplements and treatments approved for other indications. Poll respondents used online polling to select all medications (prescription or over the counter) that they or their loved one used (past or present) to treat symptoms associated with ALD. Respondents each selected an average of 4.2 responses. Poll results are presented in **Appendix 6, Q1** and illustrated with patient comments below.

*Vitamins or supplements*

Because they don't have anything else, vitamins or supplements were the top choice of poll respondents, used by 73% of the individuals living with ALD represented in the poll results. Most individuals living with ALD would take anything that would possibly help alleviate symptoms, including biotin, vitamin D, B vitamins including B12**,** resveratrol, magnesium, antioxidants, NAC, N-acetylcysteine, and alpha-lipoic acid. A downside of vitamins and supplements is that there is no clear evidence that they make a difference.

> *"There was a MD1003 clinical trial a while back, which was basically 300 milligrams of biotin that you can take a day. I wasn't able to participate in that trial, but I got on Amazon and I ordered a bunch of biotin. I didn't want to miss out on an opportunity."* - Tim 2, age 46, man living with AMN

> *"We are just trying as we go, no real guidance with the supplements. Just I hear something will help and I give it to him. … I put [my son] on biotin. I heard about vitamin D helping. I put him on vitamin D, resveratrol, metformin. All these things that I heard are helpful, I went out and got it. And put him in because I don't want him to miss out."* – Nicki, symptomatic woman living with ALD, mother of Ganesh, age 21, living with cerebral ALD

> Janis takes a combination of vitamins for neuropathy. "*Metanx, a yet to be FDA approved supplement of B vitamins normally used to treat diabetic neuropathy, monthly B12 injections, 5,000 IUs of vitamin D and low-dose naltrexone*." She also takes alpha-lipoic acid to help with digestive issues. - Janis, age 65, symptomatic woman living with ALD

*Antispasmodics*

Antispasmodics are or were used by 53% of the individuals living with ALD represented in the poll results. Both antispasmodics and anticonvulsants work to control spasticity; antispasmodics (tizanidine or baclofen) work to relax muscles and anticonvulsants (clonazepam, gabapentin, pregabalin (Lyrica) and levetiracetam (Keppra) target the CNS. Medications for restless leg

syndrome include diazepam (Valium) and pramipexole (Mirapex). Some combine medications. A downside is that efficacy varies for different individuals.

> Eric's intrathecal baclofen pump was a life changer for him. "*I went from being so spastic that eating and breathing had become difficult. My legs had pretty much a complete mind of their own when walking and even laying down quite often. Now, my legs move much more smoothly, I can stand up straight, eating and breathing have gone back to normal. …I know that I am probably a rarity in the amount of change that was had from it*." - Eric, man living with AMN

> "*He has a Baclofen pump for his spasticity. … It doesn't really help much. I assume it must be helping a little maybe, but the spasticity is so difficult*." - Nicki, symptomatic woman living with ALD, mother of Ganesh, age 21, living with cerebral ALD

> "*The things that bother me the most are the neuropathy pain and the clonus, the Myoclonic foot jerks, the constant twitching and leg cramping. I've tried several things over the years for pain and a lot of anti-convulsant medications, gabapentin, Lyrica. I've had to combine those with some SSRIs to see if I'd get more benefit out of that. That didn't seem to work. I've tried Baclofen, that seems to help a little bit. And then Keppra for the foot jerks seems to help so I can sleep a little bit better*. … *Clonazepam to help me sleep at night for my spasticity*. … *The clonazepam has helped, but stretching combined with the clonazepam has really made a difference*." - Tim, age 56, man living with AMN

### *Pain medications*

Pain medications are or were used by 45% of the individuals living with ALD represented in the poll results to treat symptoms of pain and neuropathy. They tried Advil, NSAIDS, Tylenol, Lyrica (pregabalin), Cymbalta (duloxetine), Pamelor (nortriptyline), Elavil (amitriptyline), cortisone injections, hydrocodone, as well as low dose naltrexone. Pain medications can take a while to work and may only help alleviate some of the pain.

> Back and leg pain and muscle weakness affect Janis's mother. "*She now takes a cocktail of Lyrica, Cymbalta, Baclofen, and Norco [hydrocodone] for what she contributes to even being able to get out of bed in the morning*. … *But she is still in constant pain despite the many medications that she takes.* - Janis, age 65, symptomatic woman living with ALD, and caregiver for her mother who is living with ALD

> *"The part I can't seem to handle is this pain. I've done just about all the pills, patches and shots but of course none worked. I'm not suicidal but my pain is so bad I don't really care if I wake up in the mornings anymore because I know what my body has to endure from the minute I wake up till I'm able to sleep. That is the scariest part of this disease for me and my family."* - Alisa, symptomatic woman living with ALD

> *"NSAIDs/Tylenol are the only treatment that have provided any degree of pain relief (mild at best)."* - Kamran, man living with AMN

Julie has chronic sciatic pain. "*In 2019, I had a few treatments, a cortisone injection and when that didn't work, two medial branch blocks. These treatments would take about a month after the procedure for the medication to be fully absorbed into my system. The idea then was that the pain would be relieved enough for me to begin physical therapy. For me, none of the treatments worked. In the month after each treatment the pain would return as if I had no treatment. After this, I did not see any other option for my back pain and was using my walking stick daily*. - Julie, symptomatic woman living with ALD

### *Medical or recreational marijuana, cannabidiol (CBD) products*

CBD and marijuana were used by 45% of the individuals living with ALD represented in the poll results to relieve pain, spasticity, numbness and to promote sleep and increase well-being.

"*I take CBD when I go to sleep to help with leg and bladder spasticity and that's a little bit helpful*." – Ben, man living with AMN

*"I was experiencing severe numbness in my feet and stinging in my legs. I would awaken every night between 2 - 4 am. This went on for almost 70 days. … I decided to start taking THC gummies before going to sleep. This has helped immensely. After months without a full night sleep, I was finally sleeping well. The result is complete calmness and I sleep through the numbness and stinging. Hopefully this will work for a long time since there is no treatment for numbness at this time."* - Shari, symptomatic woman living with ALD

Janis uses "*CBD oil to help with insomnia that is often brought on by leg spasticity and cramps.* - Janis, age 65, symptomatic woman living with ALD

*"Marijuana also helped his emotional wellbeing*." – Cheryl and Frank, parents who lost both sons to cerebral ALD

### *Bladder medications*

Bladder medications are or were used by 38% of the individuals living with ALD represented in the poll results. Medications include Myrbetriq (mirabegron, extended-release tablets), Enablex (darifenacin), Gemtesa (vibegron), Ditropan (oxybutynin), hyoscyamine sulphate to address urinary urgency, $\alpha_1$ blockers doxazosin and alfuzosin which relax the head of the bladder, and Botox. Many used these medications in combination, and several reported success.

*"I have also finally had some relief for urinary incontinence using a new medicine called Gemtesa. Previously I failed all the anticholinergic meds and Botox in the bladder. I didn't think it would help but it has made a big difference."* - Amy, symptomatic woman living with ALD

"*I use Gemtesa, which helps with urgency and has made a big impact, doxazosin at night, which helps with keeping the flow. They go hand in hand. It's a balancing act. Hyoscyamine sulfate, which again, helps me at night with getting up less."* - Tim, age 56, man living with AMN

"*With regard to my neurogenic bladder issues, I was prescribed to take Myrbetriq 50 milligrams and alfuzosin 10 milligrams every night. ... Thanks to all these changes, I now only pee seven times during the day instead of 11. I now only pee one time at night instead of three, totalling only peeing eight times a day, instead of 14. I now only pee my pad maybe once a week, if that, instead of several.*" - Sheila, symptomatic woman living with ALD

### *Sleep medications*

Sleep medications are or were used by 35% of the individuals living with ALD represented in the poll results. They described using antispasmodics such as baclofen or tizanidine (Zanaflex) and anticonvulsants (clonazepam) as well as marijuana products to help with sleep.

*"I have trouble falling asleep, because I get severe periodic leg spasms once in bed. Once I started taking pramipexole and Zanaflex, my restless legs calmed, but the spasms still came. I was suggested to try marijuana, which I did. And now I do need a puff or two at night to relax my leg spasms to be able to sleep*." – Cynthia, symptomatic woman living with ALD

*"Tizanidine is helpful for deeper sleep; however, the medication has not extended the total time that I remain asleep*." - Kamran, man living with AMN

*"I take clonazepam at night for spasms. Game changer. And by not waking to those, I didn't have to go to the bathroom, because I wasn't awake so I didn't feel, 'I was awake better go anyway'*." - Barbara, symptomatic woman living with ALD

### *Corticosteroids*

Corticosteroids are or were used by 28% of the individuals living with ALD represented in the poll results to treat adrenal insufficiency but also sometimes for pain.

"*I take daily supplementation of steroids. Basically, the steroids are keeping me alive because adrenal insufficiency is a serious business and steroids are not ideal. Physiologically, long-term steroid use is harmful. I've also initially dealt with issues around insomnia, some weird mood cycles.*" - Ben, man living with AMN

"*[Justin] also had adrenal problems for which he took two drugs, fludrocortisone, and dexamethasone*." – Frank and Cheryl, parents who lost both sons to cerebral ALD

*"We give him a lot of supplements, we give him steroids for his adrenal insufficiency, had to do a lot of learning very quickly*." - Nicki, symptomatic woman living with ALD, mother of Ganesh, age 21, living with cerebral ALD

### *Botox injections*

Botox injections are or were used by 25% of the individuals living with ALD represented in the poll results to treat spasticity, sleep issues as well as bladder issues. Botox wears off quickly and doesn't work for everyone.

"*Some of the things that have been the most helpful are Botox injections in her legs to try to help with spasticity and just general function as well. … When she first gets them, it helps especially with her sleep*." The positive effects of the Botox injections wear off quickly. *"She'll get them once every three to four months, and it will be relief for maybe two or three weeks at a time. …But then when it's starting to wear off, we notice a lot more leg spasms*." - Emma, caregiver for her mom, age 53, symptomatic woman living with ALD

*"I'm on my 3rd treatment of Botox for my bladder. It has helped quite a bit. I also take oxybutynin."* - Alisa, symptomatic woman living with ALD

*"I have done Botox for my leg cramps for seven years. … Which definitely helps."* Dorothy, symptomatic woman living with ALD

### *Bowel medications or regimens*

Bowel medications are or were used by 25% of the individuals living with ALD represented in the poll results, including MiraLAX, Senna as well as a bowel regimen.

"*I use MiraLAX every night and it helps. I never miss a night. If I do, it throws my entire day off. So simple over-the-counter*." - Tim, age 56, man living with AMN

*"Taking Senna 8.6 mg tablets works best for having a bowel movement consistently every day without being too soft*." - Sheila, symptomatic woman living with ALD

"*Bladder and bowel problems are other effects. I am normally unable to have a bowel movement, which requires me to help myself with a hand, soap and water. This is a very uncomfortable situation, but necessary in everyday life*." - Rodrigo, man living with AMN

### *Investigational drug/clinical trial*

A total of 18% of the individuals living with ALD represented in the poll results have participated in clinical trials or have used investigational drugs to try to address symptoms of ALD. They tried MIN-102, pioglitazone, and stem cell treatments. Some of the downsides include unknown efficacy, not knowing if they were being treated with the active ingredient or placebo, and lack of accessibility in some cases.

*"I'm on the experimental drug from Minoryx Therapeutics, MIN-102. I started the study in 2018 and I'm now in the open label extension and the drug really no longer has any side effect and may be of benefit."* - Ben, man living with AMN

After a stem cell perfusion from her adipose tissue helped with pain, Dorothy heard about an experimental procedure using stem cells. *"I asked if I could be a guinea pig and try it since I would have to pay cash. We tried it and the first one worked for three months and I did three more IV stem cell treatments that worked very well. …That gave me less pain and much more energy and better function for walking with my leg cramps*."- Dorothy, symptomatic woman living with ALD

Brandon's concerns reflect some downsides and uncertainties of clinical trial participation. *"But how early on do I want to join the trials? Do I jump into an early phase to have a chance to get the drug immediately? But what if I end up with a sub-optimal dosage of an AAV based drug during that trial? I may have just spent my only bullet and missed. I've made a great contribution to science, but that doesn't help me walk, does it? And if I wait? I'm accepting a certain few years of continued disease progression for the *hope* that there's a more appealing target for that single bullet later on."* - Brandon, man living with AMN

### *Other medications or procedures*

Other medications are or were used by 33% of the individuals living with ALD to treat symptoms associated with ALD. These include bone marrow transplants for cerebral ALD, ketamine, off-label medications approved for multiple sclerosis, bladder neck incision surgery, and SSRIs (mentioned elsewhere in report).

"*Justin decided on his own to begin ketamine treatment combined with counseling for his emotional needs. He went to a clinic and paid out of pocket for the drugs. He did this on a weekly basis for five treatments. The ketamine treatment and counseling seemed to help, but the effects did not last*." – Frank and Cheryl, parents who lost both sons to cerebral ALD

*"I was taking 4-aminopyridine in the generic form of Ampyra, which is prescribed to MS patients, but stopped because it only minimally helped while posing the risk of seizures."* - Julie, symptomatic woman living with ALD

"*Eventually it was decided that I undergo bladder and neck incision surgery to help improve the flow of urine. Once again, this treatment failed to improve my bladder symptoms that were now becoming progressively worse*." - Harry, age 63, man living with AMN

### *I have not used medications*

Few individuals, 8%, living with ALD represented in the poll results have not used any medication to treat symptoms associated with ALD.

*"As a result of worsening abdominal issues, I have discontinued all medications/supplements for two weeks. It is disappointing to express that no significant change in my physical symptoms have resulted from the discontinuation. Therefore, I may discontinue all of the medications permanently."* - Kamran, man living with AMN

## An additional ALD insight not captured by the polls

The following theme was mentioned repeatedly during the meeting and in the patient comments yet was not reflected in the poll results.

**Individuals living with ALD would try anything to cure this disease for themselves and for others who are afflicted**. Many have invested so much time and effort in trying different treatments and medications in order to find relief from their symptoms.

> "*If we can regain anything, he would be willing to try anything*". - Nicki, symptomatic woman living with ALD, mother of Ganesh, age 21, living with cerebral ALD

> *"I think most of us are willing to try pretty much anything we can to get a little bit of benefit. … I'm willing to sacrifice my body, myself to help our community, to help prevent anyone else from having to go through and deal with what we have to. I want everybody to know that we want to prevent people in the future from having to deal with what we do*." - Tim 2, age 46, man living with AMN

## Exercise is the top non-medical approach used to manage ALD symptoms

However, despite regular exercise used to maintain function, patients experience decline and increasing disability. Other top approaches for managing ALD symptoms include walking supports: canes, walkers and leg braces. Poll respondents used online polling to select all the approaches (besides medications) that they or their loved one have used to help manage symptoms associated with ALD (past or present). Poll results are presented in **Appendix 6, Q2** and illustrated with patient comments below. Poll respondents selected an average of four responses each, and not a single poll respondent indicated that they did not use any alternative approaches.

### *Physical therapy*

Physical therapy was the top choice to help manage the symptoms of ALD, selected by 80% of the individuals living with ALD represented by the poll results. Throughout the meeting, many described how movement, stretching and exercise made a huge difference to their mobility. Many specifically mentioned working with a physiotherapist, others use different exercises to keep moving including Pilates, swimming, cycling and boxing. A downside is that despite regular exercise, patients still experience a decline in physical function. Also, few physical therapists have experience with those living with ALD.

> "*I would say the biggest help for me has been really exercise, sticking to physical therapy and rehab, and really being active and moving every day, so keeping the flexibility and the core strength*." Ben enjoys Pilates, swimming and cycling. "*I have a recumbent bicycle, but I'm trying to be flexible and creative around what I do, but the ability to exercise every day and keep that core strength and flexibility and movement control are essential*." - Ben, man living with AMN

> "*I have been on an exercise regimen for the last three years, which has helped a lot with my stiffness. I've found that I really enjoy Pilates and that helps me to stay on my feet. … I'm so thankful for my instructor who I'm able to get with twice a week*." – Patrick, man living with AMN

"*I have to start my day with a series of stretches just to decrease that spasticity, I stretch for about 20 minutes. And that allows me to be able to put weight on my legs and take a few steps. …As long as I keep moving, I'm able to keep my muscles a little bit relaxed."* - Jana, age 51, symptomatic woman living with ALD

### *Cane or walker*

A cane or walker is or was used by 73% of the individuals living with ALD represented by the poll results to balance and walk. Several use their canes and walking sticks as visual cues to others. Others used mobility supports such as knee scooters.

> *"I rely on a three-legged cane and I can't walk far. My walking gait looks uncoordinated. I bump things and drop things*." – Mary, symptomatic woman living with ALD

> "*Once I leave then the house, I use a cane... A lot of the time, I can walk without [it]. I don't plant the cane, but then if I'm stopping or somebody's coming near to me, I will put it to the ground. So that I'm balanced, I'm not going to fall over."* - Patricia, symptomatic woman living with ALD

> *"To help me adapt to the new normal, I started walking with a walking stick in public to prevent falls about three years ago due to neuropathy and balance issues. This has decreased my falls significantly, but I still fall. I don't use the walking stick at home, but I have learned to just take my time, don't rush, and try to remember to pick up my feet over thresholds*." - Sheila, symptomatic woman living with ALD

### *Leg braces*

Leg braces and ankle foot orthosis (AFOs) are or were used by 43% of the individuals living with ALD represented by the poll results to help prevent tripping and falling, to help with weakness and foot drop.

> *"Because of the broken ankle and my weakness in my legs, I now have a total AFO brace, with special shoes and everything for that darn right leg."* – Jamie, age 56, symptomatic woman living with ALD.

> *"I currently use a cane, and I also use bilateral foot braces or leg braces that help me with my foot drop*." - Tim 1, age 56, man living with AMN

> Ken's specialist referrals, "*Led me to getting a prescription for an ankle foot, orthotics [AFO] leg brace, which assisted in picking up my feet to prevent me from falling. I've been using the braces for about four years and they have been one of the best aids to date*." - Ken, age 38, man living with AMN

### *Counseling or psychotherapy*

Counseling or psychotherapy is or was used by 43% of the individuals living with ALD represented by the poll results to maintain a positive attitude, to be present despite pain and fatigue, and before making enormous decisions. Others have benefited from peer support and support groups.

*"I work with a counselor to try to live in the moment and manage my expectations*." - Holly, symptomatic woman living with ALD

"*I used to struggle with feeling like I couldn't be fully present in specific moments throughout the day because I was distracted by pain, distracted by fatigue, distracted by balance issues. Not knowing whether I was going to need a restroom. I mean, all the combination of these symptoms. Something that my counselor really, really helped me with was, she shared with me this idea that if you feel like you can only be 50% present in the moment, just accept that, that is the reality that you're living with, but do your best to commit yourself to that 50%. If that's all that you can do, instead of beating yourself up about it, recognize, that's okay, that's my reality*." - Aaron, age 36, man living with AMN

*"I think it's really important to share how real the worry of developing cerebral disease is particularly for men with AMN. There's a great community. ALD Connect does a great job of connecting, symptomatic women have their own groups, men with AMN, have their own groups. We have monthly community calls that we participate in and it really gives people an opportunity to develop relationships with one another.* - Aaron, age 36, man living with AMN

### *Acupuncture*

Acupuncture is or was used by 38% of the individuals living with ALD represented by the poll results to treat symptoms associated with ALD, but this was not mentioned during the meeting or in any of the submitted comments.

### *Wheelchair*

Wheelchairs are or were used by 35% of the individuals living with ALD represented by the poll results to treat symptoms associated with ALD. Some only needed a wheelchair after their symptoms progressed. Some also use motorized scooters and power wheelchairs.

