MLD Externally Led Patient-Focused Drug Development Meeting

Additional Patient Comments

The Metachromatic Leukodystrophy (MLD) Externally-Led Patient Focused Drug Development (EL-PFDD) meeting held on October 21, 2022 was organized and hosted by a collaboration of MLD patient advocacy groups and researchers including Cure MLD, the Calliope Joy Foundation, MLD Foundation, United Leukodystrophy Foundation and the Global Leukodystrophy Initiative.

The meeting represented an important opportunity for the MLD community to share patient, family and caregiver perspectives on the challenges and unmeet treatment needs of those who live with MLD every day. The patient and caregiver perspectives gathered from the October 21, 2021 EL-PFDD meeting are summarized in an accompanying *Voice of the Patient* report, https://mldpfdd.org/. To ensure that as many voices as possible were heard, an online comment submission portal was open for one week before and four weeks after the MLD EL-PFDD meeting. Comments that were submitted through the online comment submission portal are presented in this document, and selected comments are included in the main body of the *Voice of the Patient* report.

Respondents are identified by their first name only. Comments were sorted by MLD subtype and treatment approach (gene therapy, enzyme replacement therapy [ERT], bone marrow transplant [BMT] and no therapies). Comments were edited only slightly for spelling and punctuation. Comments that did not address the Meeting Discussion Questions from **Appendix 3** of the *Voice of the Patient* report were not included.

Late infantile MLD

Victoria, mother of two children living with late infantile MLD, two-year-old Oliver who received gene therapy and six-year-old Adeline who did not

- "I am pleased with the outcome of Oliver's gene therapy. However, Oliver is delayed and shows signs of MLD. I wish I had known more about the possible outcomes of gene therapy. The good and bad."
- "Addi is completely dependent on us for all of her care, in addition she also suffers from acute respiratory failure."
- "Newborn screening and a treatment to completely prevent symptoms."

Les, father of two sons with late infantile MLD, Cathal, who passed away at age six and Ciarán, who received gene therapy and is now six

- "My son Cathal lived a short and painful life like so many of these beautiful children. He died aged 6, 2 years ago. The most difficult symptoms he endured after his rapid decline aged 2-3 were **gut pain** from digesting and passing his liquid percutaneous endoscopic gastrostomy (PEG) feed and the **muscle spasticity** he suffered from. He cried more than any child should but he met all the worst MLD could throw at him with a cute smile on his face."

Amy A., mother of three children with late infantile MLD, 12-year-old Giovanni and 8-year-old Cecilia who both received gene therapy and Liviana, who passed away at the age of five years

- "Liviana - loss of all abilities and life. Giovanni and Cecilia - none [with gene therapy] "
- "Broad gene therapy access, newborn screening or genetic screening (parental or at birth)"

Kendra, mother of two girls living with late infantile MLD, Keira, a two-year-old (gene therapy) and Olivia, four-years-old (enzyme replacement therapy

- "ERT for Olivia was not helpful (wish the doctors administering had known about gas anesthesia and its affects on children with this disease...believe it interferes with their findings/outcomes). They also claim the internal port causes no pain to the patient but immediately upon removal we saw her return to her happy self."
- "Gene therapy has been a miracle for Keira. She has developed completely normal, without symptoms and is living the life of a "normal" 2 year old child, doing things her older sister with MLD was never able to accomplish as the disease quickly took away her abilities."
- "Loss of mobility, loss of speech. Both have impacted her life greatly and the lives within our family. Simple acts such as bathing her have become a two-person job because she has grown and cant (purposefully) move a muscle. Traveling is no longer a possibility as we have to stay close to home for hospice care in case something does happen and her health takes a turn. So our other daughters tend to miss out on those opportunities. As parents we can guess what she wants/needs but at this point it's even too late to utilize the ACC device she received which uses eye movements to express thought. I could go on and on...."
- "In relation to the Augmentative Communication device - this is something an MLD patient should have BEFORE they begin to lose symptoms. Otherwise, it can be very difficult to navigate their understanding and use of the device. Combined with staffing issues of today, ours has been rendered almost useless for our 4 year old daughter Olivia."
- "Gene therapy is the light at the end of this tunnel for children who are non-symptomatic. The ultimate solution would be a cure for those who are initially showing symptoms. There should be no reason a child should die from this disease when gene therapy is an available option."
- "The weekly travel with Livvy to receive ERT all while she was rapidly regressing was much harder for us as a family than having to move to Italy as a family for Keira to receive gene therapy."
- "[wish the doctors told us] That gas anesthesia can progress the disease."

Sonal, mother of six-year-old Radha, living with late infantile MLD (enzyme replacement therapy)

- "ERT has helped Radha remain stable without further regression and has even helped her regain some previously lost skills. She has not required hospitalization since enrollment in the ERT trial."
- "Feeding difficulty, immobility, lack of head control."
- "Therapies that not only cure the disease but reverse the damage which previously occurred."
- "That heavy involvement in therapies (PT/OT/ST) can help maintain function/ slow regression."

<u>Kayla, mother of six-year-old Alexandria, living with late infantile MLD (enzyme replacement therapy)</u>

- "We feel like the ERT has slowed down the progression"
- "Her **loss of communication** is hard. Because she can't tell me what's wrong anymore. It's all guessing, and giving meds, hoping one will help. Her **loss of mobility** is also hard. We've had to make changes to our home, and buy a different car to accommodate her needs and equipment. Her **pain** is also hard, because **she can't say what's exactly wrong**. Today, she's been showing signs of discomfort, but I don't know what's wrong. I've given her what medications I have, but it's still not giving her relief."
- "Alexandria was born in December 2017. She met all of her milestones on time, until it came to walking. She was walking on her own by 13 months old, but struggled to walk without constantly falling. Signs were there, we just didn't realize it until we looked back, after her diagnosis. We knew something was wrong by 15 months, but were told she was probably just delayed a bit. Finally, at her 2 year wellness check, her new pediatrician definitely said something was wrong, and sent us to orthopedics, and neurology. Alex had multiple blood tests, genetic tests, and an MRI. Finally, we were sent to genetics. More tests, no answers. Our last test that gave us our answer was Whole Exome Sequencing. In February, 2021, Alex was diagnosed with MLD."
- "We were able to get her into the Embolden Study, with the help of Maria Kefalas, and the team at CHOP that same month. It has slowed the progression down, but did not stop it. We travel over an hour to have her infusions done every week."
- "During all of the waiting and testing, Alex did PT, OT, and Speech Therapy. But she kept getting worse. She stopped being able to walk on her own. She could walk with a walker and leg braces, but by August of 2021, she could no longer walk. By January 2022, Alex could no longer crawl. By July 2022, she could no longer sit on her own, and shortly after, she lost all speech. She still smiles and can communicate with her smiles and body movements. She will also get upset and call out or cry if something is wrong. But I'm dreading the day she can't do either."
- "**The trial we are in is as far as I'd go [in terms of risks]**. It's been so hard on her and the family. She cries and is uncomfortable the day of and the day after her infusions. It's hard to watch her and I can't stop the pain."

<u>Melanie, mother of eight-year-old Noelle, living with late infantile MLD (enzyme replacement therapy)</u>

- "My daughter Noelle has LI-MLD. She just turned 8 years old in September. She is currently a participant in the Embolden ERT clinical trial here in Canada. She was one of the oldest children to be accepted into the trial and was already far progressed - she had lost everything and was completely dependent for all of her care. We believe that receiving ERT has significantly slowed down further progression. She is still on several medications to manage her symptoms. We feel that her meds manage her symptoms somewhat but wish that her quality of life was better and that she was less drowsy. Drowsiness is a big trade off that she experiences to control her pain and seizures. Our hopes for the future include reversing the damage to the nerves and demyelination. One of the reasons we enrolled our daughter in the ERT is to buy time to hopefully live long enough to benefit from advancements in repairing brain damage. Our kids are so resilient, strong, and courageous and have endured the unimaginable and we don't want research and drug development to forget about the kids that are living with significant ongoing neurodegeneration. We still have hope that they can live lives with significant improvement to their quality of life."

<u>Pat, mother of a child with late infantile MLD (BMT)</u>

- "She had two BMT'S, I believe it took its toll but it prolonged her life for sure"
- "She is Trach/vented 24/7, can't speak but understands. She is totally dependent, and can not move or walk."
- Wants for future therapies: "Enzyme replacement therapy."
- "I moved to MN from Ohio because the doctor there had previous knowledge of the disease. It was hard leaving my family but I knew it was the right thing to do. The care we received was exceptional!"

<u>Stacy, mother of five-year-old Brooks, living with late infantile MLD (bone marrow replacement)</u>

- "I feel the BMT saved his life."
- "The **inability to talk and walk** affects day to day quality of life. Brooks is a five-year -old who knows what he wants but can't express himself which leaves everyone involved frustrated. Brooks can take steps if supported yet this requires constant 1:1 help. He has no independence anymore."
- "The most burdensome symptom for Brooks is the **inability to communicate**. Brooks' brain remains stable since his stem cell transplant in 2018. His brain knows what he wants but his body can't tell us. We've tried a number of different communication devices but have yet to find something that works due to his loss of fine motor function. Oftentimes Brooks will get frustrated and cry when he is unable to make his needs known. Simple things throughout the day can be a real source of frustration for a five-year-old who knows what he wants, but can't express himself."
- "[For future treatments] Gene therapy to help repair damage done to the peripheral nerves. Brooks needs a treatment that can improve or prevent disease progression in the peripheral nerves. If he could get a bit of function back from gene therapy, his quality of life would improve greatly."
- "[We wish the doctors told us about] Treatment options, clinical trials, different therapies to keep him comfortable such as Botox for stiffness."

- "I did research and found a doctor in Pittsburgh who was willing to try a stem cell transplant. She saved his life. It's been four years since diagnosis. He is now five years old. Currently Brooks can't talk or walk. As he grows he continually loses physical function but thanks to the transplant his brain remains intact."
- "We have so much hope that gene therapy can help our son, we just need the opportunity to try. We have nothing to lose at this point. Gene therapy needs to be available for every patient with MLD willing to try."
- "**We would risk death. This is a horrific, terminal disease. We would be willing to try anything in order to get some quality of life back**. We have nothing to lose at this point. Death is inevitable with this disease. I want the FDA to know how desperate many families are for these new treatments such as gene therapy. I want them to know that it wouldn't be fair to exclude kids who have had ERT or transplants in the upcoming clinical trials. We've done everything humanly possible to help our son. We can't be forgotten."

<u>Teryn, mother of two daughters, Lindy, who is living with late juvenile MLD (no therapies) and Darcee who passed away (bone marrow transplant)</u>

- About BMT: "BMT was the only option at the time. I felt very informed of the chance of making it through and what the hope was in the end if survived."
- "Despite having a near match sibling donor and engrafting (so a successful transplant) Darcee passed away from **graft vs. host** complications of her GI tract and side effect reactions to the anti-rejection drugs eventually leading to bleeding, bladder damage, ascites, and heart failure."
- The main symptoms were: "Ability to only communicate by facial expression and body language- dependent on others to guess what Lindy wants or needs. Reliant on others for everything- dressing, eating, care. Inability to walk, move - trapped in body."
- For future treatments: "**Ability to communicate** would be huge. Severely delaying the loss of walking. Stopping destruction completely."
- "MLD does not progress the same in everyone. MLD is individual. Even siblings do not follow the same decline at the same rate. There are other influencing factors not yet understood. Lindy was diagnosed at age 8 but is still alive and interacts with her environment 34 years later after diagnosis. **When your child is dying you are willing to take more risk to help them live and flourish. There is a willingness to try more unconventional, unproven therapies. MLD tears families apart and effects the entire family (siblings and extended family)**. Life is never the same after a diagnosis of MLD."

<u>Leah, mother of a daughter, living with late infantile MLD (no therapies)</u>

- The symptoms that impact her daughter the most are "**lack of communication, trunk and head control.**"

<u>Beth, mother of a daughter, living with late infantile MLD (no therapies)</u>

- "**Respiratory** - constant congestion, frequent pneumonia, around the clock respiratory treatments; **gastrointestinal**- frequent vomiting, weight loss, pancreatitis; **paralysis** - she couldn't move at all on her own."

- "I would love to see a treatment that could not only **stop the progression** of the disease, but also **repair the damage**."

Kristin, mother of Grayson who passed away with late infantile MLD (no therapies)

- "Grayson just recently passed away in January 2022. He kept having **UTI's** but they were staph infections and harder to treat. We had a hospital stay to treat the infection with an IV antibiotic came home heading in the right direction and then a couple days later he had no desire to breathe. Lived on BIPAP 24/7 until we decided that was no life to live and his body was showing signs of shutting down. Retaining fluid, not going to the bathroom and he just looked miserable. Stopped care with BIPAP and he passed that day."
- Symptoms: "At the beginning it was the **spasticity**. He was in **constant pain** and uncomfortable through that stage. Grayson was in constant pain, it was hard to try and enjoy life when he was constantly hurting and all he wanted was to be home in his safe place. Nutrition was huge with the **slow gut motility**, everyday was a constant battle to figure out if he was tolerating it and if we should be mixing it up by changing formulas, volume, rate, etc. And then respiratory was the next biggest issue. These kiddos work so hard to breathe."
- "We need better symptom management and more care teams that are willing to help better and have more knowledge on this disease or at minimum Leukodystrophy type diseases."