"*At the age of 28, [our son] began to have issues with ALD, especially with his gait and walking, which required the use of a cane. He had problems with walking, balance, fatigue. First came the cane, then the walker, soon the wheelchair*." - Frank and Cheryl, parents who lost both sons to cerebral ALD

"*Falls became more severe, spasticity worsened. A wheelchair became necessary in order to go out for any distance*." – Barbara, symptomatic woman living with ALD

"*In terms of non-medical, non-prescription things, my mom having a wheelchair has been incredibly helpful. She spends about 90% of her time in her wheelchair, just to prevent those falls because she doesn't have very good function in her legs. … So just having her wheelchair has given our family more freedom in terms of being able to go out and do things or just do more stuff together in general*." - Emma, caregiver for her mom, age 53, symptomatic woman living with ALD

### *Occupational therapy and Speech therapy*

Occupational therapy is or was used by 25% and speech therapy is or was used by 15% of the individuals living with ALD represented by the poll results to treat symptoms associated with ALD.

> *"Matías had a clinical doctor who was his mainstay, a nurse, a kinesiologist who dealt with the muscular part, a respiratory kinesiologist, and a speech therapist who worked a lot on the facial muscles. These specialists formed a multidisciplinary team that provided the necessary care for Matías."* - Alicia, mother of a deceased son with adult cerebral ALD

### *Urinary catheter*

A urinary catheter is or was used by 13% of the individuals living with ALD represented by the poll results to treat symptoms associated with ALD.

> "*I have learned to deal with the bladder through Botox injections and clean intermittent catheter, but it's still challenging*." - Eric, age 43, man living with AMN

> *"Mark also had numerous urology issues due to AMN, which required intermittent or external catheterization. And as a result, he suffered permanent sexual dysfunction and recurrent urinary tract infections. This did irreparable damage to his bladder and kidneys*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

### *Other approaches*

Other approaches are used by 38% of the individuals living with ALD represented by the poll results. Individuals living with ALD use many different types of approaches to assist with symptoms of ALD and adaptations to help with daily life.

**Visits to medical specialists, pelvic floor treatments and percutaneous tibial nerve stimulation were approaches used to address bladder and bowel issues.**

> "*I chose to learn pelvic floor exercises from a therapist who specializes in bladder and bowel problems*." – Mary, symptomatic woman living with ALD

> "*While I see my urologist on a regular basis, the best advice has come from a physiotherapist specializing in pelvic floor muscle relaxation. Using various strategies, this has helped to improve urine flow and alleviate the pain associated with passing urine. My urologist has also suggested I try percutaneous tibial nerve stimulation that involves electrical stimulation, which has helped to improve bladder control in some patients*." - Harry, age 63, man living with AMN

**Dry needle treatments and electrical stimulation were used to help with spasticity, balance and walking**.

> "*My physiotherapist has tried dry needle treatment to my legs and buttocks, but this only provides temporary relief of my muscular cramps*." - Harry, age 63, man living with AMN

> "*I use an assistive device, which is basically like a leg sleeve called the Cionic Neural Sleeve that gives functional electrical stimulation and that's helped quite a bit with my foot drop and my hip flexion and to achieve better stride. But considering that all these are mildly helpful, but at the end of the day, not very effective and mostly palliative*." - Ben, man living with AMN

**Personal care aids and home modifications as well as vehicle modifications make life easier, but don't address underlying symptoms.**

> *"We have an aid that helps me because I can't physically move him by myself*." - Nicki, symptomatic woman living with ALD, mother of Ganesh, age 21, living with cerebral ALD

> "*We had to change our house. We had to move and have house modifications and an accessible vehicle*. …*We bought a stair lift that gave us an extra year in the house that we had. But then we had to move quickly to a house with a bedroom on the main level."* - Nicki, symptomatic woman living with ALD, mother of Ganesh, age 21, living with cerebral ALD

> *"I had hand controls installed in my truck and continued to work in and outside of my home."* – Barbara, symptomatic woman living with ALD

**Many require medical equipment for their care**.

> "*Once I had a few bladder and bowel mishaps, I started wearing a pad or diaper for situations where I would not know when I would be near a bathroom*." - Cynthia, symptomatic woman living with ALD

> "*We had lots of medical equipment he used - cane, walker, braces, shower / toilet chair, wheelchair, ramps and grab bars everywhere, and roll in shower. …We had shelves of medical items - blue pads, incontinence items, catheters, leg bags, gloves, pressure sore items, 4 x 4 and paper tape."* - Connie, caregiver and widow of Rex who passed away from cerebral ALD

> *"The resources were scarce: an oximeter, an oxygen tube, a manual resuscitation equipment (ambu), a "bipap" that he used permanently in recent months, and an assisted cough device."* - Alicia, mother of a deceased son with adult cerebral ALD

**Separate beds, weighted blankets and urinary jugs help with sleep**.

> When Jana is woken up with severe leg spasms, "*I can sometimes turn to the side and put some weight on that side or put a weighted blanket on. If that doesn't work, I get up again, do the massaging, the stretching*." – Jana, age 51, symptomatic woman living with ALD
>
> *"It may not be for everyone, but for my safety, and my family's peace of mind; I use a urinal jug at night and empty it in the mornings. It also leads to better sleep since not having to try to make it to the restroom and getting wide awake. This of course is easier for men than women to take advantage of."* - Eric, man living with AMN
>
> "*We installed a hospital bed on the first floor to make getting around the house easier, but that also meant that he and I slept apart*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

**Some required nutritional supplementation especially when their disease progressed.**

> *"He was fed by tube, we gave him a nutritional supplement in powder form (Ensure) and oil. He lost weight and we tried other dietary supplements, but he couldn't [tolerate] them.*" - Alicia, mother of a deceased son with adult cerebral ALD
>
> "*I can't eat without coughing and gagging*. … *Now swallowing impacts my living and my ability to get enough nutrition into my body. Dining was one last social thing I could still do. My husband misses us going out and feels badly eating food while I drink my meals using powders to make shakes*." – Barbara, symptomatic woman living with ALD

Additional approaches include maintaining a positive attitude, dietary changes such as giving up red meat, caffeine and alcohol, hyperbaric (high oxygen) treatments, hot/cold applications.

## Current ALD regimens are not very effective

Poll respondents used online polling to indicate how well their current regimen treated the most significant symptoms of ALD and to select the top three biggest drawbacks of their or their loved one's current treatment strategies. The results of these two poll questions are presented in **Appendix 6, Q3** and **Q4**. Some treatment downsides were already mentioned in the sections describing specific treatments. Other downsides are illustrated with patient comments, below.

*Not very effective at treating target symptom(s) and only treats some (not all symptoms)*

When asked to select the most significant downsides of treatment, 'not very effective at treating target symptoms' was selected by 69% of individuals and 'only treats some (not all) symptoms' was selected by 63% of individuals living with ALD represented by the poll results.

This response was entirely consistent with the results of poll Q3: When asked how well their current regiment treated the most significant symptoms of ALD, not one single poll respondent indicated that their current regimen provides 'complete relief' and only 2% said that it helped 'to a great extent'. Almost half, or 44% of poll respondents indicated that their current regimen

helps 'somewhat', 38% indicated that their current regimen helps 'very little', 9% indicated that it 'helps not at all'.

> *"Rex used and tried so many medications and supplements that gave small amounts of relief."* - Connie, caregiver and widow of Rex who passed away from cerebral ALD

> *"The medication that I have been prescribed to help with pain are ibuprofen, and Tizanidine, 2 mg once a day. These do not help very much*. - Marion, symptomatic woman living with ALD

> "*I have resorted to over-the-counter cannabis-based products to help with sleep as well. But what I've found with those products is that you're on them and you feel great, and then once they wear off, the pain in your lower body tends to come back a little bit stronger*." – Patrick, man living with AMN

> "*When I have a lot of pain in my legs, there is no point in taking medication (such as pregabalin), as they do not contribute to reducing the pain*." - Rodrigo, man living with AMN

### *Side effects*

Side effects were selected by 40% of individuals living with ALD represented by the poll results as a top drawback of current treatment strategies.

> *"The disease is a balancing act (at times quite literally) of AMN symptoms with the side effects of the drugs to combat them. It's Baclofen for me, for now. It eases spasticity, sure. But too much may bring on a further unsteady gait, getting fatigued more easily, and increased constipation. Or is it the disease progressing? It's a delicate dance in the dark; with bad balance to boot."* - Brandon, man living with AMN

> *"I have severe burning neuropathy in my feet and legs and numbness in my toes. I've gone through some trial and error with medications to treat this. I had some relief from gabapentin for a while after almost two years I began having stomach issues*." - Shari, symptomatic woman living with ALD

> *"Mybetriq can cause constipation."* - Sheila, symptomatic woman living with ALD and mother of a son who died from cerebral ALD

### *Limited availability or accessibility*

Limited availability or accessibility was selected by 34% of individuals living with ALD as a top drawback of current treatment strategies. There are no treatments to specifically address ALD. Some treatment options are not available due to insurance or jurisdictional restrictions.

> "*Justin was very intelligent and he began his extensive research on ALD. He knew about the Minoryx trial but decided he couldn't wait. This let him first to consider stem cell treatment. Nothing was available in the United States so he went to Mexico…. He thought about treatments in Asia, South America, Africa and Europe, not as many restrictions as the United States. He investigated drugs. ALD continued to claim more*

*and more incontinence, leg pain, muscle spasms, and emotional issues*." – Frank and Cheryl, parents who lost both sons to cerebral ALD

### *High cost or co-pay, not covered by insurance*

High cost or co-pay, not covered by insurance was selected by 26% of individuals living with ALD represented by the poll results as a top drawback of current treatment strategies. For many, requests for wheelchairs and medications were denied by insurance companies. Others pay out of pocket for their own medications.

> *"The power wheelchair … took a year and a half to get. We were rejected, but we got it".* - Nicki, symptomatic woman living with ALD, mother of Ganesh, age 21, living with cerebral ALD

> "*Justin decided on his own to begin ketamine treatment combined with counseling for his emotional needs. He went to a clinic and paid out of pocket for the drugs. He did this on a weekly basis for five treatments*." – Frank and Cheryl, parents who lost both sons to cerebral ALD

### ***Requires too much effort and/or time commitment***

The response option was selected by 11% of individuals living with ALD represented by the poll results as a top drawback of current treatment strategies. For Nicki, Botox injections and Baclofen pump refills for her son take up a great deal of time and require a lot of effort.

> *"He has a Baclofen pump for his spasticity, so we have to go every month and he has to get that refilled every month. And that's kind of a process. … It takes about three or four hours out of our day to go get it refilled. … We have to plan because we have to have his day planned with his meals and his other medicines. …My husband has to take off work to take him or I have to take him with another person because we can't lift him and put him on the table. I can't do it by myself, so I need help, so I have to make sure I have help with that. It's challenging."* - Nicki, symptomatic woman living with ALD, mother of Ganesh, age 21, living with cerebral ALD

### ***Route of administration***

Route of administration was not selected by any individuals living with ALD represented by the poll results as a top drawback of current treatment strategies yet was mentioned in the comments. Ganesh chokes on his pills.

> *"He has trouble swallowing and I give him about 35 pills a day with all the supplements I give him plus the prescription meds. I have to give it to him with apple sauce. He has choked before and it's happened and luckily, the person that was with me was able to get it out. But sometimes, we have to wash it down [because of] trouble swallowing the pills."* - Nicki, symptomatic woman living with ALD, mother of Ganesh, age 21, living with cerebral ALD

### *Other drawbacks*

Other drawbacks were selected by 11% of individuals living with ALD represented by the poll results as a top drawback of current treatment strategies. Some of the inherent drawbacks mentioned, were that treatments that work for one person don't always work for others and that the benefits of treatments such as CBD or Botox wear off after a short period of time. Not everyone is eligible for the clinical trials or treatments.

> *"The problem is he doesn't qualify because he has cerebral ALD, he doesn't qualify for all of these things or he's over 18 or whatever. There's nothing for him. He said a million times, he's willing to be a Guinea pig. He wants to help people so no one else has to go... He wants to be helpful too."* - Nicki, symptomatic woman living with ALD, mother of Ganesh, age 21, living with cerebral ALD

### *Not using any treatment*

Throughout the meeting, between 6-8% individuals living with ALD indicated that they are not using any treatment. As mentioned previously, some abandoned therapies because of a lack of efficacy.

> *"The symptoms progressed slowly until he was 29 years old. He stopped walking, but never gave up. He was undergoing rehabilitation until he realized that he could not fight the disease. He left the gym and made his psychologist understand that there was no point in continuing."* - Alicia, mother of a deceased son with adult cerebral ALD

## Future ALD medications: increase walking ability, stop disease progression, and prevent cerebral ALD

> *"There isn't most likely going to be a wonder pill that will fix all the issues, but even a change to just a few of the symptoms would provide a better quality of life."* - Ken, age 38, man living with AMN

> Allen shared his treatment goals. "*Mine is pretty much similar to everyone. It's just quality of life*." - Allen, man living with AMN

Short of a cure, people living with ALD want future medications to help maintain their quality of life by increasing their ability to walk, stopping disease progression, and preventing cerebral ALD. Poll respondents used online polling to select the top three specific things that they would look for in an ideal ALD treatment. Poll results are presented in **Appendix 6, Q5** and illustrated with patient comments.

### *Increased ability to walk*

Increased ability to walk was the top characteristic of an ideal ALD treatment, selected by 71% of individuals living with ALD represented by the poll results.

> "*My son, Jason will soon be 42 years old. His message is, 'I want to be able to walk.*' – Kathy, mother of a man living with AMN

*"I dream every night that I can walk normal again. I cannot."* - Janisse, symptomatic woman living with ALD

*"For treatment, I would love it if it could help my walking gait. I really miss a lot of things that I used to do. I used to play basketball. I used to run when I was younger. I had this disease and just some way to regain that would be nice."* - Allen, man living with AMN

### *Slow or halt decreasing progression*

Slow or halt decreasing progression was selected by 55% of the individuals living with ALD represented in the poll results as an ideal ALD treatment goal. Many individuals living with ALD agreed with the words of Ben, a man living with AMN, that their goal for a medication is to "*Stop the progression of the disease, reverse some or all of the symptoms."*

"*Short of a complete cure, our mission should be to stop the progression of the disease in men, women and children*." - Patti, symptomatic woman living with ALD

*"Number one, stop progression is the biggest thing. I've said it before when he was progressing, if we can stop it now, then that would just be huge. He could still have quality of life and everything would be great."* - Nicki, symptomatic woman living with ALD, mother of Ganesh, age 21, living with cerebral ALD

"*I would love to be able to halt the disease progression. Mine for the last three years has come on so strong and so fast. But if we can do anything just to slow or stop the progression would be wonderful*." - Jamie, age 56, symptomatic woman living with ALD

*"Of course, my hope is that one day science progresses to the point of a cure. ... More realistically I would eagerly pursue something to halt or slow the diseases progression. Will my life be totally normal? No. That ship has sailed. I'm comfortable with that."* - Brandon, man living with AMN

Individuals living with ALD suggested several approaches to achieve this goal including remyelination and repurposing efficacious medications from other diseases.

"*Remyelination, I would like my body to return close to normal function even if it were only for 10 years or so*." - Ted, man living with AMN

*"Short of a cure, slow or stop progressing just like everybody else said. I would agree with that. Remyelination is what we need also. I think if we slow or stop, we're going to be able to gain that back, some remyelination."* – Eric, age 43, man living with AMN

### *Prevention of cerebral ALD*

Prevention of cerebral ALD was selected by 38% of the individuals living with ALD represented in the poll results as an ideal treatment for ALD.

*"Speaking for me personally, the most important treatment will help prevent cerebral progression of ALD. I can adjust and adapt to AMN symptoms, but I can't do cerebral ALD. Sure, I'd like the ability to run again and be a track star to speak, but given that or*

*the option to be free of cerebral disease, I pick the latter."*- Ken, age 38, man living with AMN

*"I hope and pray that we can find something to keep this condition from becoming cerebral ALD so no one else has to endure this horrid condition and loss."* - Connie, caregiver and widow of Rex who passed away from cerebral ALD

*"What I would like to see as [outcomes] of a clinical trial, the three main ones that really especially hit our family …is the prevention of [cerebral] ALD, the increased walking and reduced pain."* - Mary M., caregiver for her husband who is living with ALD

### *Improvement in balance*

Improvement in balance was also selected by 38% of the individuals living with ALD represented in the poll results as an ideal treatment for ALD.

"*I dream that medical scientists would create a miracle cure for ALD. If not, hopefully they'll develop drugs to restore balance and slow disease progression*." - Mary, symptomatic woman living with ALD

*"Please make a cure or treatment to avoid these bad symptoms in the legs (weakness and lack of balance) as well as for urinary and bowel problems."*- Carla, symptomatic woman living with ALD

### *Control of my incontinence*

Control of my incontinence was selected by 31% of the individuals living with ALD represented in the poll results as an ideal treatment for ALD.

"*I'm not aware of any clinical trials for ALD/AMN patients in Australia, but I would be willing to participate in drug treatment trials that may help alleviate my bladder symptoms or halt the progression of my muscular symptoms*." - Harry, age 63, man living with AMN

"*Incontinence is another big thing to be managed a little bit better. There's not that constant anxiety in your daily life of having to plan out your day because of your incontinence issues*." – Emma, caregiver for her mom, age 53, symptomatic woman living with ALD

### *Reduced spasticity*

Reduced spasticity was selected by 24% of the individuals living with ALD represented in the poll results as an ideal treatment for ALD.

*"I wish I could stand more then 10-15 minutes at a time, last longer then 20-30 minutes without having to get to a bathroom. Walk without assistance of a walker, stand up taking a shower*." - Jamie, symptomatic woman living with ALD

*"I'd love to see new treatments for painful neuropathy and to relieve muscle spasticity. Also anything to lessen the debilitating fatigue. I'd happily participate in any and all trials available for medications to help with these issues."* - Holly, symptomatic woman living with ALD

### *Reduced pain*

Reduced pain was selected by 17% of the individuals living with ALD represented in the poll results as an ideal treatment for ALD.

"*I would really love for us to be able to find a better solution to address the stinging and the numbness that really have an impact on our day-to-day everyday life*." - Patrick, man living with AMN

*"I would love the chance to have one day without pain and to be able to run again…even just one more time."* – Amy, symptomatic woman living with ALD

*"Due to the day-to-day variation in the severity and onset of mechanical pain, an as-needed/fast-acting muscle pain reliever/relaxer, that does not need to be titrated, would be beneficial (For example: participating in a scheduled 2-4 hour physical activity with predictable reduction in pain, and without drowsiness/disorientation)."* - Kamran, man living with AMN

### *Help with sleep*

Help with sleep was selected by 10% of the individuals living with ALD represented in the poll results as an ideal treatment for ALD. Sleep issues were discussed extensively throughout the meeting. Medications to address incontinence, spasticity and pain are likely to also aid with sleep.

"*Uncontrolled leg movements, bathroom trips, and muscle cramps made a restful night's sleep impossible for myself and my husband*." – Barbara, symptomatic woman living with ALD

### *Restored ability to be intimate with a partner*

Restored ability to be intimate with a partner was selected by 5% of the individuals living with ALD represented in the poll results as an ideal treatment for ALD.

*"Some of the other things that I really would need help with is the quality of life. Things like the incontinence, the sexual dysfunction stuff that I think give some dignity back to us with ALD and AMN. I think that would be a starting point for us."* – Eric, age 43, man living with AMN

### *Other treatment goals and improvement in speech*

Other treatment goals and improvement in speech were each selected by 2% of the individuals living with ALD represented in the poll results. Some of the other treatment goals that were already mentioned included improvement of quality of life, and a lessening of debilitating fatigue. Additional recommendations include treatments to include movement, A very big topic

was improved treatments aimed specifically at women, including greater inclusion for women in clinical trials, and physiotherapists who have knowledge and experience with ALD.

**Treatment accessibility for everyone**

> *"I can only hope that treatment would be potent and available as soon as symptoms develop. I hope that this treatment will halt AMN in its tracks, not just mask symptoms or slow down the pace of the disease. And it must be made available to every affected patient, regardless of age, gender, racial background, or income. ALD does not discriminate, and neither can we."* - Miranda, mother of a son with ALD diagnosed through Newborn Screening

**Treatments targeted specifically for women with ALD**

> *"The best-case scenario right now as a woman with ALD is to hope that we can get through a trial and that it works for the men with AMN and that maybe, we may be able to find someone willing to write it off script or off label for us later once it's approved."* - Kathleen O'Sullivan-Fortin, founding board member of ALD Connect, a caregiver and a symptomatic woman living with ALD

> "*I would like to see drugs and therapies developed that would help all patients struggling with ALD. I would really like the medical community and researchers to take a hard look at the ALD women's population of patients who have been overlooked for years. We are tired of being invisible. I would like to see a clinical trial to determine if the thyroid gland is affecting the female ALD population as I know so many women, including myself and my mother who are on medication. I would like to see drugs that are available for MS patients to be tested for ALD and AMN. And lastly, I would like to be included in any future conversations about ALD or AMN*." - Janis, age 65, symptomatic woman living with ALD

> *"What I'd like to see in treatments or medications for females with ALD would be physical therapists who are actually trained for our symptoms and be available when we do research."* – Julie, symptomatic woman living with ALD

## Incorporating Patient Input into a Benefit-Risk Assessment Framework

The FDA uses a Benefit-Risk Assessment Framework which includes decision factors such as the analysis of condition, current treatment options, benefit, risk, and risk management. The Framework provides an important context for drug regulatory decision-making and includes valuable information for weighing the specific benefits and risks of a particular medical product under review.

**Table 1** speaks to the challenges of living with ALD. It serves as the proposed introductory framework for the Analysis of Condition and Current Treatment Option to be adapted and incorporated in the FDA's Benefit-Risk Assessment. This may enable a more comprehensive understanding of this unique condition for key reviewers in the FDA Centers and Divisions who would be evaluating new treatments for ALD. The data resulting from this meeting may help inform the development of ALD-specific clinically meaningful endpoints for current and future clinical trials, as well as encourage additional researchers and industry to investigate options for treatments.

The information presented captures the perspectives of patients living with ALD presented at the July 22, 2022, meeting. It includes information from the caregiver survey and polling results, as well as comments submitted before, during, and after the meeting through the online portal.

Note that the information in this sample framework is likely to evolve over time.

**TABLE 1 ALD Benefit-Risk Table**

| | EVIDENCE AND UNCERTAINTIES | CONCLUSIONS AND REASONS |
|---|---|---|
| ANALYSIS OF CONDITION/ IMPACTS ON ACTIVITIES OF DAILY LIVING | **Adult patients with ALD struggle to obtain an accurate diagnosis**. Early symptoms are often dismissed or misattributed. Until very recently, women with ALD were mistakenly believed to be asymptomatic; they often feel invisible and excluded from drug trials.<br><br>**ALD is progressive.** ALD increasingly impacts the lives of those living with the disease as well as their families. Some individuals are severely affected. Cerebral ALD robs people of their cognition and the ability to care for themselves and leads to death.<br><br>**ALD is a complex disease that affects multiple body systems.** Symptoms are unpredictable and life changing. | **ALD has a heavy disease burden.** Mobility challenges, including balance and gait issues and spasticity, as well as bladder and bowel unpredictability have enormous quality of life impacts.<br><br>**The impact of ALD on families is particularly severe**. Many patients who are living with symptoms of ALD/AMN are also caregivers for children or other family members with the disease. Psychosocial impacts and burnout are common.<br><br>**People living with ALD and their families are burdened with many worries**: that symptoms will get worse, that they will lose the ability to walk, that they will develop cerebral ALD and that they will fall. |
| CURRENT TREATMENT OPTIONS/ PROSPECTS FOR FUTURE TREATMENTS | **There are no FDA approved treatments for adult manifestations of ALD**. Instead, individuals living with ALD have tried any available approach to mitigate health effects, including vitamins and supplements.<br><br>**Most treatments are not very effective and only help address disease symptoms "somewhat".**<br><br>**Exercise is one of the approaches that individuals living with ALD use to remain healthy**. They also use numerous other tools, adaptations, supports and strategies. | **Individuals living with ALD urgently and desperately need better treatments**. Many expressed a willingness to try experimental therapies or to participate in clinical trials – even in the control arm – just to advance treatments for this community. Short of a complete cure, they wish for treatments to help maintain their quality of life. They want a therapy to increase their ability to walk, to slow or halt disease progression and prevent the development of cerebral ALD. Women need to be included in research and clinical trials. |
| | ***See the Voice of the Patient report for a more detailed narrative.*** | |

## Conclusion

> "*The ALD community are some of the strongest people I know, and we deserve a big change in the future."* - Ken, age 38, man living with AMN

The Adult Manifestations of Adrenoleukodystrophy (ALD) Externally Led Patient Focused Drug Development meeting brought together a wide community of adults living with ALD and their family members and caregivers. The meeting provided an opportunity for adults with ALD, AMN and cerebral ALD to share their personal insights and experiences and shine a spotlight on their symptoms and struggles, concerns, disappointments and hopes. As a result, we now have a deeper understanding of ALD and its impact. The hope is that this meeting will encourage future research, and successful new product development for people living with ALD, who urgently need more options.

> *"We welcome more of the medical community to take a walk in our shoes and understand the challenge we face with each literal step we take. Help us take greater strides so that we and those who receive a diagnosis in the future will be lucky enough to move past hope and on to realizing potential life-changing therapies*." - Brandon, man living with AMN

> "*My life is very different from how it used to be before I developed symptoms. But I still try to live as full of a life as I can. I have two young children that I share with my wife, and taking care of them, I'm not able to get them out to do all of the things that somebody who is able bodied might be able to do. But I think that it really is about focusing on what we can do, what we still can do, and trying to live the best that I can*." - Aaron, age 36, man living with AMN

> "*Three years have passed since Mark died. … No matter how many times Mark fell, we found a way to laugh together as he got up. I think of the tears in his eyes when we got married, the smiles on his face when he completed marathons in his racing wheelchair, and how he inspired our family and so many others with his resilience and laughter and kind natured spirit. He truly was a gem of a human being. And I will miss him and grieve his loss every single day for the rest of my life. I ask that you please remember our story and our tremendous unmet needs when you review new treatments for ALD and AMN. Thank you*." - Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

# Appendix 1: Meeting Agenda EL-PFDD for ALD

**Externally-Led Patient-Focused Drug Development Meeting**

**July 22, 2022**

**Adrenoleukodystrophy (ALD) in Adulthood**

| | |
|---|---|
| 10:00-10:05 AM | **Welcome Remarks**<br>*Kathleen O'Sullivan-Fortin*<br>*Symptomatic woman with ALD, ALD Connect Board Member* |
| 10:05-10:15 AM | **FDA Introduction to PFDD**<br>*Wilson Bryan, MD*<br>*Director, Office of Tissues and Advanced Therapies, FDA* |
| 10:15-10:30 AM | **Clinical Features of ALD and AMN & Therapeutic Approaches**<br>*Florian Eichler, MD*<br>*Associate Professor of Neurology at Harvard Medical School,*<br>*ALD Connect Board Member* |
| 10:30-10:35 AM | **Meeting Overview and Introduction**<br>*James Valentine, JD, MHS, Meeting Moderator* |
| 10:35-10:40 AM | **Demographic Polling**<br>*James Valentine, JD, MHS Meeting Moderator* |

**Topic 1: Living with ALD: Men with adrenomyeloneuropathy, cerebral ALD, symptomatic women with ALD**

| | |
|---|---|
| 10:40-11:05 AM | **Pre-recorded Panelists** |
| 11:05-12:30 PM | **Polling and Audience Discussion**<br>• Zoom Discussion Starters (live)<br>• Patient/caregiver audience remote polling<br>• Moderated audience discussion (telephone and written comments) |
| 12:30-1:00 PM | **Break** |

**Topic 2: Approaches to Treatments for ALD and AMN: Men with adrenomyeloneuropathy, cerebral ALD, symptomatic women with ALD**

| | |
|---|---|
| 1:00-1:25 PM | **Pre-recorded Panelists** |

1:25-2:40 PM Polling and Audience Discussion
- Zoom Discussion Starters (live)
- Patient/caregiver audience remote polling
- Moderated audience discussion (telephone and written comments)

2:40-2:50 PM **Meeting Summary**
*Larry Bauer, RN MA*

2:50-2:55 PM **Concluding Remarks & Next Steps**
*Kathleen O'Sullivan-Fortin*
*Symptomatic woman with ALD, ALD Connect Board Member*

## Appendix 2: Panel Participants, Discussion Starters and Callers

**Session 1: Living with ALD: Symptoms and Daily Impacts**

**Patient/caregiver testimonials**

- Mary, symptomatic woman living with ALD
- Allen, man living with AMN
- Barbara, symptomatic woman living with ALD
- Eric, age 43, man living with AMN
- Laurie, widow and caregiver of Mark who passed away from cerebral ALD at age 44

**Zoom discussion starters**

- Jana, age 51, symptomatic woman living with ALD
- Tim 1, age 56, man living with AMN
- Patricia, symptomatic woman living with ALD
- Aaron, age 36, man living with AMN
- Connie, widow and caregiver for Rex who passed away from cerebral ALD at age 62

**Callers**

- Emma, caregiver for her mom, age 53, symptomatic woman living with ALD
- Ken, age 38, man living with AMN
- Jessie, symptomatic woman living with ALD and caregiver for her son with ALD
- Holly, symptomatic woman living with ALD

**Session 2: Current & Future Approaches to Treatment for ALD**

**Patient/caregiver testimonials**

- Janis, age 65, symptomatic woman living with ALD, and caregiver for her mother who is living with ALD
- Ken, age 38, man living with AMN
- Julie, symptomatic woman living with ALD
- Harry, age 63, man living with AMN
- Cheryl and Frank, parents who lost both sons to cerebral ALD. Cheryl, symptomatic woman living with ALD

**Zoom discussion starters**

- Emma, caregiver for her mom, age 53, symptomatic woman living with ALD
- Tim 2, age 46, man living with AMN

- Nicki and Ganesh. Nicki, symptomatic woman living with ALD, and mother of Ganesh. Ganesh age 21, living with cerebral ALD
- Jamie, age 56, symptomatic woman living with ALD. Caregiver for her son with a cerebral ALD who passed at the age of 21.
- Ben, man living with AMN

**Callers**

- Tim, age 56, man living with AMN
- Patrick, man living with AMN
- Mary M., caregiver for her husband who is living with ALD
- Eric, man living with AMN
- Allen, man living with AMN

## Appendix 3: Meeting Discussion Questions

**Session 1: Living with ALD: Symptoms and Daily Impacts**

1. Of all the symptoms and health effects of ALD, which 1-3 symptoms have the most significant impact on your or your loved one's life?

2. How does ALD affect your or your loved one on best and on worst days?

3. How has your or your loved one's symptoms changed over time? How has the ability to cope with the symptoms changed over time?

4. Are there specific activities that are important to you or your loved one that you cannot do at all or as fully as you would like because of ALD?

5. What do you fear the most as you or your loved one gets older? What worries you most about you or your loved one's condition?

**Session 2: Current and Future Approaches to Treatments**

1. What are you currently doing to manage your or your loved one's ALD symptoms?

2. How well do these treatments address the most significant symptoms and health effects of ALD?

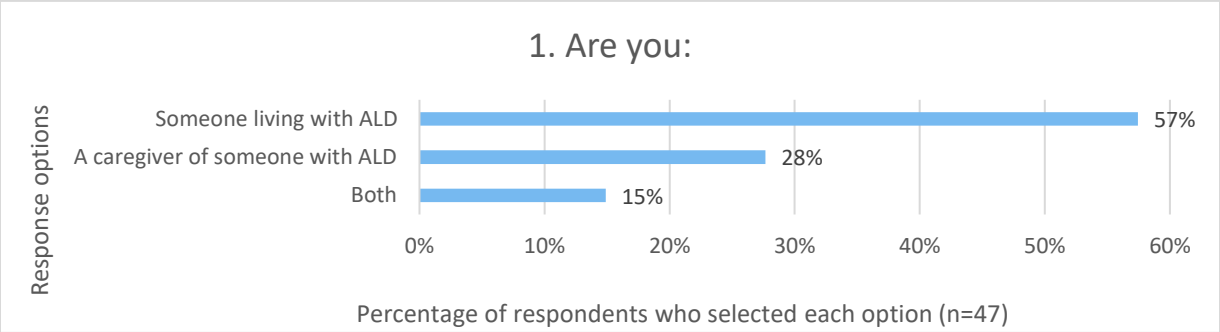
3. What are the most significant downsides to your or your loved one's current treatments and how do they affect daily life?

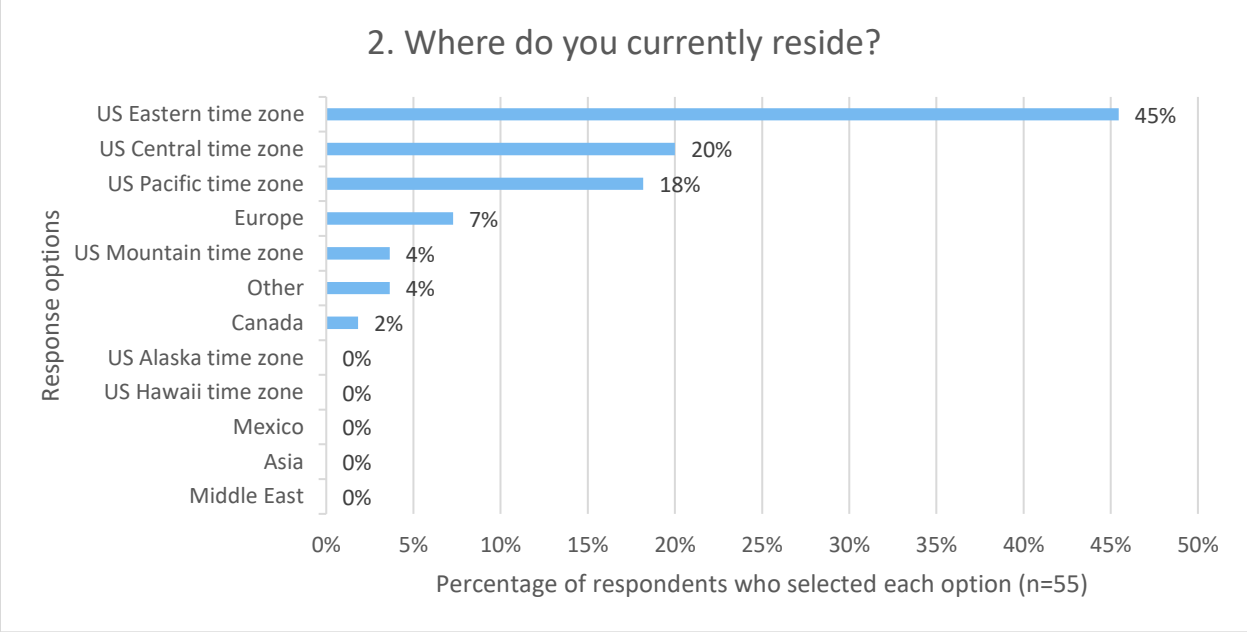
4. Short of a complete cure, what specific things would you look for in an ideal treatment for ALD? What factors would be important in deciding whether to use a new treatment?

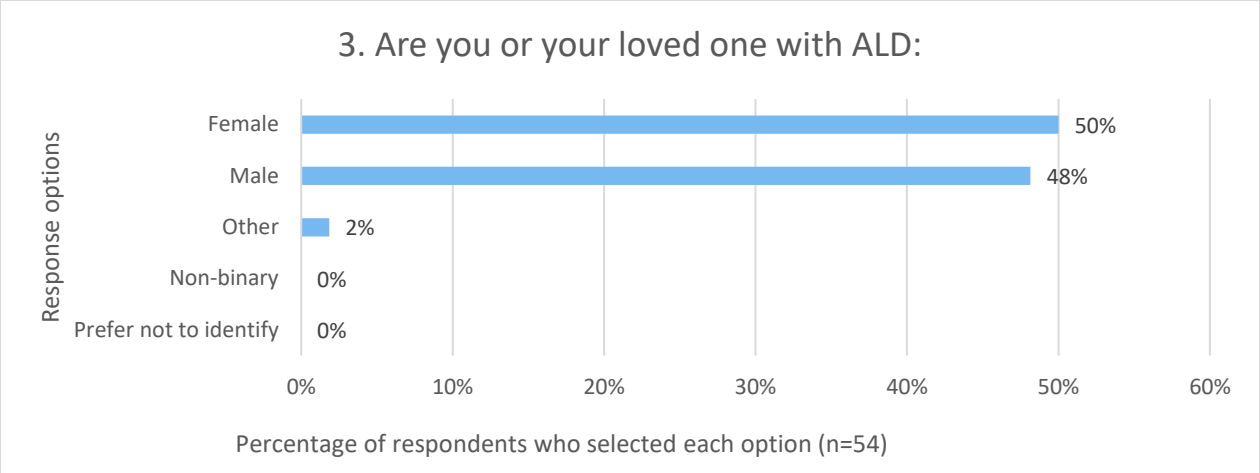
## Appendix 4: Demographics

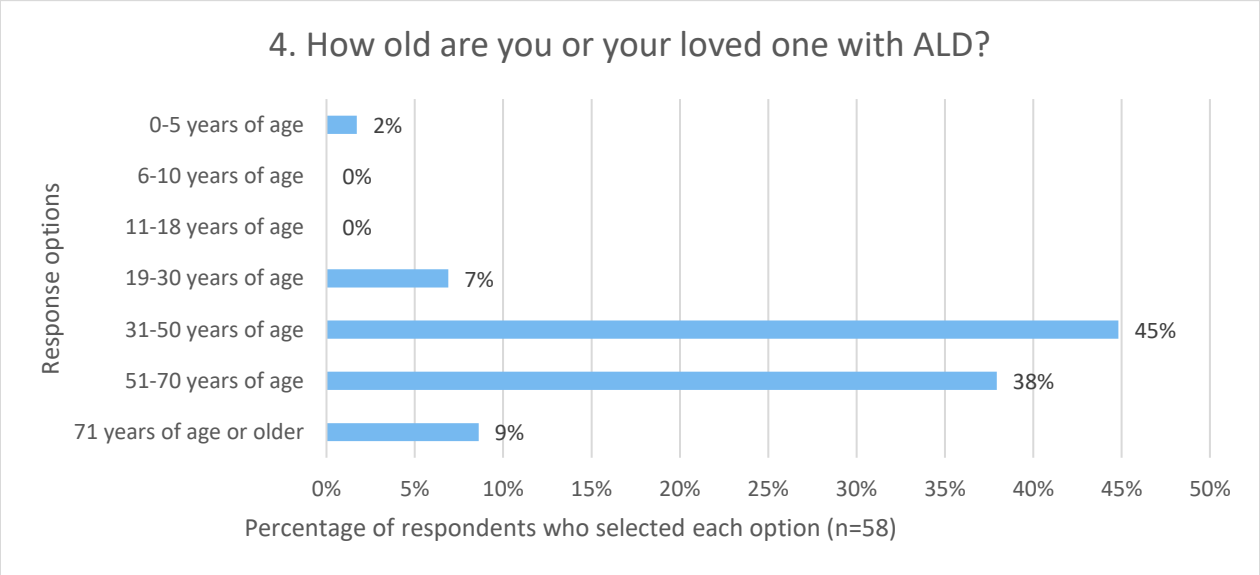
The graphs below include all attendees who chose to participate in online voting. The number of affected individuals and caregivers who responded to each polling question is shown below the X axis (N=x).