Nicole, mother of Gabby, living with late infantile MLD (no therapies)

- "Gabby is unable to walk, speak, eat or participate in any ADLs. She is completely dependent on her parents and caregivers. She is constantly monitored by machines and needs rescue interventions such as pulmonary treatments and oxygen to help her breathe and assistance such as catheterization and suppositories to help her void. "
- "Early diagnosis so these children have a chance with gene therapy. Without any intervention they lose all their abilities in a short amount of time."
- "How fast the progression is. That this disease is painful. I wish we had assistance on how to get her the care she needs and that doctors knew what care she would need when she needs it."

Katie, mother of a son living with late infantile MLD (no therapies)

- [Her son's major symptoms are] "GI motility, suctioning secretions, seizures"

Trisha, mother of a son living with late infantile MLD (no therapies)

- [Her son's major symptoms are] "Progression, Pain, inability to move and or verbalize needs"

Carrie, mother of a daughter living with late infantile MLD (no therapies)

- Symptoms: "Pneumonia- UTI - CDIF"

- "For future treatments we would like to see anything! Any treatment that's odds were greater than or equivalent to natural progression of the disease. Newborn screening and ANYTHING that could tip the odds in our favor."

Laurie, mother of a daughter living with late infantile MLD (no therapies)

- "Can barely move, can't speak & in constant pain."
- "This disease is horrible for the entire family but mostly on the individual. Newborn babies should be tested."

Kaprice, mother of a daughter who passed away from late infantile MLD at the age of eleven (no therapies)

- Child was most debilitated by "scoliosis, not being able to communicate with words, feeding tube."
- "They [the doctors] had no idea what the disease was. Told us to take her home and make her comfortable and that she wouldn't survive past five. She was 10 days shy of her 11th birthday."

Asmahan, mother of six-year-old Norah, living with late infantile MLD (no therapies)

- "1. **Muscle contractures** - difficulty with positioning her without pain. Need frequent adjustments. Cannot hold her for long period 2. **Vomiting** - we need to intervene with suction so she doesn't choke or aspirate. It limits her calories count, needs to clean her and clothes. 3. **Loss of Communication**: losing her eyesight and hearing loss affected the ability for her sibling to stay connected to her. We don't know how she is feeling or have any pain. It is hard to see her sisters unable to communicate with her and maintain a relationship with her."
- For future treatments: "Improved quality of life. Ability to connect with family."
- "Norah was not eligible for gene therapy by the time she was diagnosed at age 2. We had reached out to Milan and were heartbroken to hear she had progressed too far to benefit from treatment. We did not pursue bone marrow transplant at the time as our understanding was the treatment would slow down the progression but not halt it nor improve her quality of life. Since then, we have focused on palliative treatment to ease her pain and make her as comfortable as we can afford. Existing palliative treatments such as medication, tube feeding, botox injection every three months support her comfort partially. It feels like a moving target.

Lexi, mother of a four-year-old son living with late infantile MLD (no therapies)

- "**Communication**; frustrating because he still knows what he wants and likes to do but cannot express himself. As his mom, I can usually figure out what he's communicating but nobody else is able to. **Motor function**; cannot function as a normal four year old, probably harder on us (as parents) but I feel like he could still know he is missing out on certain activities he used to like. **Ability to eat**; as a family we like to bond over food- going out to eat, having cookout parties, trying new places. Used to bring a lot of joy but another thing we are no longer able to do."

- "Having treatment options readily available would be incredibly helpful to the MLD community. The only part that makes getting the treatments in time difficult is the lack of knowledge in the general medical field. Most non-specialty doctors have no clue about MLD let alone treatment options."

Aria, mother of a daughter who passed away from late infantile MLD

- "Our daughter Liviana passed away from LI MLD in September 2013. Even today, a little over 9 years since we lost her, I still see and feel the missed milestones. She would be a freshman this year, in the same school with two siblings. She would be playing sports, borrowing her sister's clothes, and spending time with friends. She would be sassy, as she was before we lost the sound of her voice. The loss of her life is painful for the entire family. The grief bubbles up when least expected. Her siblings feel the pain of missing growing up with their sister beside them."

Vijayakumar, parent of a daughter living with late infantile MLD (no therapy)

- "She [her daughter] got a high fever on 1st Jan 2018 and it was for three days and after that she faced a lot of problems in **her talking** and **walking** and other activities as well. We are very much waiting to understand the medicine availability."

Matthew father of Loie, who passed away at the age of three and a half years from late infantile MLD (no therapies)

- "#1 is the **pain** we know she experienced 24 hours a day. This was one of the hardest things to deal with, as no child should experience pain, especially on a regular basis. Keeping her medicated to the point of virtual numbness was difficult to administer, as well as watch. #2 is the **ability to eat**. This was a significant issue that we struggled with on a daily basis, especially once our daughter received a feeding tube. Almost on a weekly basis we had to change her diet to react to her changing symptoms and nutritional needs."
- "I would look for an improved quality of life, but more importantly, a way to **stop the progression of this disease** prior to any symptoms being observed."

Tara, mother of nine-and-half-year-old Cece, living with late infantile MLD (no therapy)

- "Respiratory, storming, loss of all abilities"

Tyler, father of four-year-old Lybie, living with late infantile MLD (no therapy)

- "Easier and quicker gene testing. Lybie was misdiagnosed twice before MLD was found. If a more comprehensive gene test was standard in these situations it would help catch it quicker."

Kelsey, mother of six-year-old Teagan, living with late infantile MLD (no therapy)

- "Teagan's loss of her ability to walk, talk and eat by mouth. She has lost all of her ability to be independent in any way, and that is truly heartbreaking. Teagan was always super advanced and she is so incredibly intelligent. So as symptoms began, to see the frustration in her face was gut wrenching."

- Desire for: “A cure. A way to stop this. A way to save our children and give them the lives they deserve.”
- “MLD needs to be tested for at infancy. This would give all of our kids a fighting chance to qualify for treatments.”