While the response rates for these polling questions is not considered scientific data, it provides a snapshot of those who participated in the ALD EL-PFDD meeting and is intended to complement the live and pre-recorded comments throughout the meeting.



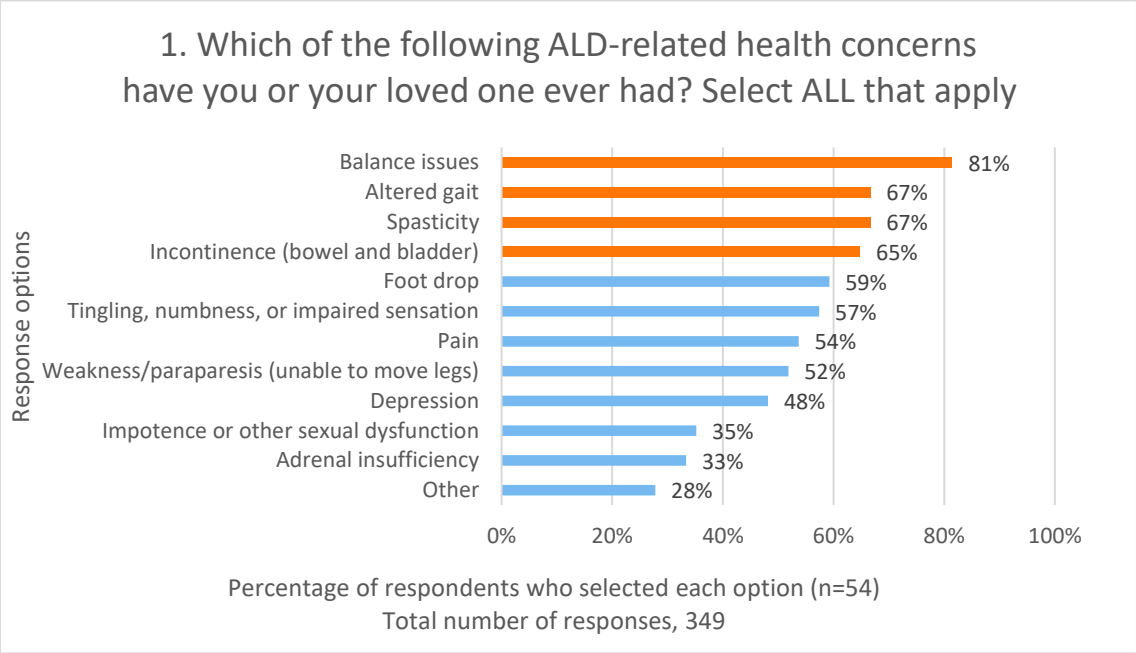

3. Are you or your loved one with ALD:
Response options
Female
Male
Other
Non-binary
Prefer not to identify
50%
48%
2%
0%
0%
0%
10%
20%
30%
40%
50%
60%
Percentage of respondents who selected each option (n=54)


4. How old are you or your loved one with ALD?
Response options
0-5 years of age
6-10 years of age
11-18 years of age
19-30 years of age
31-50 years of age
51-70 years of age
71 years of age or older
2%
0%
0%
7%
45%
38%
9%
0%
5%
10%
15%
20%
25%
30%
35%
40%
45%
50%
Percentage of respondents who selected each option (n=58)

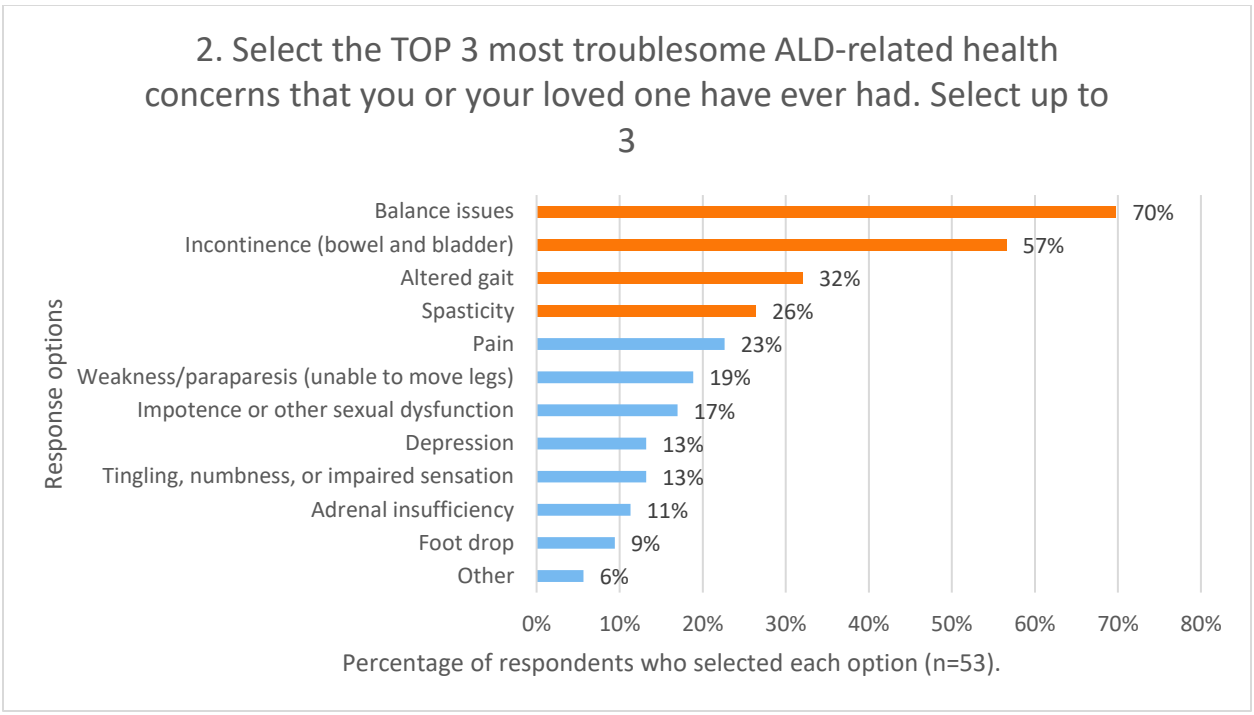
## Appendix 5: Session 1 Polling Results

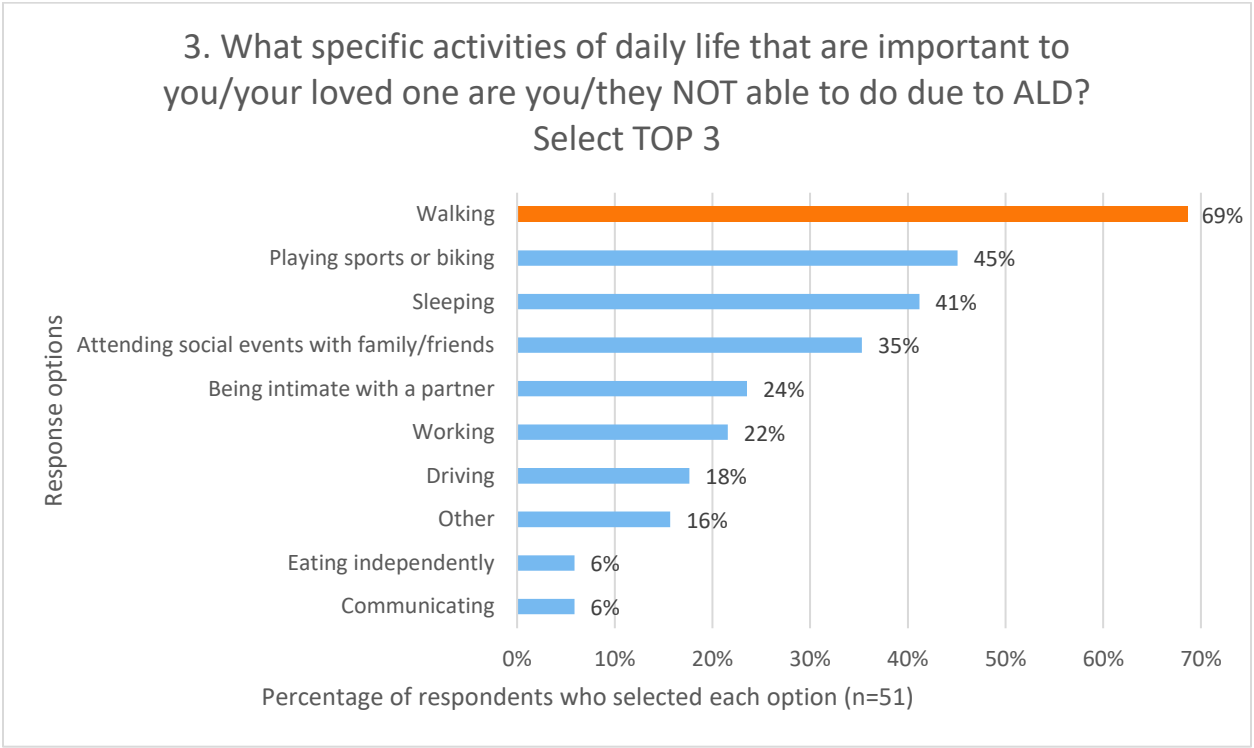
The graphs include those attendees who chose to participate in online voting. The number of patients who responded to each polling question is shown below the X axis. For most questions, poll respondents could select more than one response. The total of poll responses is also shown below the X axis.

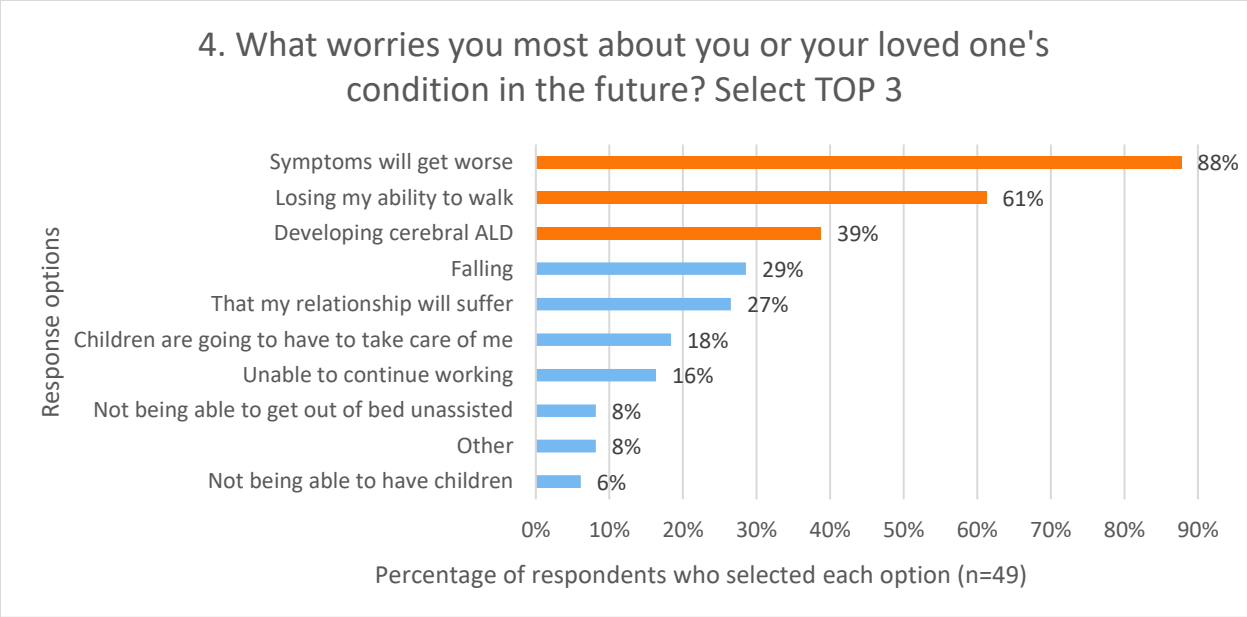
While the response rate data for these polling questions is not considered scientific data, it provides a snapshot of who participated in the ALD EL-PFDD meeting and is intended to complement the live and pre-recorded comments throughout the meeting.




Respondents each selected an average of 6.5 responses to this poll question.


2. Select the TOP 3 most troublesome ALD-related health concerns that you or your loved one have ever had. Select up to 3
Response options
Balance issues 70%
Incontinence (bowel and bladder) 57%
Altered gait 32%
Spasticity 26%
Pain 23%
Weakness/paraparesis (unable to move legs) 19%
Impotence or other sexual dysfunction 17%
Depression 13%
Tingling, numbness, or impaired sensation 13%
Adrenal insufficiency 11%
Foot drop 9%
Other 6%
0% 10% 20% 30% 40% 50% 60% 70% 80%
Percentage of respondents who selected each option (n=53).

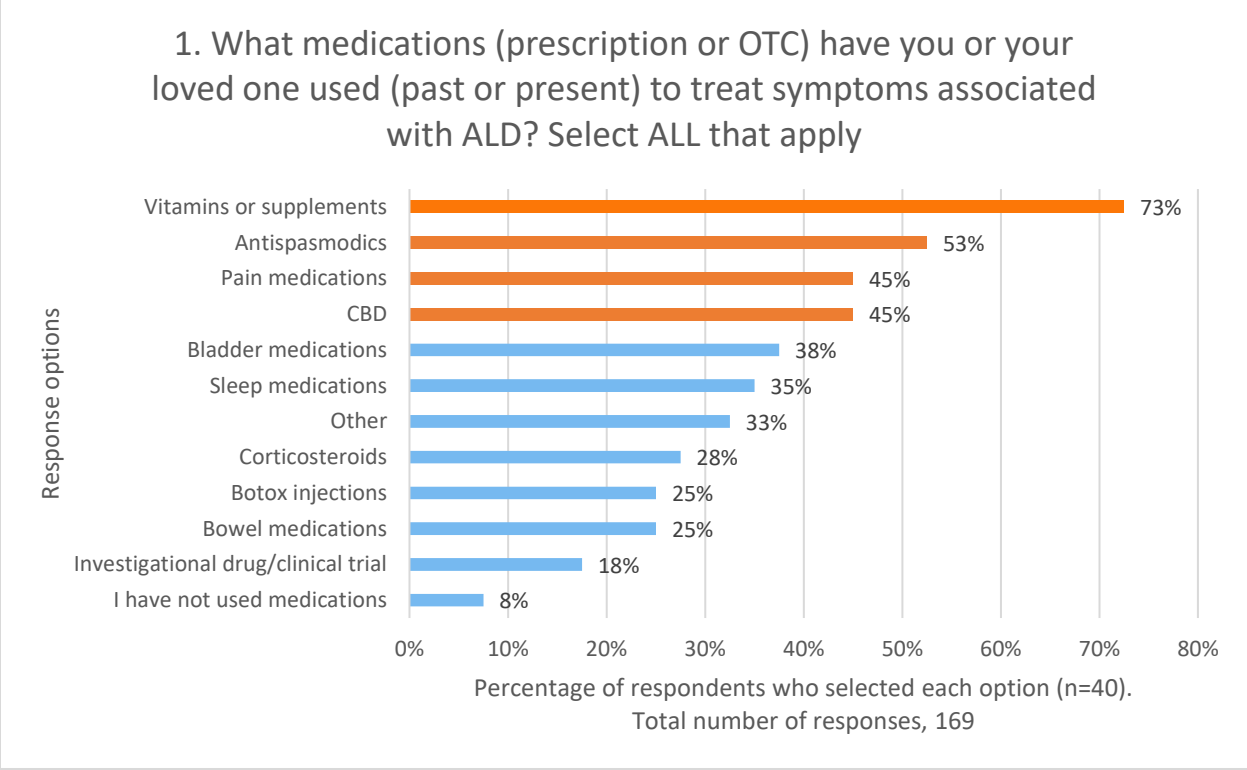

3. What specific activities of daily life that are important to you/your loved one are you/they NOT able to do due to ALD? Select TOP 3
Response options
Walking 69%
Playing sports or biking 45%
Sleeping 41%
Attending social events with family/friends 35%
Being intimate with a partner 24%
Working 22%
Driving 18%
Other 16%
Eating independently 6%
Communicating 6%
0% 10% 20% 30% 40% 50% 60% 70%
Percentage of respondents who selected each option (n=51)


4. What worries you most about you or your loved one's condition in the future? Select TOP 3
Response options
Symptoms will get worse
Losing my ability to walk
Developing cerebral ALD
Falling
That my relationship will suffer
Children are going to have to take care of me
Unable to continue working
Not being able to get out of bed unassisted
Other
Not being able to have children
88%
61%
39%
29%
27%
18%
16%
8%
8%
6%
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
Percentage of respondents who selected each option (n=49)

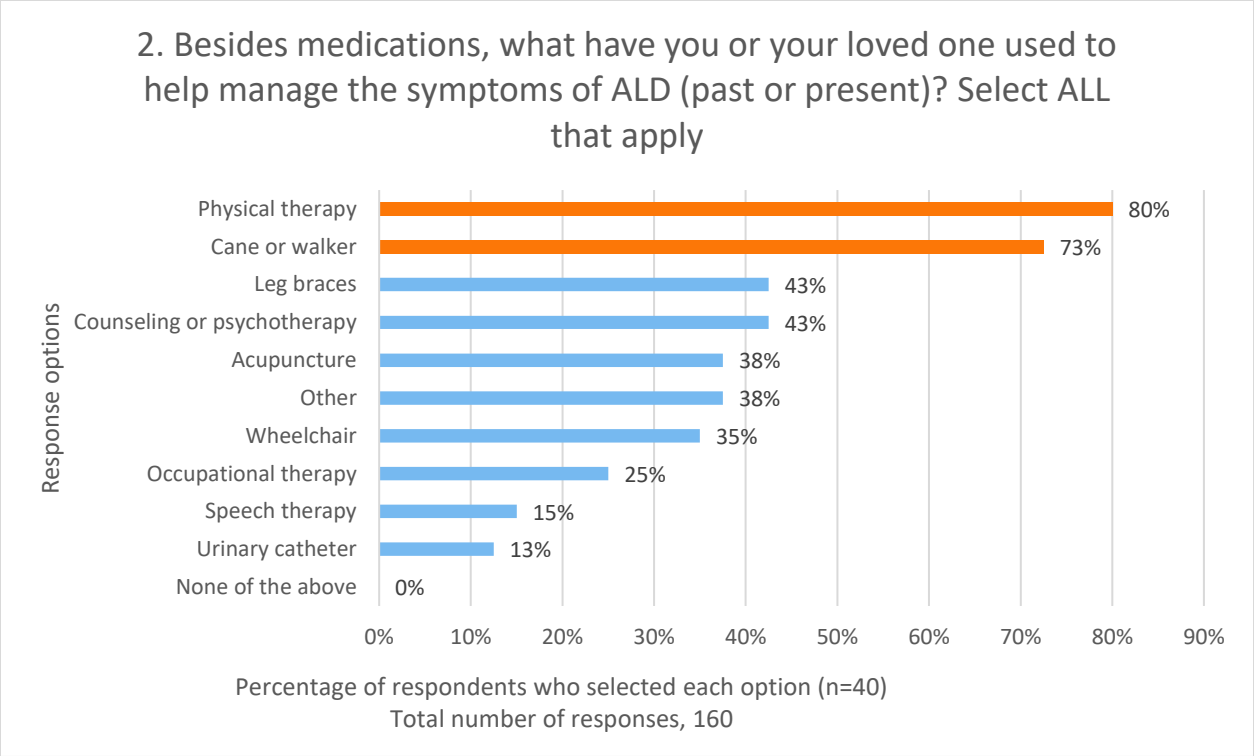
## Appendix 6: Session 2 Polling Results

The graphs include those attendees who chose to participate in online voting. The number of patients who responded to each polling question is shown below the X axis. For most questions, poll respondents could select more than one response. The total of poll responses is also shown below the X axis.