Early juvenile MLD

Amy B., mother of two children living with early juvenile MLD, a seven-year-old who received gene therapy and a nine-year-old son who received a bone marrow transplant

- “Walking problems, leg fatigue, inability to run."
- “My boys responded really well to treatment thus far. However they have not gone through puberty yet and it has only been 4 years"

Jennifer, mother of Jana living with early juvenile MLD (gene therapy)

- “One of the worst symptoms that my daughter has is the **tone** and **muscle spasms**. Most days the tone is controlled by baclofen, but there are times that the tone kicks in so bad she screams in pain. Her arm sticks out straight, I can feel her shoulder blade sticking out on her back. Her leg gets so tight that she cannot control it to bend it. It is always difficult to figure out what is causing the tone to kick in extra. It could be being cold, scared, not feeling well, constipated. When the tone kicks in so bad she screams and becomes unable to communicate.”“Worries for the future: This is such a hard question, because it is so hard to think about the future when every ounce of energy we have is spent trying to get through each day right now. But I worry what if something happens to my husband and I. What happens to my daughter? I don't feel like I have anyone in our family who would be capable of caring for her.”
- “My daughter Jana was diagnosed with MLD one year ago. We were fortunate to receive gene therapy through compassionate care use at the University of Minnesota Masonic Children's Hospital. We are grateful to the doctors at CHOP for a quick diagnosis and to the FDA for the use of gene therapy. Unfortunately we hit a hurdle for insurance approval. Insurance companies should not be the ultimate decision maker for patients. It is an outrage when some of the county's top doctors in the field get overruled by a paper pusher behind a desk at an insurance company more worried about their bottom line rather than quality of life. My daughter ultimately received gene therapy, but she was mildly symptomatic. While waiting for gene therapy and during treatment there was also some decline. She now requires adaptive equipment, daily medications and therapies. Despite this, we are beyond grateful that this disease has stopped progressing and that our daughter is still with us. Most importantly our daughter is grateful to be alive and is happy.”
- “The **loss of speech** is devastating. This makes communication difficult as she lacks the fine motor skills to use an iPad as a method of communication. We primarily use thumbs up and thumbs down. She loved to sing and now takes several minutes to get a sentence out. People assume she is dumb because she can't speak. She is still extremely intelligent and has a lot to say, but her body lacks the mechanics to speak at a normal pace. It frustrates her to speak at turtle speed.”

- "The nerve damage also causes her to feel "lost in space". Being on an exam table terrifies her, if her feet are not touching something while she is sitting up she panics. Her legs splay out and she screams in fear and throws her arms up. It is difficult to calm her. This impacts her ability to sit on the toilet, so she is currently in diapers."
- "We knew **all of the risks going into gene therapy. We knew there would be some decline in the process as she was symptomatic**. If we had to do it all over again we would still choose gene therapy as it is better than doing nothing and letting your child slowly lose all function and die. This disease progresses so fast, my only regret in the process is the insurance portion. I feel they delayed my daughter's treatment."
- "This disease affects the whole family, but just the child who has it. It is devastating for parents to watch their child slip away. It is confusing and life changing for siblings and extended family. Your whole life and whole being is now this disease. You learn to live each day as it comes, because you don't know what the disease will bring from day to day. It kills every single hope and dream you ever had for your child and for yourself. Where you once pictured wedding dress shopping with your daughter, you are now hoping for the day she will pick up a fruit snack again. There is a lingering guilt, how did we not see this sooner. But in reality, many in the medical field struggle to diagnose."

<u>Gary, father of six-year-old Celia Grace living with early juvenile MLD, the first child to receive gene therapy in the United States</u>

- "I feel good about the outcome [of gene therapy]. Celia is developing normally and is having no symptoms."
- "Celia Grace is asymptomatic at this present time. We was able to catch the disease early due to a gallbladder problem. She is living a normal happy life thanks to gene therapy. "
- "When we found out our daughter had MLD we felt like our world was turned upside down. We felt numb. God paved the way for our daughter to live a normal life. God placed Wonderful doctors and medical staff in our life. Celia Grace was able to receive gene therapy under compassionate use with special approval from the FDA. The only other option we had was to move to Italy for several months to receive gene therapy which is approved for the treatment of MLD. I pray that no other family has to worry about a treatment option if they receive news that their child has a horrific disease like MLD."

<u>Georgina, mother of a daughter living with early juvenile MLD (gene therapy)</u>

- Major symptoms: "Non-ambulatory, incontinence, processing speed"

<u>Francoise, parent of a son living with early juvenile MLD (bone marrow transplant)</u>

- "[The symptoms my son faces are] the **bladder and bowel issues**- he is in pull ups ever since transplant. He has accidents with bowel maybe 4 x a month and is 5/7 nights wet. His **lack of executive functioning** is difficult as he needs help with EVERYTHING as he forgets what steps are next. He needs help just like a toddler."

<u>Shanna, mother of Gavin, who passed away from early juvenile MLD (bone marrow transplant)</u>

- “We were very optimistic about the stem cell transplant and the actual treatment was successful for my son. But **he ultimately died of graft vs host**, while recovering from the stem cell transplant. We knew all of the risks but we just wanted to save our son, we did look into gene therapy in Milan but Gavin was too far progressed for that option.”
- Daily burden: “"His **breathing was labored** and he needed oxygen to survive. He was **unable to walk** because although the treatment was successful with ARSA he was too far progressed in his peripheral nerves to be successful. He had a G tube because of his **inability to eat enough** to stay healthy. All of these symptoms kept Gavin from living life to the fullest and we were exhausted with all of the cares for him."
- “My dream future treatment for children with MLD is Gene Therapy with early detection.”

<u>Jennifer, mother of Emma who passed with early juvenile MLD (bone marrow transplant)</u>

- “I don't know that anything can prepare a parent for the pain and trauma that your child will go through when receiving and trying to recover from treatments and complications. The biggest hurdle was coordinating care at home. I was still trying to find my footing and find a routine that I could pass along to her father and others who came to care for her when the time came. Dealing with insurance, ensuring that supplies were in stock, making sure she was comfortable and entertained and had the best quality of life she could have given her situation felt like I was running a marathon with no breaks and little help and few people that understood. Traveling out of state and then having to go back home and establish a new TEAM of people for care, that is where I felt the most stressed and helpless.”
- “Emma has passed and I don't know what I could have done differently. If we didn't seek a bone marrow transplant, we would be left wondering if that path would have helped her. She went into **septic shock** while in Minnesota that caused a lot of damage and felt like it made her MLD progress rapidly. I believe there were multiple types of bacteria cultured. She was in PICU for several weeks, but recovered and was able to breath on her own again. She did need a **feeding tube** and **lost the ability to walk**. She also **struggled to talk** and had a lot of **spastic movements** in her hands and legs. With her therapies, they would work on her endurance because she would get mentally exhausted even before she was physically exhausted. Once we were cleared to go home, there were several days where we moved around the house in her wheel chair and bed, but we were not equipped to do anything like before. Her sister tried to entertain her, but we spent a lot of time cuddling together in bed because her stomach pain kept coming back. This was not uncommon and we were phasing down her TAC medicine which often led to runny stools. Then one morning when I went to give her some nausea medicine before she woke up, she was cold to the touch. We performed CPR and called the paramedics, but she was pronounced dead at the hospital. No autopsy was performed and cause of death was **heart failure**.”
- Wishes for future treatments: “**Communication** is the biggest. I often had to interpret non-verbal signs to understand what a problem was or where pain was. Ways to help a child express themselves would be so helpful to a tired parent who is afraid of missing something that they can't let others help out of fear.”
- “I feel like the chemo recovery was downplayed [in the BMT].”