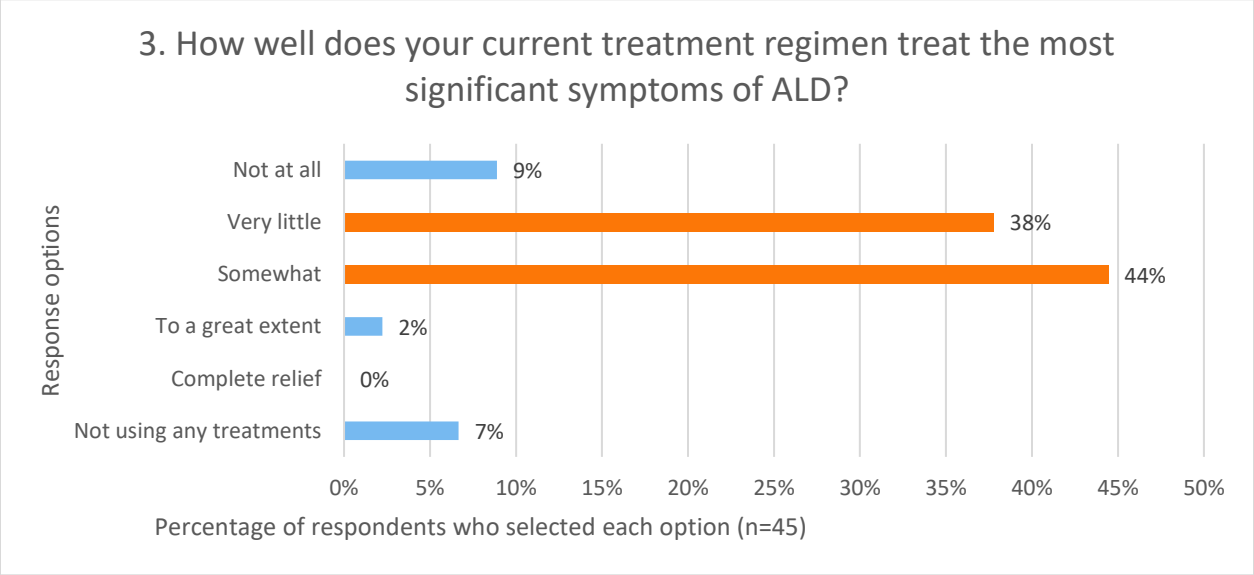
While the response rate data for these polling questions is not considered scientific data, it provides a snapshot of who participated in the ALD EL-PFDD meeting and is intended to complement the live and pre-recorded comments throughout the meeting.

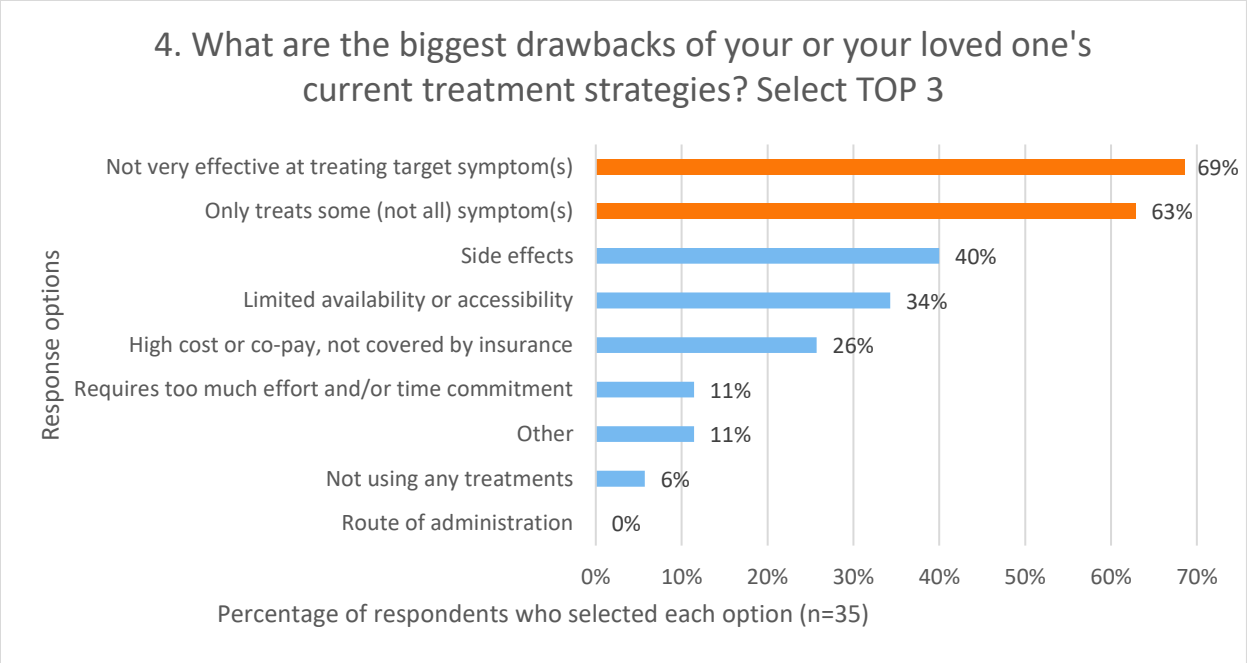


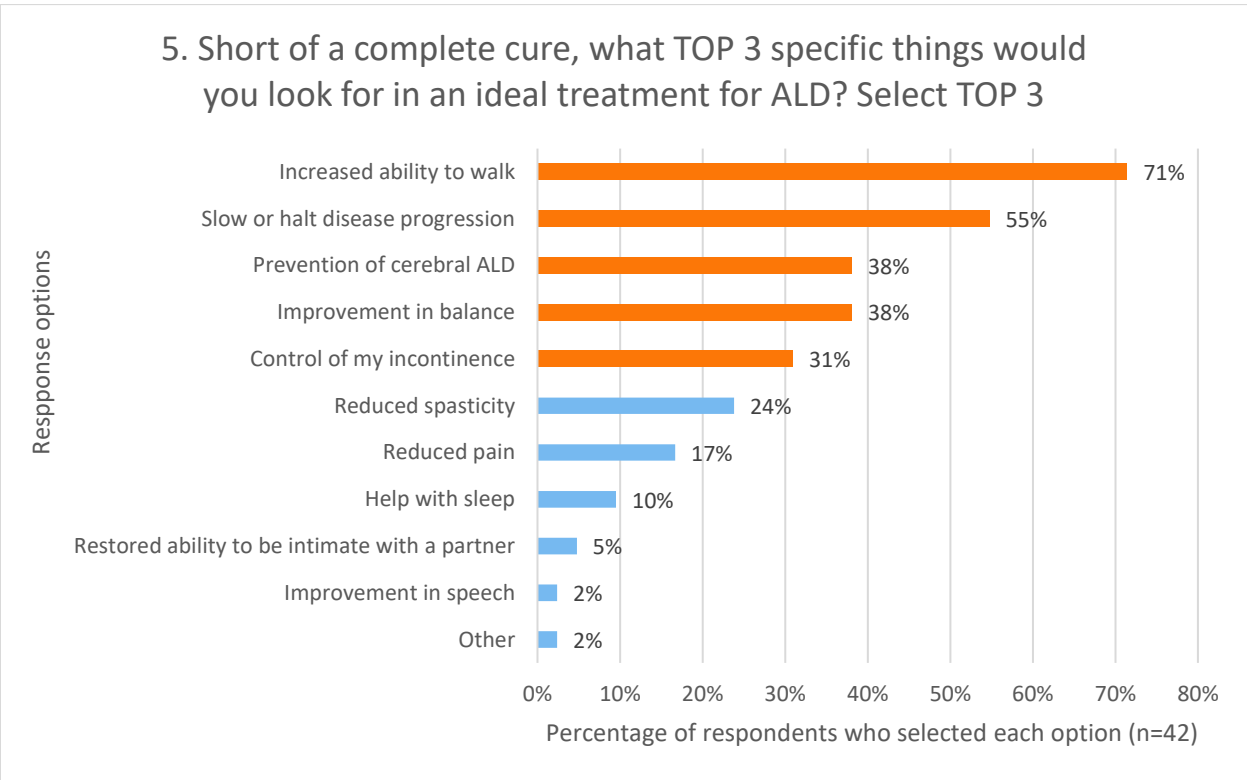

Respondents each selected an average of 4.2 responses to this poll question.




Respondents each selected an average of 4.0 responses to this poll question.




4. What are the biggest drawbacks of your or your loved one's current treatment strategies? Select TOP 3
Response options
Not very effective at treating target symptom(s)
Only treats some (not all) symptom(s)
Side effects
Limited availability or accessibility
High cost or co-pay, not covered by insurance
Requires too much effort and/or time commitment
Other
Not using any treatments
Route of administration
69%
63%
40%
34%
26%
11%
11%
6%
0%
0% 10% 20% 30% 40% 50% 60% 70%
Percentage of respondents who selected each option (n=35)


5. Short of a complete cure, what TOP 3 specific things would you look for in an ideal treatment for ALD? Select TOP 3
Respponse options
Increased ability to walk
Slow or halt disease progression
Prevention of cerebral ALD
Improvement in balance
Control of my incontinence
Reduced spasticity
Reduced pain
Help with sleep
Restored ability to be intimate with a partner
Improvement in speech
Other
71%
55%
38%
38%
31%
24%
17%
10%
5%
2%
2%
0% 10% 20% 30% 40% 50% 60% 70% 80%
Percentage of respondents who selected each option (n=42)

## Appendix 7: Additional Comments from ALD Community Members

In order to allow as many voices as possible to respond to the Meeting Discussion Questions presented in **Appendix 3**, individuals living with ALD were invited to submit comments through the ALD Connect website, by email and through an online portal which was open for two weeks before and four weeks after the ALD EL-PFDD meeting. Submitted comments are presented in the following section.

Respondents are identified by their first name only. Submitted comments are sorted by the respondent. Comments were edited slightly for grammar, spelling and punctuation and those that did not address the meeting discussion questions were removed. Comments submitted in Spanish include English translations.

Selected comments and excerpts were included in the main body of the *Voice of the Patient* report.

**Ted, man living with AMN - One comment submitted by email**

*Of all the symptoms of adrenoleukodystrophy, which 1-3 symptoms have the most significant impact on you or your loved one's life?*

- Bladder control

- Loss of balance and muscle control in the legs

*How does adrenoleukodystrophy affect you or your loved one on best and on worst days? Describe your best days and your worst days.*

- Worst days are when my wife wants us to go enjoy time with friends and I am not confident I can manage through the evening.

*Are there specific activities that are important that you or your loved one cannot do at all or as fully as you would like because of adrenoleukodystrophy?*

- Going for a walk downtown.

- Going to a concert, or play, or dance, or any similar event. I have to manage how much I hydrate and when I will be able to get to the bathroom

*How has your loved one's ability to cope with the symptoms changed over time?*

- She has taken responsibility to carry things for me and not let me get up and help around the house.

*How well do these treatments treat the most significant symptoms of adrenoleukodystrophy?*

- There are no treatments other than cortisol replacement, which is quite effective.

*Short of a complete cure, what specific things would you look for in an ideal treatment for adrenoleukodystrophy? When considering a new treatment, what factors are important to you?*

- Remyelination. I would like my body to return close to normal function, even if it were only for 10 years or so.

**Kamran, man living with AMN - One comment submitted by email**

**Current Age:** 51 years old
**Age at Onset of Symptoms:** Subtle symptoms of fatigue and inability to condition during late 30s. Stumbling over left lower extremity in early 40s.
**Age at Formal Evaluation:** 45 years old
**Age at AMN Diagnosis:** 48 years old (diagnosis complicated by coexisting radiographic cervical stenosis/thoracic syrinx, leading to several neurosurgical recommendations for cervical fusion)
**Most Significant Symptoms:**

- Mechanical pain/stiffness: Pain with movement
- Muscle weakness
- Fatigue/Poor recovery following physical activities
- Lesser symptoms include restless legs, occasional burning sensation over feet, poor sleep
- Questionable AMN-associated symptoms include frequent lower abdominal pain and IBS
- Indirect symptoms as a result of abnormal gait/use of assistive devices/overuse include shoulder/elbow/knee/hindfoot/low back pain

**Assistive Aids:** Cane/walking sticks for community ambulation; no aids or "wall surfing" in my home
**Attempted Treatment Modalities:** Home exercise program, NSAIDs/Tylenol/Baclofen/Tizanidine, heat/cold application, bracing, numerous supplements
**Most Frustrating Aspects of Condition:**

- Difficulty with simple activities of daily living and work duties (pain with bending/twisting/squatting and need for extended breaks between chores)
- Unable to play sports and do physical activities with children
- Unable to predict how I will feel at any given moment, regardless of following same daily eating/sleeping/exercise/medication routine
- Year-to-year progression in symptoms

**Best days** are characterized as being able to focus upon my work, children, chores without thinking about my condition (becoming less frequent)
**Worst days** are characterized as struggling to stand from a seated position, buckling at the hips/knees which may result in falling, and need to lay recumbent for most of day
**Activities that I am unable to, or have difficulty to, participate in:** Hiking, skiing, cycling, weightlifting, travelling/sightseeing, landscape photography, social interactions
**Ability to Cope:** Fair. I am extremely fortunate to be financially stable. However, the ability to cope becomes difficult as new limitations arise. The progression of symptoms appears to accelerate.

**Success of Attempted Treatment Modalities:** NSAIDs/Tylenol are the only treatment that have provided any degree of pain relief (mild at best). Baclofen use has no perceptible symptomatic benefits; however, use may decrease the frequency of calf/quad/hip flexor strains that I experience. Tizanidine is helpful for deeper sleep; however, the medication has not extended the total time that I remain asleep.

As a result of worsening abdominal issues, I have discontinued all medications/supplements x 2 weeks. It is disappointing to express that no significant change in my physical symptoms have resulted from the discontinuation. Therefore, I may discontinue all of the medications permanently.

**Ideal Medical Treatments:**

- Due to the day-to-day variation in the severity and onset of mechanical pain, an as-needed/fast-acting muscle pain reliever/relaxer, that does not need to be titrated, would be beneficial (For example: participating in a scheduled 2-4 hour physical activity with predictable reduction in pain, and without drowsiness/disorientation)
- Neurologic deficits alone (in my opinion) do not explain the prolonged recovery periods that follow physical activity. It is possible that this may be related to mitochondrial dysfunction. Treatments targeted to expediting this recovery may result in more functional condition, which will have a secondary benefit on mood/mental status
- A medication that can decrease the excitability of neurons that result in unexpected and reflexive hip/knee buckling

**Brandon, man living with AMN - One comment submitted by email**

I was diagnosed with AMN in August of 2021; followed shortly thereafter with a conclusive genetic test. I've learned a lot about this mysterious disease over the course of the last year and want to give the medical community a glimpse into what it's like to live with the early(ish) stages of AMN.

One of the more exhausting things about AMN is how ever-present it is. It's there every time I stand up and have to take a beat to wait for my legs to loosen before walking. Don't have time? Get ready for an awkward, stiff, robotic shuffle. When life requires me to stand for too long, the disease checks in too. AMN legs get tired and need a break. Now we're back to sitting for a while. I'm reminded of it every time I have to pick up something off the floor. Between the tightness in my lower back, and holy hell my hamstrings, a simple bend isn't really an option. It's a hand on a knee or a nearby surface. Really makes a guy in his mid-30s feel old. Thankfully our dog doesn't mind a simple game of fetch taking a little longer than it used to.

Imagine having to think about every step you take, constantly having to calculate and calibrate your gait. Too fast and you risk tripping over your own feet. Too slow and... my god this is taking forever. Am I in this person's way? I hope they hold this flight for me.
The double-edged sword of the disease is that it typically progresses at a slow pace. On one hand we are able to constantly adapt to our new, ever-diminishing abilities before we're even

aware of them. On the other hand, it can be cruel because we're constantly reminded of this progression, and there's nothing we can do to stop it.

I could dunk a basketball in high school and now I couldn't tell you the last time I tried to jog. Or jump. Actually, that was in physical therapy, and it felt bizarre and unnatural.

It seemed odd to be in physical therapy after my AMN diagnosis, but without a single instance or event to land me there. I'd never been before, and admittedly my initial thought was "how much could this really help?". As it turns out a great deal. While I was doing exercises that seemed mundane, I was quickly humbled by my inability to do them. While I'd been a little lax on my physical conditioning the last few years, the disease hadn't taken a day off. This wasn't getting older, losing a step, or being a little out of shape. My legs and feet that could once complete agility drills and scoot (fairly well) around a dance floor were simply incapable now.

Despite all that and knowing the likely course of the disease that I'm ill-fated for, I know that in many ways I'm one of the lucky ones of the AMN/ALD community.

I'm lucky I got into a career that is almost exclusively done from behind a desk; and doing it remote or from home? No problem. So long as I am of sound mind (fingers crossed) and can communicate, my ability to perform at work is more or less uncompromised. I'm also fortunate to work at a company with outstanding employer-funded health insurance and the flexibility to take appointments and pursue a diagnosis as needed without penalty or lost wages; both luxuries that I know aren't plentiful.

I'm lucky that most of my hobbies happen to be intellectual in nature. I can't say that I ever had a desire to run a marathon or compete in an Ironman. Now I'll never have to worry about getting pressured into a 5k.

I'm lucky that I was only diagnosed a year ago at the age of 35. I got to enjoy a childhood blissfully unaware of the potential danger lurking. No constant testing or worried parents for me.

I'm lucky I only had one year before my correct diagnosis of swimming through misdiagnoses, where doctors had no idea what or if anything was wrong with me, or were so convinced that I had something else that I was on the doorstep of expensive and potentially unnecessary genetic testing.

I'm lucky to have world class medical care all around me in Dallas, Texas. Once the diagnosis did look more serious, I had no trouble seeking out a (better) second opinion.

I'm lucky to have a neurosurgery resident in the family that spotted my odd gait on a hike and recommended that maybe I should see a doctor about it in the first place. A routine physical can't hurt.

I'm lucky that on the eve of my first routine physical exam in years, the one that kicked off this whole journey, I went on a first date with a woman who turned out to be the love of my life. I'm beyond lucky that she's leaned into this diagnosis with me and has supported me emotionally (and who am I kidding, increasingly more often physically). She's the most amazing, supportive partner that I could ever ask for.

I'm lucky.

I wonder how many of my brothers and sisters in the AMN/ALD community would say the same.

Of course, my hope is that one day science progresses to the point of a cure, or something like the Neuralink renders my atrophied spinal cord unnecessary.

More realistically I would eagerly pursue something to halt or slow the diseases progression. Will my life be totally normal? No. That ship has sailed. I'm comfortable with that. It would be amazing to be able to continue to walk for the rest of my life, but the reality is, I don't know if I will be that lucky.

Gene therapies likely carry the most hope right now. There's a drug or two in the works. But how early on do I want to join the trials? Do I jump into an early phase to have a chance to get the drug immediately? But what if I end up with a sub-optimal dosage of an AAV based drug during that trial? I may have just spent my only bullet and missed. I've made a great contribution to science, but that doesn't help me walk, does it? And if I wait? I'm accepting a certain few years of continued disease progression for the *hope* that there's a more appealing target for that single bullet later on.

For me, for the time being, the disease is a balancing act (at times quite literally) of AMN symptoms with the side effects of the drugs to combat them. It's Baclofen for me, for now. It eases spasticity, sure. But too much may bring on a further unsteady gait, getting fatigued more easily, and increased constipation. Or is it the disease progressing? It's a delicate dance in the dark; with bad balance to boot.

The AMN/ALD community is made up of great people. It's a supportive, tight-knit group that really tries to make the best of the hand we've been dealt.

We welcome more of the medical community to take a walk in our shoes and understand the challenge we face with each literal step we take. Help us take greater strides so that we and those who receive a diagnosis in the future will be lucky enough to move past hope and on to realizing potential life-changing therapies.