Yvonne, mother of daughter, living with early juvenile MLD (bone marrow transplant)

- "The symptoms that affect my child the most are loss of motor skills, especially walking and speaking"
- For future treatments: "peripheral nerve treatments"

Susan, mother of Daniel, who passed away at the age of seven years from early juvenile MLD

- "The top three would be loss of mobility, digestion issues, and autonomic storming. These three symptoms made the last years of Daniel's life painful and plagued by medical complications. I'll share my previous testimony."
- "I would look for a treatment that halts the progress of the disease. A treatment that only alleviated the neurological pain and storming and/or the digestive issues would greatly improve quality of life."

Krystle, mother of nine-year-old Amelia, living with early juvenile MLD (in the process of getting therapies)

- "Our daughter Amelia started having **difficulty in school** with focus and ability to write. While getting Amelia ready for the school year in September 2021 we noticed she could no longer write her name. The school had her IEP meeting in December and said Amelia had a **cognitive delay**. Amelia began **walking on her toes** and we made a neurologist appointment. Amelia started falling down the stairs and broke her toe. She kept falling and then Amelia's legs gave completely out. Since we were not able to get medical help in IL we took Amelia to the children's hospital in Madison WI where Amelia was diagnosed within an hour with a quick MRI scan. We then took Amelia to Duke University for three weeks for an extensive medical evaluation. They said we could try the stem cell transplant but the outcome would not be great. If Amelia survived the chemotherapy, survived the risk of infection, and by the time the stem cells would graft Amelia would be in a very bad quality of life and dependent on many systems to keep her alive. This is a decision no parent should EVER have to make. We decided to not put Amelia through that horrible risk with such a terrible outcome."
- "Amelia lived as a healthy little girl for eight years. Today she is a nine-year-old girl that is slowly losing all of her abilities. Amelia is **incontinent**, losing the ability to use her legs and hands, and has started difficulty drinking and eating. Amelia's short term memory has also taken a big loss. Amelia is upset and does not understand why she used to be healthy, she used to be able to walk miles and can now barely walk a few feet. This is cruelty to the child and it is cruel to the parents and family to watch. We have to watch Amelia slowly lose all of her abilities until she dies in a few years. This could have been prevented with genetic testing at birth. How is there no medication, therapy, SOMETHING to help our symptomatic MLD daughter!?!? This is cruel and inhumane to have to go through. We need medication or therapeutic drugs that can help symptomatic MLD patients reduce the disease and help stop progression."

- "Peripheral nerve medication would help MLD patients greatly. The nerves are greatly affected and medication to slow progression is desperately needed for symptomatic patients."
- "Every child should have the right to try gene therapy. Genetic testing at birth should be mandatory across the globe. We are watching our daughter slowly die. Our daughter is upset. Amelia does not understand why her legs used to work and now they do not. This is cruel and inhumane to watch our daughter go through this with no available medication. Our family and friends are devastated. This impacts more than just the MLD child. In the United States we should have available treatment for this terrible disease. There needs to be more help for children with neurological treatments. We finally took our daughter to an emergency room in Madison WI where they finally diagnosed Amelia. The United States needs to get on track like other countries have."
- "I would move anywhere or go anywhere for treatment. If there were temporary side effects we would try it. An example is gene therapy where the child might lose functions temporarily but gain it back after grafting is completed."

<u>Debbe, mother of 12-year-old Annabel, living with early juvenile MLD (no therapy)</u>

- "Complete physical inability, including not only inability to walk, eat, control bodily functions, or even meaningfully move her limbs to control a communication switch, which to a child who was completely normal in all abilities through age seven is devastating in itself. But by far the most devastating effect is the loss of ability to communicate, even while retaining most cognitive abilities. Five and a quarter years into the disease's progression, our child can communicate only by inconsistent eyeblinks and occasional smiles, rendering even a communication device that could completely enable this function an impossibility. The mental/emotional impacts of suddenly being "locked in" to a world where they can no longer express themselves, while apparently retaining full ability to think and hear (most MLD kids do lose most functional eyesight at some point) renders this disease absolute torture for those who suffer it."
- Desires for future treatments: "Two things: ability to identify the gene mutation BEFORE it starts to do damage to the myelin sheath (eg, screening at birth), then gene replacement therapy to cure the enzyme deficiency that leads to the damage which causes the symptoms."
- "Our doctors told us a stem cell transplant might be available, but the people we talked to at our hospital (Lurie Children's) about a stem cell transplant (SCT) were not at all experts on MLD. I feel our doctor, who ran a 'leukodystrophy clinic' had an obligation to put us immediately in touch with the foremost experts in the country performing this procedure on MLD patients so that we didn't lose precious time searching for them on our own. Fortunately, the MLD Foundation assists families greatly with this, but for some reason, we didn't find them until 5-6 weeks in, and by the time we got to the right experts to evaluate whether she was a good candidate for SCT, she was so symptomatic the experts were unsure how beneficial the procedure would be. We were aware of gene therapy and it was our first choice, but there was no clinical trial open to her at that time. I feel that if we had been able to make a decision on giving her gene therapy within the first week of her

diagnosis, we would have gone forward with it and it could have been a game changer to her life, and therefore to the life of everyone in our family (she has a twin sister and a brother 2 1/2 years older whose childhoods have also been enormously impacted by their sister's disease)."