**Rodrigo, man living with AMN - One comment submitted by email, one comment submitted online.**

**Comment submitted by email**

Thanks for the opportunity to join this quite relevant debate regarding ALD and AMN. I am 47 years old and have AMN. I have a comprehensive understanding about my condition and the issues associated with AMN and cerebral ALD. I would cite two effects as the issues that have the most impact on my daily life. Pains in the legs, with burning, tingling and numbness. When the temperature is hot the pain is more intense, in the cold I feel much better. When I have a lot of pain in my legs, there is no point in taking medication (such as pregabalin), as they do not contribute to reducing the pain. I was used to live in Sao Paulo, a huge city in Brazil. Now that I changed to Curitiba, a small, quiet and great city, my quality of life enhanced a lot and my pain almost disappeared. Bladder and bowel problems are other effects. I am normally unable to have a bowel movement, which requires me to help myself with a hand, soap and water. This is a very uncomfortable situation, but necessary in everyday life. Although I like to stay at home and avoid crowded places, I like to go out, travel and discover new places. I still walk and use a walking stick when I felt the need to help avoiding to fall. My wife is always scared about possible accidents that could prevent me to walk. I feel that she is always scared about possible accidents and the disease evolving to cerebral ALD. Thanks for the opportunity to share some insights from my daily life.

**Comment submitted online**

The different symptoms we are discussing are common and changing depending on multiple issues. The access to reliable information, as ALD Connect allows, is extremely relevant in my perspective. Information is fundamentally relevant to me so I can better manage my challenges and live better.

**Michael, man living with AMN - One comment submitted by email**

I'm Michael, age 59 ALD/AMN for 36 years. The disease over the 36 years has taken me from good athlete to just a few walking steps per day. I lost my ability to run @1990. Other challenges include bladder and bowel issues. I am unable to stand independently and need to hold support to stand up. I am able to swim okay, but loss of strength over the years is making it more difficult. Thank you for your interest and concern.

**Brett, man living with adult cerebral ALD – One comment submitted by email**

1. I had to quit working/running because of ALD.

2. I no longer work/run because of ALD.

3. I wish I could work/run but I can't because of ALD.

4. ALD has impacted my relationships with wife.

5. I missed out on playing with my 13-year-old twin boys because of ALD.

I received a bone marrow transplant in Boston in November of 2013. I live in San Diego. I'm 45 years old.

**Artemio, man living with AMN and arrested cerebral ALD – One comment submitted by email**

1. I had to quit drinking coffee because of ALD.

2. I no longer run and play soccer because of ALD.

3. I wish I could be with my friends hanging out without any accident, but I can't because of ALD.

4. ALD has impacted my relationships with my dad's side of my family because I cannot tell them I have this genetic disorder.

5. I missed out on going outdoors/nature because of ALD.

**Julie, symptomatic woman living with ALD and mother of a son with childhood cerebral ALD – One comment submitted through the website**

ALD has greatly impacted and continues to affect/impact many aspects of my life and the life of my family. Complications of AMN took the life of my dad when he was only 58. I have not had my dad for over half of my life. My son has ALD and has grown up only knowing life as a medically-complicated child/now teenager. The first ten years of his life were filled with MRI's, bloodwork, tests, Lorenzo's Oil research study which kept him on a very strict diet, and eventually a harrowing journey of bone marrow transplant. Thankfully the transplant was successful; however, his adrenal insufficiency that comes along with ALD greatly affects his daily life. He is an endurance athlete who loves to run, but his AI medical needs prevent him from doing what he loves to the extent he loves to do it. He has gone into adrenal crisis on several occasions and never knows how he will feel from day to day or if he will be able to finish a run with his cross-country team or not. This has a great impact on his mental well-being as well…he trains and trains but is so discouraged by not being able to keep up with his peers and struggling, while they succeed. He has to fight through adrenal sickness and daily frustration.

He also has fears about developing AMN as he gets older. I myself have symptoms as a woman with ALD…neuropathy in my feet and legs, one leg/foot often drags, tripping is a daily worry, as well as bladder control and balance issues…I've had all of these to some degree since I was in my 30's. I keep exercising as much as I can since there is no treatment for women, and I greatly worry about mobility as I get older (I am 49).

**Celeste - mother of a deceased son with childhood cerebral ALD – One comment submitted by email**

Because of ALD my son fought 7 years and 4 months, he was too late for BMT but we made sure his life after ALD diagnosis was filled with love. He was diagnosed 01-16-2015 he passed due to complications of parainfluenza 3 on 05-18-2022. I hate ALD.

**Miranda, mother of a son with ALD diagnosed through Newborn Screening - One comment submitted through the website**

My name is Miranda McAuliffe. My six-year-old son was diagnosed with ALD at birth thanks to Aidan's Law being passed in New York and newborn screening for ALD being implemented in 2013. Right now, he is currently asymptomatic. He is monitored diligently every six months with MRIs of the brain and blood work to check for adrenal insufficiency.

When parents learn of this diagnosis for their child at birth, they are told that their son may develop the childhood cerebral version of this disease or the adult version known as AMN. It is an awful message to be delivered to a new parent. While I delegate most of my worrying time to the cerebral phenotype and his monitoring protocol, the thought of AMN is always lurking in the back of my mind. Sometimes I get mad at myself for not worrying more about AMN. After all, statistics tell us that AMN is more likely than childhood cerebral ALD to present itself in a male with the ABCD1 gene mutation.

My son can switch from bi-annual to annual MRIs at the age of twelve. I trick myself into thinking I can worry less at this age, but who am I kidding? The threat of cerebral ALD is always there (even for AMN patients) and the deterioration from AMN can creep up at any age – as early as the second decade of life for some. If my son gets sick in childhood, he can be treated with a bone marrow transplant or hopefully (FDA review pending) gene therapy. The landscape for AMN treatment is much less concrete...and so much more dismal.

I am sure by this point in the program you have heard from numerous patients about the lack of treatment options for AMN. This devastates me as a mother. The most important thing I can be doing today is sharing with the FDA that my son represents HUNDREDS of PRE-symptomatic boys that will one day grow up to be men not unlike the men you have heard from today. This applies to a majority of the ALD newborn screen girls as well. Newborn screening is a gift to not only me but to every stakeholder involved in making treatment options available for men with AMN and symptomatic women with ALD. As of this writing, 29 states are screening their babies for ALD, a disease with an incidence rate of 1:15,000. In approximately three more years, I anticipate all 50 states will be screening. These babies will not grow up to suffer a diagnostic odyssey. When their symptoms begin to show they will know exactly what they have....and they will be seeking treatment. The point I am trying to get across is to please, in your minds, magnify the voices of all of these patients you are hearing today. Double them, maybe even triple them. By helping patients and their clinicians discover treatment options, you are unburdening families and a healthcare system that is currently greatly tolled by the slowly devastating and deteriorating disease that is AMN. This will only get worse if we do not keep pace with newborn screening advocacy efforts that are currently underway.

As the mother of a pre-symptomatic boy, I can only hope that treatment would be potent and available as soon as symptoms develop. I hope that this treatment will halt AMN in its tracks, not just mask symptoms or slow down the pace of the disease. And it must be made available to every affected patient, regardless of age, gender, racial background, or income. ALD does not discriminate, and neither can we.

Thank you for listening to my concerns.

**Jesse, symptomatic woman living with ALD and caregiver for her son with ALD – One comment submitted through the website**

I am the mother of a 23-year-old son with cALD. He had a transplant 15 years ago and although the transplant was successful, it was a late diagnosis and he is fully dependent. I am his caregiver and I have ALD symptoms that are currently more a nuisance, but getting more pronounced. I am worried about what the future holds for me, my son and my ability to care for him.

**Janisse, symptomatic woman living with ALD – One comment submitted by email**

I am a 62-year-old female with 3 grandchildren. I long to sit down and play with them and get up on my own or chase after them. I cannot. I dream every night that I can walk normal again. I cannot. My hope is that anyone with ALD receives help in any form that fits their individual need.

**Jamie, symptomatic woman living with ALD, mother of a deceased son with cerebral ALD – One comment submitted by email**

*I had to quit*

Hiking, water skiing, riding a bicycle, line dancing, long country walks, gardening, cooking holiday meals

*I no longer*

Work my dream job, ride horses, show farm animals, go to the lake with the kids, go to the river with the kids. Enjoy long walks, fly kites with the grand kids. Go fishing at the lake.

*I wish I could*

Stand more then 10-15 minutes at a time, last longer then 20-30 minutes without having to get to a bathroom. Walk without assistance of a walker, stand up taking a shower

ALD has impacted my life with all of my relationships.

*I missed out on*

lake trips, river trips, fishing trips, hiking outings, camping.

*I worry about*

waking up not being able to walk, becoming completely incontinent, needing help to take care of myself.

*I have to*

Get rides to go to medical appointments, have my groceries delivered, depend on others to help me clean the house, have people take care of my yards, have help with the garden.

Have help with almost everything.

**Julie, Symptomatic Woman with ALD – One comment submitted by email**

1. I had to quit running my usual list of errands because of ALD. I have to choose which errand(s) I can do in a certain amount of time.

2. I no longer work out in the evenings because of ALD. I'm too fatigued.

3. I wish I could walk the distances I used to walk but I can't because of ALD.

4. ALD has impacted my relationships with my colleagues at work.

5. I miss out on group activities because of ALD.

**Cynthia, symptomatic woman living with ALD – One comment submitted by email**

I am a woman with Adrenoleukodystrophy, ALD.

The first time someone in my immediate family was diagnosed with ALD was in the early 1980's. I was 30 years old. My youngest brother, Jeff, had a car accident while having leg spasms. He was 27 years old. The CAT scan in the ER showed white plaques in his brain. He was initially diagnosed with MS.

A week or so later, Jeff, had a respiratory infection and it hit him hard and was difficult to heal.

There was one pediatric neurologist in our area, who knew about ALD and he recognized my brother's symptoms. The adrenal deficiency is what tipped him off.

Our family was referred to Dr. Moser at John Hopkins and when we all went for bloodwork. Out of the 6 children in my family, 3 boys and 3 girls; the youngest, a boy, me and my older sister all had the elevated long chained fatty acids.

Back in the 1980's, we were told that only males get symptoms of the disease, women are "carriers only."

I learned about the symptoms and progression of an adult male with ALD by taking care of my brother, never paying attention to symptoms I may have been having.

**My First suspicion**

I started having issues controlling my bladder and bowels when I was 50. After experiencing several embarrassing situations, I went to my PCP. He referred me to a neurologist, Dr. Ruffing, who not only knows about ALD and has treated one woman with symptoms**.**

Right after my appointment, I went home to look up women with ALD and only found one article from a Dutch woman. She had all of my symptoms I was having which validated my diagnosis.

**My Initial Symptoms**

Once I knew that women with ALD did get symptoms, I now knew why I was experiencing challenges.

**#1 Balance;** I always wondered why I could never balance on one foot even after many yoga classes and PT; this embarrassed me because I was an aerobics instructor and had strong legs. I also fell several times at home, and even in one of my aerobic classes.

#2 **Incontinence both bladder and bowel**; Once I had a few bladder and bowel mishaps, I started wearing a pad or diaper for situations where I would not know when I would be near a bathroom

# 3 I started getting **severe leg spasms** every afternoon or every evening, depending on how active I was each day.

#4 I have had **restless leg syndrome** since my early 30's, which caused my husband to sleep in another bed.

# 5 I have **trouble falling asleep**, because I get severe periodic leg spasms once in bed. Once I started taking pramipexole and Zanaflex, my restless legs calmed, but the spasms still came. I was suggested to try marijuana, which I did. And now I do need a puff or two at night to relax my leg spasms to be able to sleep.

**Main Social changes:**
I am a nurse and had to go on disability because I could no longer do nursing tasks.

My husband and my activities together were bicycling outside in warm weather, hiking in the cold and teaching spin, pilates and strength classes at the gym.

In my early 50's I was having trouble keeping up with my riding group. I fell back to a slower group in the club, but felt my husband and I were spending too much time away from riding together. E-BIKES were my savior. With an E-bike I can ride with my husband and friends again.

My legs are too weak to hike and my whole body is tired by 4-5 pm so I don't hike or teach classes at the gym anymore. My husband still goes to the gym every evening. I stay home.

Once I started having symptoms, I spent over a year depressed and angry that I could no longer do the activities that I loved to do.

We had a dog. I wasn't able to walk her for her last year of life. She pulled me down whenever she saw a squirrel.

My house seemed too quiet after our dog, Maggie, died. I was no longer strong enough to take care of another dog, so I got two cats instead. They are giving me a lot of happiness.

**Now**

**Things can do:**
Bike with power assistance, electric bike.
Walk slow and short distances with a cane for balance
Swim

**Things can no longer do:**
Put pants, socks, undies or shoes on standing up
Can't travel alone easily, need wheelchair to get around
Can't hike, I am only able to walk about 2.5 miles before my legs cramp.
I miss tours and activities when we travel. I am unable to walk around museums so I sit somewhere and wait.

**I have fallen 3 times with severe injuries:**
- broke 3 toes, swelled and painful
- I broke both hips (different occasions 1 year apart) and had to have two total hip replacements. My recovery for each injury was longer than most because of my balance and unstable walking
- I can't walk a buffet line holding a plate of food walking with cane. I do need help
- I have a handicap license plate because I can't walk far

**Dorothy, symptomatic woman living with ALD – Two comments submitted by email and one submitted online**

**Comment 1 submitted by email**
As a woman with symptoms, it is difficult to be rare with no one around with the disease and no medical providers with any experience with the disease; it becomes frustrating at best. I have done Botox for my leg cramps for 7 years at Shepherd Rehab Ctr that has never had a patient with the disease at all. I was fortunate to have a neighbor neurosurgeon that had gone to Europe to look into stem cell treatments for pain for his daughter and did an adipose stem cell injection for my back pains and was able to introduce me into trying placental stem cells IV therapy which has been exceptional for the last 6 years until the company was called by the FDA and essentially told to submit the stem cells for medical clearance and they had to close all production leaving me with no treatment for a year now. I have had a major increase in symptoms and fatigue which has been significant to say the least.

I would like the FDA to consider stem cells that might be close to MS therapy for ALD patients since I now have seen the improvement in function to the point I can walk with a walker very well, walk about .4-.5 miles a day, teach at a major hospital in Atlanta, entertain, and otherwise able to do a lot more than expected. Since no stem cells for the year I have digressed greatly and developed foot drop and have to go back to a leg brace that I ceased using years ago.

I think having more ways for other patients to have connections is vital to share what might improve their lives. Using a scooter around my house lets me do about everything I need to get things done. Getting therapies established is tantamount to improvement of everyone's lives. This disease, although rare, may have strong ties to MS therapy that could help start more investigative studies for ALD.

As someone who dared to try something to assist at my own cost, I have been pleased to have done it and share its information, but wish that again the FDA realize when those that have been proven are removed should be given a fast track for approval so those affected can have others use the treatment options if possible.

Weakness and fatigue are difficult issues. Inability to lift objects anymore is depressing and no longer able to stand for long periods is another issue. I was told by my orthopedic surgeon after I had four back surgeries for stenosis unrelated to ALD that I should just get a wheelchair and go retire to the beach. That was 6 years ago and still never did that, continue to teach Infertility care at Morehouse and do clinics and patient care despite his recommendation. My only issue now is fatigue and hope there is a stem cell therapy I can try so I can go my usual full 100% at the age of 73.

**Comment 2 submitted by email**
I am 72 and have experienced some cramping over time in my calves that have become worse since age 64. I used Skelaxin which is very helpful but just went way up in price this month to $300 from $100 for 60 tablets.
I started BOTOX injection in my calves at Shepherd Rehab Center for almost 7 years now which definitely helps. Medicare has lately started wanting not to pay for it as well.

I also had stem cell perfusion from my adipose tissue done in early 2016 by a neurosurgeon who had learned the procedure in Europe to help his daughter who had severe pain in her ankle after a fracture during soccer injury. Both her treatment and mine to my back (after 2 back surgeries) worked very well for my pain. I asked if there was any other treatment that might help for ALD (which of course he never had a patient with the diagnosis) but told me about placental stem cells from BioBurst that had gone through multiple studies for pain. I asked if I could be a guinea pig and try it since I would have to pay cash. We tried it and the first one worked for 3 months, and I did 3 more IV stem cell treatments that worked very well. I decreased to 3 per year then over the last 2-4 yrs only needed twice a year that gave me less pain and much more energy and better function for walking with my leg cramps.

Lately, in June 2021 I had the IV stem cells and it worked very well. I came back in December for the second dose, but I had gotten my booster full dose Oct 21 and when I returned for the Botox and stem cells I had absolutely NO results for the first time ever in getting either one of the meds. I went on and did March 2022 Botox that finally did better, but I did notice I was extremely exhausted that I have never experienced before.

In June I was to get Botox and the stem cells but unfortunately, they had been called by the FDA to cease production and sales and to submit their stem cells to be evaluated as a drug. They have sent all the info to the FDA in March but do not expect it to be passing any time soon. In the meantime, I am having severe weakness in my legs, have difficulty walking with my walker and still exhausted and sleeping huge amounts per day.

Everyone has noticed my decline which has been rapid. I am seeing if there is an MS stem cell study that might have been done that would possibly help and I am glad to try that again as the only person in all of Shepherd Center that they have had with ALD and they are highly ranked as a rehab center in the US. I have yet to meet anyone with the disease or heard of it.

My son has ALD – Mature onset with Addison's for 4 years now.

I am a physician, Reproductive Endocrinologist and Infertility in OB/GYN for 42 years and have had extensive physical therapy and thank goodness, Botox. The stem cell dilemma is obviously my greatest concern at this point.

I would be glad to meet and discuss issues with the FDA about stem cell treatment and its efficacy I have experienced. I do believe MS and ALD have much in common and might ask about going to the large MS practice at Shepherd as well just to see if I might benefit from any of their meds.

**Comment submitted online**

Attempt to get FDA or others to do stem cell or other meds for treatment.

Have ALD patients be able to participate in proposed studies.

**Carla, symptomatic woman living with ALD – One comment submitted by email, one comment submitted online**

**Comment submitted by email**

3 symptoms that really bother me:

1) weak legs, I can't walk fast, lack of balance

3) urinary function

3) constipation

4) neuropathic back pain

My life has changed since I was 46 years old, I had fell and started a low back pain and weakness. Now I'm 55 years old and is worst. I can't walk, I fall down all the time. I hurt my coccyx and now I am taking pregabalin or Lyrica.

Please make a cure or treatment to avoid bad symptoms in the legs (weakness and lack of balance). Also medicine for urinary and bowl problems.

**Comment submitted online**

I'm 55 years old and I suffer 8 years ago with ALD
Symptoms:
1. Lost of balance and falls;
2. Can't walk;
3. Urinary and bowel problems.

It is hard to live with ALD. My life has changed a lot, I can't work and can't go for a walk alone, is terrible.
Also, to live with urinary and bowel problems is hard. I can't go anywhere, and I can't sleep either.

**Joyce, symptomatic woman living with ALD – One comment submitted by email, one comment submitted online**

**Comment submitted by email**

I am 66 years old. I am a symptomatic woman and I am thrilled for this opportunity. I have urinary incontinence. I am wheelchair bound. l cannot stand. I live in an Assisted Living facility where I work full time as receptionist, payroll and benefits and H.R. person. If there is a possibility for any improvement in my mobility, I may work a few more years.

**Comment submitted online**

Thank you, thank you, thank you! And God Bless you for organizing this meeting. It means so much to be heard. Thank you, Kathleen for emphasizing the fact that women need treatment options too. My heart was so touched today.