- "I want the FDA to understand the horrors of this disease. Within the first two weeks of her diagnosis, I spoke to an MLD parent who was a physician. Before her daughter's diagnosis, like my many friends who are physicians, she had never heard of this disease. She warned me that this was the most horrific disease out there, nothing like cancer that got all the publicity and celebrity visits to children's hospitals. Sadly, she has been proven right by my daughter. Although we believe we have been able to mostly control her physical discomfort arising from the disease, there is nothing anyone can do to relieve the mental/emotional torture and resulting despair of no longer being able to function, and especially communicate, while maintaining most cognitive functioning, other than to continue to recognize these people as the still-thinking, existing people they are through daily interactions and stimulation. It would honestly be easier to bear as a parent or other loved one if they lost mental functionality, as well, and you could comfort yourself that they were sort of "out there" and unaware of the world around them. At least for our daughter, that is not the case, and that is excruciating."
- You saw that basically everyone--presenters and those responding to the poll--agreed that inability to communicate was the very most devastating effect of MLD. Although I touched on this, I wanted to re-emphasize WHY this is so devastating. It is excruciating emotionally and inexpedient clinically when they are crying or otherwise indicating something is wrong, to not be able to have them tell you where it hurts, what is wrong. But to me as a mother of a child who was diagnosed only at seven and therefore had a full range of experiences in addition to a well-above-average vocabulary, it is the knowledge of what torture it must be for this person whom all in contact with her agree seems to have maintained the majority if not all of her cognitive abilities, to be utterly unable to express her thoughts, feelings, and often even preferences as she goes through life. I know if I had MLD, this would be the factor that drove me to utter despair and hopelessness. We have tried everything out there, and nothing works at this point, which just stabs my heart when I think about what a game changer this could be for my daughter. I would LOVE to see more R&D devoted to this area alone, especially given the fact that most experts agree that most of these children, certainly the ones diagnosed as juveniles, maintain many of their cognitive abilities."

<u>Michelle, mother of six-year-old Willow living with early juvenile MLD (no therapies)</u>

- "The most difficult symptom that has effected Willow's life is **losing the ability to walk along with muscle control**. She requires full head-to-toe body support 24hrs a day. We've been unable to try a stander or gait trainer because Willow's father accidentally injured her ankle while applying her AFO's. She is due for tendon-lengthening and botox later this month which, after healing, will give her the opportunity to try this equipment. The second greatest impact has been from Willow's **insufficient swallowing**. This was truly the scariest symptom for me because it made the likelihood of asphyxiation much greater. She had a g-tube placed in October 2019 and during that procedure also had a nissan fundoplication

fold & gallbladder removal. Prior to g-tube, Willow suffered from severe dehydration sending her to the ER twice. I COULD say the third most difficult symptom to live with has been incontinence, sensitivity to temperatures, hypertonia, bruxing or drooling, but that's not true. Harder than any of those is her **losing the ability to speak**. Willow's cognitive skills are present, but she can't speak for herself. She can't sing or laugh out loud. I would give anything to hear her speak to me. We've worked with an eye gaze device for a year and have seen progress, but anyone who wants to communicate with her has to do 100% of the talking. I tell this to all of her caregivers, because the easiest thing to accidentally do is forget to talk to her."

George, father of 11-year-old Ronan, living with early juvenile MLD (no therapy)

- "Lack of motor function, Inability to speak, swallow, or clear congestion, and blindness"
- "Treatment that can **arrest symptoms or reverse damages** would be helpful for sufferers of this disease."
- "How to plan for emotional hardship on an MLD family, and the significant challenges of modifying transportation, home, school, and schedule to care appropriately for a growing child patient."
- "My family, including the patient, live in rural/remote Alaska, a four-hour drive from the care system we are impaneled in. Our ED and PICU are 250 miles away. Our experience is unique, and may have a different care perspective to share."
- "As a parent and primary caregiver, I just want to mention risk. Our experience is that all symptom reduction therapies (OT, PT, AFOs etc.) or medications that don't reduce the myelin degenerative processes may slow symptoms for a while, but don't improve underlying disease processes. They give some comfort to the patient for a time, but don't provide hope. **Where therapeutic methods that arrest or reverse that degenerative processes exist, hope exists. As a caregiver of a patient with advanced MLD, our risk tolerance is extremely high.** We would like to just share that our family would take big risks to treat the myelin erosion if there are solutions considered or developed for trial or implementation in the future in advanced cases."

Late juvenile MLD

Corrine, mother of Trent, who passed away at the age of 29 from late juvenile MLD (no therapies)

- Biggest symptoms: "His inability to communicate, his inability to move voluntarily, his inability to respond to stimuli. The long process of losing communication is eventually loss of voluntary response, then involuntary response. Our son could laugh or smile, or groan later because that's involuntary. Eventually, unfortunately, all communication is gone, even involuntary."
- "I hope future treatments will stop the disease before it continues to progress, or it is eventually cured."

- "It is a terrible disease. We had 19 years of watching our normal child lose every ability. We cared for him at home until he died at age 29 (he was diagnosed at age 10). I have no regrets in how we cared for him, but I am sorry this awful disease took my normal boy and turned him into a living vegetable. I wouldn't wish this disease on anyone."

<u>Cache, father of two daughters with late juvenile MLD, three-year-old Hazel who received gene therapy and 10-year-old Lia who received a bone marrow transplant</u>

- "We really wanted to do gene therapy for Lia. Unfortunately, she was unable to receive it because it was not yet approved by the FDA. Lia's BMT outcome so far has been better than most experiences we've heard from other families - there was no graft vs. host or rejection issues. Her new immune system appears to be producing an adequate amount of enzymes needed to break down sulfatides. We're hoping that the BMT was successful enough to stop any further progression and nerve damage. Our youngest daughter, Hazel, underwent gene therapy in Italy a few months after Lia's BMT. Her recovery has been much better than Lia's. Her chemo treatment was much more mild and she didn't need any medications to address rejection. Hazel was jumping on her hospital bed the same week she had the gene therapy. She ran back to the hotel the day she was released from the hospital. Lasting effects of chemo have been minimal physically and cognitively. Lia had a very difficult experience due to the severity of her chemo. She spent nearly all of her four week hospital stay in bed, with an occasional short and exhausting walk down the hall and back. It's been almost seven months since transplant and she still cannot do many basic functions she was able to before transplant: she walks slowly and needs to hold on to someone for walks around the block. Lia cannot use the bathroom, shower, dress, or brush teeth independently. It's difficult for Lia to hold a fork or a pencil. (Hazel just learned how to draw a heart on her own this week.) Lia still requires diapers every day. I don't think we had an adequate understanding of how serious and lengthy Lia's recovery would be. Compared to Hazel's recovery, Lia has been put through significantly more trauma and suffering. We don't know how much of this difficulty is caused by chemo or by MLD, but we do know that her MRI results on March 1, 2022 showed no progression in scarring on her brain from her first MRI in August 2021. In retrospect, we feel strongly that gene therapy would have been a much better option for Lia."
- "In comparison to our oldest daughter's BMT, gene therapy has been exceptionally better in treatment and results. The effects of chemo and recovery were much less severe and dangerous. Gene therapy also is expected to stop any further progression of MLD, where a BMT could possibly stop, but only slows progression in most cases. Where gene therapy was not FDA approved, we had to decide if we wanted to seek immediate treatment by taking Hazel to Italy for treatment, or gamble precious time seeking conditional FDA approval and then attempting to convince our health insurance to pay for treatment. Only one patient in the USA had been successful in obtaining treatment at the time we made our decision. MLD is a rapidly degenerative disorder and every day we waited for treatment increased the risk that Hazel would lose cognitive and physical abilities."
- "Loss of cognitive and physical functions. Lia's outcome has been better than most children diagnosed with MLD. Still, every day is a struggle for her. Her learning ability, short term

memory, and processing speed have been significantly affected. Before the onset of symptoms, Lia was a top academic performer in school, often scoring in the 99th percentile on standardized testing. As of September 2021, she scored a FSIQ of 69. She dreamt of being a pediatrician one day, but now the rest of her education experience will be in Special Education. Physically, Lia loved being active - bicycling, running, jumping, dancing, alpine skiing. All of these she was able to do until she had her BMT. Currently, she cannot do any of these activities and cannot walk around the block without assistance. The most difficult thing for Lia is that she remembers what it was like before the onset of MLD. She grieves over the loss of the person she was and becomes frustrated when she can't complete a task or formulate a thought that was easy for her at one time."

- "We are amazed with the progress that has been made with science's ability to rewrite the human genome. Even so, we are hopeful for continued advancements in treatments, looking forward to when MLD gene therapy can be completed much faster, at a lower cost, and en-vivo (eliminating the need for chemotherapy.) MLD can now be identified and eliminated before the onset of symptoms (as well as many other genetic disorders.) The cost of mapping the human genome has dropped dramatically. Making prenatal/neonatal genetic screening widely available can prevent unnecessary debilitation, suffering, and death from happening to hundreds of thousands of children every year."
- "I wish our doctors would have had gene therapy widely available and FDA approved to treat our oldest daughter."

<u>Deborah, mother of a 22-years-old daughter with late juvenile/adult-onset MLD (no therapy)</u>

- "Would also like to talk about improving speed-to-diagnosis, avoiding misdiagnosis, and right to try treatments even if not in target audience for trials"
- "My daughter was funny, joyful, high-achieving, an amazing artist (drawing, painting, photography), a competitive dancer for many years, and an honors graduate from high school just after turning 16 with the intent of becoming a surgeon. Although she had started showing social awkwardness, forgetfulness, attention issues, and trouble distinguishing reality from thoughts when she was an early teen, we chalked this up to teen behavior. Things seemed to really progress at 19-20, and the diagnosis process began with medications for ADHD, depression, and bipolar disorder, but none of that helped. We pushed for an MRI because it was such a stark difference from the daughter we knew, and during the pandemic it took a while to get to the MLD diagnosis."
- "Cognitive symptoms are the primary issue - memory (reading a page many times, what happened earlier today or last week or last month), ability to sequence tasks (showering, dressing), attention/focus (seems like staring into space, wandering off)."
- "STOPPING THE PROGRESSION IS CRITICAL while progress is made on other fronts - it is okay to have an interim outcome for our loved ones be a disease plateau until something better comes along because that is more than we have today!"
- "Risk tolerance for my adult daughter with cognitive symptoms would include trying any therapy that has minimal risk/downside. For example, gene therapy or enzyme replacement that has had positive results for another subtype or pre-/early-symptomatic patients would be acceptable (but not BMT/HSCT with significant hospitalization/chemotherapy required

or risk of graft-vs-host disease). Physical and emotional stress are associated with periods of decline so surgeries and chemotherapies and risk of host-graft disease are unlikely to be considered by or for her in her present disease state."

- "I have great expectations for neuroscience research to not only rectify the ARSA gene mutation(s) to increase enzyme levels but to also clean up the sulfatide debris and regrow myelin to address all phases of disease progression AND all subtypes. I hope all these mechanisms are being investigated and clinical trials opened; for example, other methods of enzyme delivery (e.g., liver), treatments and delivery platforms for other leukodystrophies and lysosomal storage diseases, and treatments (or variations) already available or in development for MS / Alzheimers / MCI / dementia / metabolic diseases. Maybe the CGT/biotech/pharma companies need a greater incentive to come up with these rare disease treatments and get them into clinical trials more quickly - I think many parents of those with MLD would support the FDA allowing for some fast-track modifications to the NDA/BLA process for rare disease clinical trials. I definitely think these companies need to be incentivized to broaden the eligibility criteria that relate to disease progression and subtypes (especially late-juvenile and adult)."

Adult onset MLD

Cindy, mother of Josh (1978-2009) who died of adult onset MLD, and Karen aged 42 who is living with adult onset MLD (bone marrow transplant)

- "Our son Josh, had the adult onset, 1978 -2009. His childhood was very normal. Worked for a couple of different jobs. Never could hold on for long. Couldn't figure it out. Josh was a very intelligent young man. Took him to several doctors to see what was going on. First thought it was MS. Then they sent us to Mayo clinic in Jacksonville, FL. diagnosed him with MLD in 2003. He stayed home with us. Symptoms started to develop. **His motor skills started to be affected.** Then his body started to fail. Pretty soon he was in a wheelchair, I was having to feed him. Finally, he developed bed sores. It was time to take him to Hospice. He had a grand mal seizure that lasted 1 1/2 hours. From then on he was unconscious. He died 16 days after he was in Hospice."
- "Our daughter, Karen has the adult onset born in 1981. She also had a very normal childhood. Things were pretty normal for a while. Then the symptoms started to happen. **Falling down, driving was not a good thing for her.** She would cut corners short and dent the car. Her husband decided to find out what was wrong. With the MLD with her brother, it didn't take long to figure it out. In March 2018 she was diagnosed with MLD. Decided on the bone marrow transplant. Starting looking for a donor. Finally found that her little sister was a perfect match. Nov. 28th was the date of the transplant. She got really sick with a high fever and threw up quite a bit. Stayed in the hospital for a couple of days. Then came home. It seemed like the transplant was going to be successful. But about 6 months later it started going downhill. First with not being able to walk for a long period of time, to using a wheelchair all the time. Now she is in such pain from her legs being curled up in the fetal position. They can't be straightened out. She is in so much pain. As of this date 10-8-2022 she is in a wheelchair and in such pain from MLD. Any help would be welcomed."