**Nancy-Anne, symptomatic woman living with ALD – One comment submitted through the website, one comment submitted by email**

**Comment submitted through website**

I started experiencing ALD 18 years ago by limping. It took 5 years to determine a diagnosis. I am unable to walk on my own without a walker. I have no balance, no independent mobility, and no bladder control. In Toronto, there are no doctors who have adult patients with this disease. I educate my specialists if they are interested. I hope that my daughter, who has the gene, and her two daughters who are school age kids, and their future children, will be able to have a healthy life if they have an activated gene through the treatments that will be available in the future. Thank you.

**Comment submitted by email**

1. I had to quit work because of ALD.

2. I no longer feel because of ALD.

3. I wish I could walk but I can't because of ALD.

4. ALD has impacted my relationships with my doctors who are uninformed about ALD and my ability to participate with people in work and social activities.

5. I missed out on being an active and participatory grandmother, community volunteer, writing tutor, conductor of workshops, soprano in our seniors choir, hostess and visitor to/with family and friends because of ALD

2. I no longer feel alone because of ALD Connect.

**Patti, symptomatic woman living with ALD –One comment submitted through the website, one comment submitted by email**

**Comment submitted through website**

Short of a complete cure - our mission should be to STOP the progression of the disease in men, women and children!!!

**Comment submitted by email**

In response to the prompt:

1. I had to quit always being VERY optimistic because of ALD.
2. I no longer walk unassisted because of ALD.
3. I wish I could play on the floor with my grandchildren, but I can't because of ALD.
4. ALD has impacted my relationships with my entire family and friends.
5. I missed out on babysitting my grandchildren because of ALD.

**Sheila, symptomatic woman living with ALD and mother of a son who died from cerebral ALD – One comment submitted by email**

I am a 55-year-old woman with ALD. I have leg issues, neurogenic bladder, constipation, low energy, short term memory loss, and mental health issues. I was only diagnosed with ALD at age 48 when my son was diagnosed with Addison's Disease and Cerebral ALD at 18 ½. After being a caregiver for my son with ALD, who has now passed, I learned a lot about handling ALD symptoms, and I am now using that knowledge for my own symptoms. I am also using advice from my ALD specialist, my family, and other symptomatic ALD women during ALD Connect Community Zoom calls. I have incorporated many lifestyle and nutritional changes which have helped to improve my symptoms.

With regard to my leg issues, I have shuffled my feet since my early 20's and I've had a few falling issues in my 40's and 50's. Recently over the past few years, I've had significant increase in falling issues, my gait is significant for scissoring of legs, difficulty turning, balance issues, right foot drop, and pain in the right thigh. The recent falling issues had become an embarrassment for me when I am in public, but also dangerous due to easy bruising and easy bleeding from my Von Willebrand's Disease. In the house I have difficulty walking over thresholds and walking down the stairs with laundry. In the yard, I can get very wobbly doing

gardening and clean up, but have only fallen a few times in the yard. I made my neighbor very nervous when he saw me wobbling in my yard carrying a bag of mulch over my shoulder. Recently at a wedding, I had problems dancing, so my husband had to hold onto me the whole time. That was a shame, because I love to dance. My husband also had to help me get over the waves at the beach to a calmer spot out in the water. But even then, he had to hold onto me the whole time as water came in and out. It was like he was flying a kite, and I was the kite. After sitting for a couple of hours watching TV at night, I was getting right thigh pain. I needed to find a way to adapt.

To help me adapt to the new normal, I started walking with a walking stick in public to prevent falls about 2 years ago due to neuropathy and balance issues. This has decreased my falls significantly, but I still fall. I don't use the walking stick at home, but I have learned to just take my time, don't rush, and try to remember to pick up my feet over thresholds. I have been having my husband carry the laundry down the stairs for me, but I bring it up myself by using our hamper as a walker going up each step. It works. I have been walking 3 miles a day, every day, to build up my strength and practice walking so I don't end up in a wheelchair. If the weather doesn't cooperate, I sit and do the peddler for 1 ½ hours. I also stopped eating red meat to prevent my occasional right side abdominal pain from my diverticulosis, which my sister suggested. I also started eating salad every day for the same reason. Now that is not an ALD issue, but I noticed that once I stopped eating red meat and eating salad every day, not only did my abdominal pain from diverticulosis not happen anymore, my right thigh pain from ALD stopped as well. I will just keep chugging along with my walking stick and hope for the best.

With regard to my neurogenic bladder issues, I was having frequent urination, where I would pee 11 times during the day, sometimes up to 3 times at night, totaling 14 times per day. I also had urinary urgency and incontinence, and would pee my pad several times a week. These issues made it difficult when we went on vacation down to visit my older son and tour Washington DC. There was a lot of walking and sightseeing involved, and I would always need to stop and find a bathroom. I felt bad for always slowing us down. I needed to spend less time in the bathroom, and more time living. To help get my bladder issues under control, I first started by giving up caffeine and limiting my alcohol intake. I was drinking 5 cups of coffee a day for energy, and drinking 2 glasses of wine a night with dinner to help me sleep. Then I participated in an ALD Connect Symptomatic Women with ALD community call. They recommended giving up caffeine and alcohol to help with urinary issues. I gave up caffeine and reduced my alcohol intake. This helped reduce frequent urination, urgency, and incontinence a bit. My ALD Neurologist recommend I keep a log with all my urinary, bowel, liquid, and dietary stats to try and find a balance and so I have proper info when I saw my Neuro-Urologist. I began seeing a Neuro-Urologist, who recommended I drink a minimum of 60 ounces of liquid (mostly water) a day, which was up from the 46 ounces of liquid I was doing. That set me back a bit, but then I had a Urodynamic study done. I was then prescribed to take Myrbetriq 50mg and Alfuzosin 10mg every night after my last bite of dinner with a full glass of water. Thanks to all those changes, I now only pee 7 times during the day, instead of 11; I now only pee 1 time at night, instead of 3; totaling only peeing 8 times a day, instead of 14; I now only pee my pad maybe once a week, if that, instead of several. I am very happy with those results, considering

how many ounces of liquid I drink a day. My Neuro-Urologist said the 60 ounces of liquid a day would also help with the constipation and be healthier for me. He was right.

With regard to my bowel issues, I was not only having constipation, but incontinence as well. My younger son with ALD had that problem too. Sometimes I would only have a bowel movement every 3 days, and my poop was very big and hard like clay. Sometimes if I got out a small hard plug poop, usually a little later I would have to run quick to the bathroom, I would get out a softer poop, and I had no control. Sometimes I didn't make it in time, causing me to have a mushy accident, which is an embarrassment, and give me great anxiety. I needed to find a happy medium with bowel movements. I learned from taking care of my son that taking Senna 8.6 mg tablets works best for having a bowel movement consistently every day without being too soft for a mushy accident.

I started to just take 1 Senna pill a night, along with eating salad every day, not eating red meat, and having a balanced dinner. I also eat a banana with my breakfast every day and blueberries in my yogurt. I found this consistency in my diet makes my bowels more consistent. This improved to a bowel movement almost daily, instead of every 3 days. Once I started drinking 60 ounces of liquid a day, I was having a bowel movement every day, until I started Mybetriq for my neurogenic bladder. Mybetriq can cause constipation. I recently started taking 2 Senna 8.6 mg tablets a night to help. It seems to be working well for me.

With regards to my low energy issues, I have started feeling more tired and sluggish lately, but my bloodwork comes back fine. So, I took a page from my son, and started drinking a 20oz bottle of Powerade Zero every day to give me electrolytes and hopefully energy.

With regards to my short-term memory loss and mental health issues, they may not be a symptom of ALD, but I believe I have them due to dealing with ALD in my son and now me. My son was only diagnosed at 18 ½, was quite functional, just developmentally disabled, ended up in Neuro ICU due to seizure/pneumonia at 21 ½, slowly went downhill, and passed way at 23 ½. It was a lot to handle, physically and mentally. During this time, I began hearing sounds at night, especially when the heat or refrigerator was running. At first it was like a muffled newscast, then music, and then 3 months before my son passed, I heard voices. They have been with me ever since. I also am very anxious and worry all the time, however I learned from my son to be an optimist and not a pessimist. Once we were driving to an appointment, and I was worried I would be late. He looked at me with a smile and said, "Don't be a pessimist, be an optimist". He was a big fan of Ike from his Axis and Allies computer game. I realized he had the right idea. I try to stay positive and deal with symptoms as they happen.

I also have short term memory loss. When I wake up, the first thing I do is go to the bathroom. While in there, I take my Viactiv chew and Vita Fusion gummy vitamin. Sometimes, 10 minutes later, I won't remember if I took it or not, so I have to run in the bathroom and see if my Viactiv chew wrapper is in the trash, so I know if I took it or not. I also keep my nighttime meds at the dining room table so I remember to take them after I eat. I always use written lists and phone alarms to remember things. My MRI shows nothing that would explain why I have these two

problems. My PCP has put in a referral for a neuro-psych, but it could take up to 6 months before they even call to set up the appointment. Until then, I will keep staying positive.

All these ALD symptoms have created a lot of problems for my life and have given me worry and anxiety. I will keep going and keep trying to adapt to any new changes that come along due to ALD.

**Shari, symptomatic woman living with ALD – One comment submitted through the website**

I am a woman with ALD. I was diagnosed in 2019 by Dr. Eric Mallack at Weill Cornell Medical. ALD has affected my family since 1959 when my mother's younger brother died. I lost both my older brother in 1972 and my younger brother in 1979 from ALD. I had my genetic test in 1987 when I was 18. Clearly my grandmother and my mother had ALD and they both died from their ALD symptoms.

My symptoms began when I was 50 years old. I have severe burning neuropathy in my feet and legs and numbness in my toes. I've gone through some trial and error with medications to treat this. I had some relief from Gabapentin for a while after almost two years I began having stomach issues. I take duloxetine and it seems to be working well. However, additional neuropathy symptoms started last fall and I was experiencing severe numbness in my feet and stinging in my legs. I would awaken every night between 2 - 4 am. This went on for almost 70 days. I saw a pain management specialist but all he could suggest was having a device implanted in my back that would send signals to my spinal cord that might help reduce this. I am not up for this type of surgical procedure, so I decided to start taking THC gummies before going to sleep. This has helped immensely. After months without a full night sleep, I was finally sleeping well. The result is complete calmness and I sleep through the numbness and stinging. Hopefully this will work for a long time since there is no treatment for numbness at this time.

I'm constantly on edge worried about what the next symptom will be since none of this is predictable. There's always fear that I will end up paralyzed the way my mother did. She suffered from ALD for 10 years. Watching her go through that was devastating. I don't want my family to experience that.

I have twin daughters. I did IVF with PGD in 1998. Testing embryos for ALD was not developed yet so we could only choose female embryos. I did three cycles and the third was the charm. They were born healthy in 1999. They will turn 23 this summer. They had their genetic tests in 2017 when they were 18. The results were bitter-sweet. One has ALD and the other does not. There's always concern that my daughter will also become symptomatic. It's been a never-ending road to travel and my family is still affected. My hope is that research will one day finally end all of this suffering.

This is the effect ALD has had on my life and continues to affect me every day.

**Laurie, symptomatic woman living with ALD – One comment submitted by email**

I am a 53-year-old female with ALD. My initial symptoms started at the age of 38. They progressed slowly for the next 10 years. I started to experience problems with my gait as well as balance. I progressed from using a cane to forearm canes, a walker and eventually a wheelchair. I would like to provide a day in my life...

5/21/2022

4:43 am Woke to discomfort in my legs and inability to move

5:00 am Managed to transition to a wheelchair but was not able to transition to a toilet as my legs were too weak

6:00 am My husband woke up and had to help me to the restroom

6:00 am Experienced severe pain in my legs and numbness in my feet and took 600 mgs of Advil as well my prescribed medications for GABAPENTIN, BACLOFEN AND DARIFENCIN. I tried to stretch and work through the pain

8:00 am Still unable to stand without significant assistance. Family has gone out for an adventure on the water and I am unable to attend because of my physicality and my pain.

1:00 pm At home alone because my family is enjoying an adventure that I cannot participate in.

My struggles with ALD are absolutely impacting my daily life. My family is dramatically affected by ALD but I am the one with the worst symptoms. Please consider the dramatic effects this disease has on women and please help us. I am sure that actions now will not help me, but I only hope that they can help future generations.

**Barbara, symptomatic woman living with ALD – Seven comments submitted by email**

**Comment 1**

I had to quit working because of ALD.

I no longer can do embroidery because of ALD.

I wish I could walk but I can't because of ALD.

ALD has impacted my relationship with my husband and my friends.

I missed out on having fun because of ALD.

I don't know how to put this in one prompt but when I had to stop working people congratulated me on an early retirement. However, unlike others who may finally get to travel and golf, I stay at home unable to go independently and my friends don't think to ask me along as that means a wheelchair and someone who has difficulty speaking and eating. Not the friend they used to know. It is hard even to look at Facebook and see all the fun things people do that I can't. I am grateful for my family but being greedy sometimes I want more. I want to laugh and have fun too.

I no longer have fun because of ALD.

I don't go anywhere and can't do but realized especially this weekend after attending a cookout and watching everyone swim, play games, walk about to where they wanted to be, to talk to who they wanted to, and eat what they wanted etc.

**Comment 2**

An AMN man could be a boy who has had treatment as a boy for ALD. Not a guaranteed cure. Though I am not my son's caregiver I have witnessed his fear of this even before doctors recognized that BMT wasn't all that. He now falls, his gait is stiff and he has suffered from depression since his transplant.

**Comment 3**

When I am in my wheelchair people speak to my husband not me. Even in doctor's offices. Not all places are wheelchair accessible.

People don't know what ALD is. I've never talked about myself because people don't understand. If it were MS, people would understand, there would be medicines, insurance approved physical therapy for long term. Very isolating.

I would rather be by myself than try to blend in. Listen to others talk about their lives, their jobs, their activities, eating. My husband brought me home from a cookout because I just couldn't sit on the side in pain and watch everyone talk laugh eat and play. He was not happy with my decision, but I have been on the sidelines for so long and that day watching the other grandparents and my husband in the pool with my grandson set me over the edge. I needed to be selfish and leave. I felt relief when I was home by myself.

**Comment 4**

I take Clonazapam at night for spasms. Game changer. And by not waking to those, I didn't have to go to the bathroom, because I wasn't awake so I didn't feel, "I was awake better go anyway".

**Comment 5**

My AFOs were great for helping with toe drop and leg weakness. Downside made of plastic so very hot and made feet and ankles hurt from being unable to move especially when seated. Can't take them off in a restaurant but needed them to get into one. Needed them for work but same issues.

**Comment 6**

I'm hearing about different things used by patients but thinking how not [all] are available to everyone as ALD is not understood by everyone including insurance companies to approve long term physical therapy or other devices

**Comment 7**

Dream: Prevent disease once newborns are diagnosed

**Pat, symptomatic woman living with ALD – One comment submitted by email**

I had to quit taking hikes and regular walking about because of ALD. I no longer take walks because of ALD. ALD has impacted my relationships with my family. I missed out on so much that others take for granted because of ALD.

**Rachael, symptomatic woman living with ALD – One comment submitted by email**

It's hard to imagine my life without ALD,

I'm 27 and I've had symptoms since elementary school.

I wake up in pain, leg pain, back pain, bladder pain, fatigue and so many other little things, Before I do anything I get up and struggle to the restroom to deal with bladder issues, then I take about 10 medications with a breakfast shake, none of them cure me but they make it possible to get through the day without needing narcotics. It takes at least a half hour for the meds to kick in and then maybe I can do a few chores or go grocery shopping but not both even on a good day. My capacity to do those things has fallen over time, I get exhausted and clumsy as the day goes by and I find myself pulled away from the things I love doing, so I can rest and treat my pain. I can't work, because some days all I can do is sit, my brain and body will not cooperate. ALD effects every moment of my day. This is just mornings, and the rest of the day can be just as hard.

**Roxanne, symptomatic woman living with ALD and mother of sons who died of childhood cerebral ALD – One comment submitted through the website**

ALD has been in my family for three generations. My grandma lost two sons young, my parents lost their son, my brother, and two of my three sons died from it at age 9. I am now wondering if my health problems at age 79 are because I have ALD. It is so rare I have no one to answer my queries or help me. There were also two family members who died from AMN. Are there other symptomatic women that can connect with me??

**Jason, man living with AMN - One comment submitted by email**

I want to be able to walk.

**Charles, man living with adult cerebral ALD – One comment submitted by email**

I am a long time ALD patient. I was diagnosed in 2006. I was in a blind trial study shortly after being diagnosed, and discovered I had the active ingredient. The trial was discontinued. So disappointing!

Issues for me are:

1. I have become a burden to my family because I am no longer able to walk, have no balance or muscle control.

2. Up until 2 years ago I had a fairly active life. Able to walk, golf and travel with some limitations such as falling down on the golf course and airports due to balance issues.

3. I have been in a wheelchair for the last year. Because of the lesion on my brain that was found 1 1/2 years ago, I am unable to do simple tasks. I can no longer type, have double vision and slurred speech, eat with a spoon, and have some swallowing issues.

4. I am only 71 years old and don't know how much time I have left.

This disease is devastating. It is hard on the patient, caregiver and family. Please continue focusing hard on this disease for trials, new meds etc. I am sure it is too late for me, but am hoping something can be done soon to help those with this disease.

**Eric, man living with AMN – Three comments submitted by email**

**Comment 1**

I had an intrathecal Baclofen pump placed back in October. It has been a life changing procedure. I went from being so spastic that eating and breathing had become difficult. My legs had pretty much a complete mind of their own when walking and even laying down quite often. Now, my legs move much more smoothly, I can stand up straight, eating and breathing have gone back to normal. I lead singing at our small church and the Sunday after the surgery I had to stop mid verse because I was tapping my foot in time to the music. I had not been able to do that in over 2 years. I know that I am probably a rarity in the amount of change that was had from it. But I would recommend anyone dealing with severe spasticity to speak to their neurologist about getting tested to see if it will help them. The test is a seminal tap with placement of baclofen intrathecally, into the spinal fluid, and then reviewed every 2 hours after that by physical therapy. It doesn't relieve any pain or any balance other than leg control, but think about it.

**Comment 2**

I understand completely about the taxing on a marriage. After 3-4 years of becoming more symptomatic, my wife of 9 years filed for divorce. She stated that she had just lost her love for me. Part of this was because of the sexual problems. She wanted more than I could give her, and the loss of income I had once, had some to do with it also.

**Comment 3**

It may not be for everyone, but for my safety, and my family's peace of mind; I use a urinal jug at night and empty it in the mornings. It also leads to better sleep since not having to try to make it to the restroom and getting wide awake. This of course is easier for men than women to take advantage of.

**Ganesh, adult man living with childhood cerebral ALD – One comment submitted by email**

I am Ganesh a 21-year-old with CCALD. My prime years was until I was at 12 years old. I missed out on most high school experiences, hanging out with my friends and college experiences. I started losing my abilities at 14. Now I cannot walk or use my hands. It kills me that I am dependent on my family caretakers for everything. I have no privacy. I am never comfortable. I used to be very good at sports and video games and had a lot of plans such as graduating from college, which I still plan to do, but it's very difficult. This is not the life I am supposed to be

living. I want to get a job and get married and have children, but without treatment or a cure, I don't know what the future holds.

**Marion, symptomatic woman living with ALD – One comment submitted by email**

I am a symptomatic woman with ALD. I participated in the Lorenzos Oil Study in 2006, and was informed by Dr. Raymond that I had ALD, mild stages.

Walking, incontinence issues, and balance are my biggest issues that I am having now. Early this year, bending over to pick up items from the floor has become almost impossible. My back seizes up. I am also having a lot of back pain, which keeps me awake at night. Going from a sitting to standing is very painful, and takes me some time before I can stand up straight. I use a cane when walking outdoors now. Gardening has become a very difficult task, and just taking a walk around the block is nearly impossible.

The medication that I have been prescribed to help with pain are ibuprofen, and Tizanidine, 2 mg once a day. These do not help very much.

I would like to have physical therapy on an ongoing basis with someone who is trained and knowledgeable with ALD. Medication to help with mobility and back pain would be helpful.

ALD is becoming difficult for my husband and family, as many changes in my physical ability have changed this year. I am having a hard time with this, as I have seven grandchildren now. I want to be able to participate in their future.

I found out that I had ALD in 1985 when my brother was diagnosed with cerebral ALD, after years of misdiagnosis. He died at the age of 12 years, just months after his diagnosis. My mother died at the age of 60, 20 years ago, with a diagnosis of Parkinson's disease. I have 2 daughters who have ALD. Both have gone through IVF to have children without the ALD gene. Granddaughter age 5, and Grandson age 1 in August.

Thank you for all of the work you are doing to bring public awareness to ALD, and help us who have it.

**Gisele, symptomatic woman living with ALD and mother of two children with ALD – One comment submitted online**

Soy mamá, portadora de Ald, de 31 años, mis dos hijos con Ald 5 y 12 años con insuficiencia suprarrenal. Presentan lesión cerebral actual sin síntomas actualmente en ensayo clínico para detener su lesión. Mis síntomas en las piernas y infección urinaria

**Gisele, symptomatic woman living with ALD and mother of two children with ALD – One comment submitted online (translated to English)**

I am a 31-year-old mother with ALD. I have 2 children (ages 5 and 12) who have ALD. Currently they only have adrenal insufficiency. In the brain scans, a brain injury was discovered in both of

them, but they still did not show symptoms. They are currently participating in a clinical trial to stop the progression of the lesion. I have symptoms in my legs and urinary infections.

**Kathy, mother of a man living with AMN - One comment submitted online**

My son Jason will soon be 42 years old. His message is "I want to be able to walk"

**Amy, symptomatic woman living with ALD – Four comments submitted online**

**Comment 1**

I just wanted to share that after doing a lot of research on my own and failure of any other treatments or medications…I have found some pain relief in LDN (low dose naltrexone) especially for my neuropathic pain. It's not perfect but it does take the edge off. It works paradoxically by increasing the body's own endorphins, important now since many doctors are hesitant to consider and prescribe any pain medications such as tramadol or opioids (which I could not tolerate anyway). I purchase LDN from a compounding pharmacy and it is not covered by insurance since it is an old medicine shrouded in stigma (it is used in higher doses for opioid addiction). I do wish there was more research in LDN and similar medicines.

I have also finally had some relief for urinary incontinence using a new medicine called Gemtesa. Previously I failed all the anticholinergic meds and Botox in the bladder. I didn't think it would help but it has made a big difference. I hope this helps someone!

**Comment 2**

It is getting harder to deal with my diagnosis. Thankfully my son was spared. As my daughter gets older, I fear for her future. Personally, I would love the chance to have one day without pain and to be able to run again…even just one more time. I recall a day recently my son fell off his bike. I tried to run to him…my legs just wouldn't work. I ended up falling too. I often feel like a failure as a parent, as a wife and as a person. I cannot work due to this and other medical issues and have lost my identity. I used to be a medical professional. I am still struggling to accept that my future is likely only downhill from here.

**Comment 3**

Some of the most challenging symptoms for me as a symptomatic female is pain…sometimes severe that is often blown off by medical providers, bladder and bowel dysfunction, and balance/ proprioception and inability to walk well or run (especially in emergency).

**Comment 4**

Please please find a way to safely prevent or reverse symptom presentation and progression in females. I know it is likely too late for me, but I am heartbroken to think my daughter (or hypothetical grandchildren) and so many others may suffer. The guilt is gut-wrenching.

**Cheryl, symptomatic woman living with ALD – One comment submitted**

Symptoms that impact my life:

1) Loss of Balance

2) Gait

3) Falls

**Jerry, man living with AMN – One comment submitted online**

I have been recently diagnosed with ALD. My symptoms are currently slight with tremors in fine motor schools and gait. I'm wondering how long it will be until I start dealing with bathroom problems?

Thank you for your help

**Janis, symptomatic woman living with ALD – Three comments submitted online**

**Comment 1**

I think fatigue is a huge issue that needs to be addressed.

**Comment 2**

I remember someone once said, "I have ALD, ALD does not define me." That is a great quote for our community.

**Comment 3**

I agree with Tim about constantly being tired. I got 10 hours of sleep last night after taking a sleep aid because I was up about 6 hours the previous night. Yet, I did not feel refreshed when I got up this morning. I never feel rested anymore when I wake up. Fatigue is a major symptom that I deal with daily.

**Steve, man living with AMN – One comment submitted online**

The worst thing is back pain. I sit in a wheelchair and my back pain can never get better because I sit all day. I am 36 and I already take 18 pills a day. My pain doesn't allow me to do daily things. I have to lay down hours a day.

**Harry, man living with AMN – One comment submitted online**

I’m relatively fortunate that my AMN symptoms began fairly late (early 50s). But it also meant that I already had my two daughters who now have the ABCD1 mutation. The burden is now on them to try eliminating the condition to their future children.

**Holly, symptomatic woman with ALD – Two comments submitted online**

**Comment 1**

On my worst days, I experience severe muscle and neuropathic pain and fatigue. This makes it difficult to function normally. My husband and I loved long walks and hikes. That part of our life is over. I work with a counselor to try to live in the moment and manage my expectations.

**Comment 2**

I'd love to see new treatments for painful neuropathy and to relieve muscle spasticity. Also anything to lessen the debilitating fatigue. I'd happily participate in any and all trials available for medications to help with these issues.

**Emily, symptomatic woman living with ALD – One comment submitted online**

I started symptoms in my 30's as the mother of very young kids. The walking (tripping, loss of balance) is a serious issue and is difficult with an active family. But uncontrolled bowel frequency is the issue that most effects my current daily life. In my 30's, I started soiling myself while out in public. It's something I have to manage constantly and that severely limits my daily activities**.**

**Alisa, symptomatic woman living with ALD and mother of an adult son with cerebral ALD – Two comments submitted online**

**Comment 1**

I'm 51. my progression has been fast to me. Within 2 years I went from doing things as normal to where now I'm using a cane and holding onto walls to get around. I need a wheelchair for anything that requires more than a few steps of walking. Have had my share of falls. Adjusting to all this is a challenge but I know I have to keep it going because my son who is 28 lives with my husband and I and he has cerebral ALD. We will never put him in a facility to be taken care of so we figure things out as we go. The part I can't seem to handle is this pain. I've done just about all the pills, patches and shots but of course none worked. I'm not suicidal but my pain is so bad I don't really care if I wake up in the mornings anymore because I know what my body has to endure from the minute I wake up till I'm able to sleep. That is the scariest part of this disease for me and my family.

**Comment 2**

I have ALD and I'm on my 3rd treatment of Botox for my bladder. It has helped quite a bit. I also take oxybutynin.

**Connie, wife of a deceased man with AMN and adult cerebral ALD – One comment submitted online**

Rex's symptoms began around age 37 with numbness in his feet while running, stress incontinence during daily activities but nothing was found to be physically wrong so it was written off as aging. By age 40 he had a foot drop that wore the side of his boot off. A physician found neurological deficits and an MRI showed a bone spur growing into the spine so this became the red herring to explain. He continued to slowly progress and lose the ability to ambulate. By age 60, he progressed so much that spinal cord injury could not be the explanation. A geneticist diagnosed ALD. He used a small scooter and held on to walls to get around our home. He progressed where he could not stand or walk so we had to move from the home our children grew up in to a home that we made handicap accessible before moving in. He was unable to stand or walk at this point so we had lots of medical equipment he used - cane, walker, braces, shower / toilet chair, wheelchair, ramps and grab bars everywhere, and roll in shower. We had shelves of medical items - blue pads, incontinence items, catheters, leg

bags, gloves, pressure sore items, 4 x 4 and paper tape. Rex used and tried so many medications and supplements that gave small amounts of relief. Once Rex had cerebral ALD, he had swallowing issues, he was no longer able to fight infections (had urosepsis many times), severe nerve pain, extreme migraines (that needed injections to treat) and motion sickness just from transferring to take a shower. Those last few months of his life were heartbreaking. I hope and pray that we can find something to keep this condition from becoming cerebral ALD so no one else has to endure this horrid condition and loss.

**Dennis, man living with AMN - One comment submitted online**

What a fantastic show to watch. We all seem to be struggling with the same battles. I feel like I'm one of the lucky ones. My biggest battle is the way I walk. I'm 64 and was diagnosed about 30 years ago through a family member. I have had symptoms now for about 25 years. Prior to that I used to run marathons. I now need 2 canes to walk.

**Alicia, mother of a deceased son with adult cerebral ALD - One comment submitted by email**

Soy Alicia Bernardini, mamá de Matías Bonzon, paciente con ALD. Vivo en Argentina, provincia de Entre Ríos, ciudad de Gualeguay. Un pueblo de 50 mil habitantes cuyo sistema de salud está muy lejos de ser el de las grandes urbes.

En Matías la lesión cerebral se descubre a los 16 años. Hacemos una consulta con un traumatólogo por un problema en su cuello y nos aconsejan ver a un neurólogoy pedir una resonancia de cerebro junto con la de columna. En ese momento me dicen que tiene 6 meses de vida. Ante la desesperación, lo llevamos a dos hospitales de la ciudad de Buenos Aires, en ambos dieron la misma opinión: “No podemos determinar el origen de la lesión, ni porqué lleva una vida normal. Hubo pérdida de mielina y está cicatrizada, no hay riesgo de vida, vamos a realizar controles”.

A los 21 tiene la primera convulsión. Volvemos al mismo lugar y el diagnóstico fue EPILEPSIA. Hasta ese momento nunca hubo otros síntomas. Matías estaba terminando el cuarto año de la carrera de abogacía, las convulsiones fueron periódicas y no respondía a ninguna medicación. A los 23 años, cuando termina de cursar la carrera, comienza a tener problemas de estabilidad, dificultad para hablar (no en la pronunciación, tenía la imagen pero no encontraba la palabra), para caminar y por esta razón, se solicita una interconsulta en Buenos Aires. Sin embargo, no donde queríamos, sino donde la Obra Social nos permitió.

A los 25 años le diagnostican ALD. A partir de ahí, se hizo estudios en diferentes lugares que implicaron un calvario con la Obra Social. Cada autorización nos llevaba entre 4 y 6 meses de espera, tiempo que no podíamos perder. Los síntomas seguían apareciendo: disminución de la visión, problemas de erección, dificultades en la pronunciación, necesidad de ayuda para caminar. A pesar de los pedidos, la Obra Social nunca entendió de urgencias ni de cobertura integral.

Matías nunca pudo ejercer como abogado, su pareja con la que convivió 7 años lo abandonó, tuvo que renunciar a todos sus sueños, dejar su departamento y volver a su ciudad natal.

Los síntomas avanzaron en forma lenta hasta sus 29 años. Dejó de caminar, pero nunca bajó los brazos. Cumplía con la rehabilitación hasta que se dio cuenta que no podía contra la enfermedad. Abandonó el gimnasio y le hizo entender al psicólogo a su manera, cuando dejó de hablar, que no tenía sentido seguir.

A los 31 años, ya había perdido la movilidad de sus miembros superiores, se alimentaba por sonda, le pasábamos suplemento nutricional en polvo (Ensure) y aceite. Perdió peso e intentamos con otros suplementos alimentarios, pero no los resistía. Mientras tanto, la Obra Social nunca respondió a los requerimientos de una internación domiciliaria y el neurólogo dejó de responder diciendo que ya no había nada más que hacer.

Tenía un médico clínico que fue su puntal, una enfermera, una kinesióloga que se ocupaba de la parte muscular, un kinesiólogo respiratorio y una fonoaudióloga que trabajaba mucho sobre los músculos faciales. Estos especialistas conformaban un equipo multidisciplinario que brindaban los cuidados necesarios a Matías.

Una de las situaciones que más padecía Matías era evitar lastimarse. Su motricidad y su cognición nunca fueron a la par. Se mordía, se lastimaba y era consciente de lo que sucedía. Aprendimos a presionar los puntos exactos para poder abrir su boca.

Nuestro fuerte era la humanidad, el amor, la alegría que se transmitíamos en su cuidado. Los recursos eran escasos: un ojímetro, un tubo de oxígeno, un equipo de reanimación manual (ambu), un aspirador, un “bipap” que usó en forma permanente los últimos meses y un aparato de tos asistida.

La Obra Social nunca entendió lo que significaba internación domiciliaria, ni lo que quería decir yo en los medios de prensa o en el juzgado cuando decía QUIERO QUE MI HIJO VIVA CON DIGNIDAD HASTA SU PARTIDA.

Falleció con 30 kilos, respirando con la ayuda del “bipap” y con oxígeno cuando bajaba la saturación. Lo asistíamos para que tosiera y aspirábamos su saliva y sus secreciones en forma continua para evitar que se ahogara. Lo levantábamos y lo sentábamos en una silla de ruedas que nos prestaron, que adaptábamos de acuerdo a sus necesidades, porque nunca llegó la silla que se pidió al seguro medico.

El 22 de septiembre de 2017 lo sedaron porque ya no resistía más. Lo acompañamos todos. Algunos cuidadores se quedaron toda la noche, hicieron chistes, cantamos canciones que le gustaban a Matías, lo rodeamos de muchísimo amor. Falleció en mis brazos, tranquilo (como yo pedía) y se durmió. Eso sucedió un 23 de septiembre que jamás olvidaré.

No hubo tratamientos específicos para su enfermedad. Al principio su neurólogo hablo de la posibilidad de trasplante. Lo intentamos, pero nos dijeron que no se podía hacer.

A las familias que hoy tienen un hijo adulto con ALD les quiero decir que busquen profesionales especializados que los sepan guiar. No duden en cambiar de médico si no encuentran respuesta. Deseo que nadie pase por lo que no pasó Matías.

Mantengan la calma, agudicen los sentidos para poder ayudar a los profesionales, no teman de manifestar su opinión, los padres conocemos a nuestros hijos como nadie más.

Conserven la organización y los lazos del núcleo familiar, bríndense apoyo mutuo, no se den permiso para rendirse. Por más que el miedo y el dolor nos atraviesen como padres, nunca debemos olvidarnos que los que padecen la enfermedad son ELLOS, nuestros hijos. Ellos nos necesitan fuertes y motivados. El amor y la fe son parte fundamental del cuidado para que puedan tener una vida digna hasta el final.

Me siento muy agradecida de haber podido participar en este evento y que las vivencias de Matías puedan ayudar. Esto le da sentido a todo el sufrimiento que él atravesó. También le da sentido a la lucha incansable de Verónica y Eduardo, fundadores de la **Fundación Lautaro te Necesita**, que son los que establecen contactos, nos unen como una gran familia a todos los que convivimos con leucodistrofias desde cada rinconcito de Argentina y se ocupan de difundir y hacernos visibles, intentando mejorar la calidad de vida de nuestros chicos con cada proyecto que organizan. Todo esto ante la ausencia del Estado y las trabas de las Obras Sociales.

**Alicia, mother of a deceased son with adult cerebral ALD - One comment submitted by email (translated to English)**

I am Alicia Bernardini, mother of Matías Bonzon, patient with ALD. I live in Argentina, in a little town (Gualeguay) of 50,000 inhabitants whose health system is far from being like the big cities.

The injury in the brain of Matías was discovered at the age of 16. We consulted a traumatologist for a problem in his neck and he advised us to see a neurologist and ask for a brain and spinal MRI. At that moment the doctor told me that my son had 6 months to live. Two different hospitals in the city of Buenos Aires gave the same opinion: "We cannot determine the origin of the injury, nor why he leads a normal life. There was loss of myelin and it is healed, there is no risk of life, we are going to carry out tests".

When Matías was 21 years old, he had his first seizure. We went back to the same hospital and the diagnosis was EPILEPSY. Until that time there had never been any other symptoms. Matías was finishing his fourth year of law school, the seizures were periodic and he did not respond to any medication. At 23 years old, when he finished his law degree, he began to have stability problems, difficulty walking and speaking (not in the pronunciation, he had the image but he could not find the word) and for this reason, a consultation was requested in Buenos Aires. However, we did not go to the hospital where we wanted, but where the health insurance allowed us.

When he was 25 years old, he was diagnosed with ALD. From then on, he underwent studies in different hospitals that involved an ordeal with health insurance. Each authorization took us between 4 and 6 months of waiting, time that we could not afford to lose. The symptoms kept appearing: decreased vision, erection problems, speech difficulties, needing help to walk.

Despite the requests, the health insurance never understood about emergencies or comprehensive coverage.

Matías was never able to practice as a lawyer, his partner with whom he lived for 7 years abandoned him, he had to give up all his dreams, leave his apartment and return to his hometown.

The symptoms progressed slowly until he was 29 years old. He stopped walking, but never gave up. He was undergoing rehabilitation until he realized that he could not fight the disease. He left the gym and made his psychologist understand that there was no point in continuing.

At the age of 31, he had already lost the mobility of his upper limbs, he was fed by tube, we gave him a nutritional supplement in powder form (Ensure) and oil. He lost weight and we tried other dietary supplements, but he couldn't tolerate them. Meanwhile, the health insurance never responded to the requests for home hospitalization and the neurologist stopped responding, saying that there was nothing else to do.

Matías had a clinical doctor who was his mainstay, a nurse, a kinesiologist who dealt with the muscular part, a respiratory kinesiologist, and a speech therapist who worked a lot on the facial muscles. These specialists formed a multidisciplinary team that provided the necessary care for Matías.

One of the situations that Matías suffered the most was to avoid getting hurt. He bit himself, he hurt himself and he was aware of what was happening. We learned to press the exact points to be able to open his mouth.

Our strength was humanity, love, the joy that we transmitted in caring for him. The resources were scarce: an oximeter, an oxygen tube, a manual resuscitation equipment (ambu), a "bipap" that he used permanently in recent months, and an assisted cough device.

Health insurance never understood what home hospitalization meant, nor what I meant in the social media or in court when I said I WANT MY SON TO LIVE WITH DIGNITY UNTIL HE DEPARTS.

He died weighing 30 kilos, breathing with the help of the "bipap" and with oxygen when the saturation dropped. We assisted him to cough and aspirated his saliva and secretions continuously to prevent him from choking. We lifted him up and sat him down in a wheelchair that people lent us, which we adapted according to his needs, because the chair that was requested to the health insurance never arrived.

On September 22, 2017, doctors needed to sedate him. We all accompanied him. Some caregivers stayed with him the whole night, they made jokes, we sang songs that Matías liked, we surrounded him with a lot of love. He passed away in my arms, calm (as I wished) and fell asleep. That happened on September 23, a day that I will never forget.

There were no specific treatments for his illness. At first, his neurologist talked about the possibility of a transplant. We tried, but were told it couldn't be done.

To the families that today have an adult child with ALD, I want to tell them to look for specialized professionals who know how to guide them. Do not hesitate to change your doctor if you do not find an answer. I wish that no one goes through what Matías had to experience.

Keep calm, sharpen your senses to be able to help professionals, do not be afraid to express your opinion, parents know our children like no one else.

Maintain the organization and ties of the family nucleus, provide mutual support, do not give each other permission to give up. As much as fear and pain go through us as parents, we must never forget that those who suffer from the disease are THEM, our children. They need us strong and motivated. Love and faith are a fundamental part of care so that they can have a worthy life until the end.

I feel very grateful to have been able to participate in this event and hope that Matías's experiences can help. This would give meaning to all the suffering he went through. It also gives meaning to the tireless struggle of Verónica and Eduardo, co-founders of FUNDACIÓN LAUTARO TE NECESITA, who are the ones who establish contacts between families and specialists, unite all of us who live with leukodystrophies from every corner of Argentina and take action in spreading information and make us visible, trying to improve the quality of life of our children with each project they organize. All this in the absence of the state and the obstacles of the health insurance.