- **“We are willing to do anything to help with the adult on-set treatment”**

Margaret, wife of Michael, living with adult onset MLD (bone marrow transplant)

- “We would make the decision to do the transplant again because there was no other treatment option available. But it was very dangerous and Michael will now have **graft vs. host disease** for the rest of his life. Of course, having GVHD and having the chance of halting the progression of MLD is better than letting it run its course. But I hope someday that those with adult onset MLD will have the option of gene therapy.”
- “My husband is only 29 years old, now has a whole life of being **cognitively impaired** ahead of him, and has to spend most of his days **alone and confused** at home. I have to work, and will probably always have to work long hours because he cannot, and he can’t go out on his own because he gets lost.”

Mary, mother of an adult daughter, Kris living with adult onset MLD (bone marrow transplant)

- "We are very satisfied [with BMT]. There has been no progression in her MLD, since her transplant 8 years ago. It did not undo the damage already done, so she has a new normal, but we are all satisfied that she has few limitations compared to where she could be had the progression continued. The only thing we really didn't understand prior to making the decision for the transplant is that due to the chemotherapy she could be more prone to certain cancers. We also didn't realize that it would take almost a year for her blood counts to normalize. But the fact the progression has stopped has made everything worthwhile."
- “[My daughter’s main symptoms are]"1) **short term memory and distractibility** can affect daily task completion; 2) because she can be **impulsive** it affects decision-making which means she doesn't always think things through - this includes driving decisions- so based on her doctor's recommendation, she doesn't drive; 3) **spatially affected**- hard to find things she misplaces; or can't find something on a shelf that is there; 4) no organizational skills; 5) she was exceptionally bright and was an account clerk -very good with math, but she now has poor math skills and needs help paying bills and managing her own money."
- “[For treatments], "1) Something that would help with memory and improve the executive functioning of the brain; 2) Physical activity regimen that would accompany treatment while rebuilding those mind body connections."
- Comments about Doctors: “I wish they would have told us there were options for treatments if the illness had not progressed. I wasn't willing to accept there was no solution - and did my own research and started calling hospitals around the US to find help, which is how we found Dr. Escolar at a hospital 900 miles from our home. She gave us hope, and options and had we accepted our hometown advice. Kris would have deteriorated instead of stabilizing. A bone marrow transplant was a risk, but for us it was hope.”
- “Kris went 15 years misdiagnosed - from age 18 to 33 -she was diagnosed with various mental health disorders - and on various medications - not one psychiatrist suggested there could be a physical cause for the cognitive symptoms she was displaying as well as changes in her personality, academic and athletic ability. No one made the connection and tied together the physical, intellectual and mental decline all those years. If we had not suspected a brain tumor and requested an MRI- we would have never known - it was never

a mental condition- it had a physical cause. Every mental health professional should suggest an MRI or a blood test for AA enzyme level or urine test for sulfatides. Had Kris been diagnosed sooner- there would have been less damage to her brain. I can't help but wonder how many people there are out there that are in institutions, hospitals, homeless that are not really mentally ill but may have adult-onset MLD and if caught in time, could at least have a better quality of life. I wish there was a way to get the mental health professionals to understand - physical first."

Linda, parent of an individual living with adult onset MLD (bone marrow transplant)

- "Didn't have any choices that reflect improvement in executive function, an issue for many olders. Definitely a treatment goal."

Heather, a 35-year-old woman, and one of four siblings living with adult onset MLD (no therapies)

- "I have not had any treatments due to the likelihood of severe after effects, cognitive decline, infertility and the possibility of death."
- "Daniel [her brother, also with Adult MLD] suffered from aplastic anemia after his bone marrow transplant. He had three (failed) cord blood transplants prior to his passing at the University of Minnesota."
- "In my family, we have the adult-onset form of MLD. Our mind is taken much sooner in my experience than our bodies. The hardest impact is watching the individual's slow **cognitive decline**. In the beginning of my brother Joel's onset, I watched him slowly exhibit this, as he would forget how to complete tasks, become disoriented, and confused. He became quiet and lost his witty, funny/jokester personality. Due to this decline, he lost various labor jobs and relationships with his peers. Joel is now 42 years old and non-verbal. I would give anything to be able to speak with him again. While his decline increased, I slowly lost my brother and my best friend even though he is still alive. For myself, I struggle with the mental health effects of all of the loss we have endured in our family. I struggle with the knowledge of what is to come for others and myself if we are not able to expand treatment options to include anyone, regardless of age, in gene therapy trials. There has not been a day that goes by where I do not think about MLD. It is the persistent dark cloud hovering in the sky on a sunny day. Our family is unique in that four of my parent's five children have been diagnosed with adult-onset MLD. Of us children, most of us have had vastly different paths of decline or symptomatology presenting differently at varying age markers. We, like so many other MLD families, have suffered immense loss. My wish is for a change regarding the age criteria for gene therapy treatment. If that change were to happen, I feel many families would have hope; I would have hope."
- "For a future treatment for MLD I would look for gene therapy as I believe that is the best option to fight and cure this life-robbing disease. It is inaccessible for certain members who are inflicted with the disease, myself and siblings included."

Jamie, caregiver of a daughter living with adult onset MLD (no therapies)

- Symptoms: “Incontinence, fecal Incontinence, reduced cognitive abilities. The **Incontinence** issues mean constant work for Britt and parents in trying to head off accidents and large messes. The **cognitive** issue just doesn't allow us to communicate as we are used to doing.”

Pam, mother of an individual living with adult onset MLD (no therapy)

- “Myelin repair would be what we would like to see worked on”

Barbara, mother of Anja, living with adult onset MLD (no therapies)

- “We have a daughter where the first signs appeared at the age of 20. She was mistreated by various psychologists for seven years. When the parents asked for an MRI of the brain, the disease was diagnosed and confirmed by genetic analysis. For once, Anja only has cognitive problems that prevent her from organizing her work and living independently. The disease started with **cognitive decline**, which was stronger in the first years, but now the condition has been maintained for at least the last three years.”
- “Due to cognitive decline, Anja cannot live independently. If she's home alone, I never know if she'll actually eat lunch and I know she won't do anything smart because I always have to involve her.”

MLD, subtype not identified

Patrick, parent of a child living with MLD

- “As a parent, caregiver, and advocate for another leukodystrophy, I want to emphasize the importance of acknowledging the severe consequences and loss of life and potential that MLD presents to the afflicted. The FDA should carefully examine the MLD community's perspectives when balancing risk and benefit of potential therapies. As Laura Adang said, MLD (and truthfully many other leukodystrophies) is "relentlessly progressive." Families deserve an opportunity to save their loved ones even if it requires imperfect solutions.”