

James Valentine, JD, MHS (00:10:46):

Good morning. My name is James Valentine and welcome to the Externally-led Patient-focused Drug Development meeting on STXBP1 related disorders. I'm here in the studio with my co-host, Charlene Son Rigby, the President of the STXBP1 Foundation. We're coming to you live from the Washington DC metropolitan area, actually not too far from where the US Food and Drug Administration's headquarters are located. It's my pleasure to turn it over to Charlene to provide us with some opening remarks. Charlene.

Charlene Son Rigby (00:11:18):

Thank you, James, and hello everyone. Welcome to the Externally-led Patient-focused Drug Development meeting on STXBP1 related disorders. I'm Charlene Son Rigby and I'm president and co-founder of the STXBP1 Foundation. I'm also mom to my daughter, Juno, who has STXBP1 related disorder. Our foundation's mission is to accelerate the development of treatments for people living with STXBP1 related disorders.

(00:11:49):

A special welcome to the many staff members of the US Food and Drug Administration that are taking the time to be with us today. Thank you for giving us permission to hold this meeting. We're really excited to have you with us and we hope you learn a lot today from our amazing parents and caregivers. I also want to thank our industry sponsors, Biogen, BioMarin and Coded and Horizon for their generous support. We are pleased to have in attendance representatives from advocacy and professional organizations, pharmaceutical companies, federal agencies, and clinical and research centers from across the world. Thank you all for joining us today. Most importantly, I want to welcome the members of our audience whose lives have been directly impacted by STXBP1.

(00:12:41):

Today's meeting is the result of many months of planning and people working together behind the scenes. I want to extend my deep gratitude to everyone who has had a hand in preparing for this meeting. We are grateful to have had this opportunity to ensure that patient and family perspectives are considered in the drug development and regulatory processes.

(00:13:02):

STXBP1 has a severe impact on quality of life, affecting our children in ways that can be difficult for people outside of our families to understand. Most of our children have no or very little speech capabilities. They're not able to tell their own stories or advocate on their own behalf. Many of our children are further affected by seizures and other medical problems, sometimes so severe that they and their families experience significant challenges with daily activities and social isolation.

(00:13:37):

As you will hear today, almost all living with STXBP1 are severely affected by developmental disabilities. Almost all experience epilepsy, which is resistant to therapies for some. Often hypotonia, tremor, motor issues, sleep problems, and gastrointestinal problems further diminish health-related quality of life for STXBP1 patients. Despite these severe manifestations of STXBP1, there are no FDA approved treatments for this disorder.

(00:14:12):

As an example, my own child, Juno, is now 10. She was diagnosed in 2016 after a three year diagnostic odyssey to find out why she was missing milestones. Juno is a happy child despite her challenges. She is nonverbal. She has severe intellectual disability. She didn't walk until she was almost five. She has a significant tremor that impacts all activities including trying to press buttons on the device that she valiantly uses to communicate with us. Our family is just one of hundreds that are concerned for our children's futures.

(00:14:49):

As I said before, there are no FDA approved treatments for STXBP1. Today, you will hear just a small number of stories from our worldwide community. We hope that you will remember what you hear today and understand the urgent need for treatments for STXBP1.

(00:15:06):

I want to express my appreciation to be investigators working in labs all around the world, striving toward a better understanding of basic and translational STXBP1 science to move us closer to future clinical trials. Our hope is that this meeting will encourage future research and successful new product development for people living with STXBP1 who urgently need treatment options.

(00:15:32):

For our STXBP1 families, we invite you and your loved ones to call or write in during the program. We also ask that you stay with us throughout the day and participate in remote polling. We want to hear as many perspectives as possible and we'll do our best to get as many calls and comments in. When participating, please only use your first name and then your city and state or country. No other identifying information should be shared. Be assured that any comments we're unable to share are still very important and will be included in the Voice of Patient report, a summary of this special day.

(00:16:11):

To begin today's meeting, I'm delighted to introduce our speaker from the FDA. Dr. Michelle Campbell is the Associate Director of Stakeholder Engagement and Clinical Outcomes in the Office of Neuroscience in the Center for Drug Evaluation and Research at the FDA. This is the part of the FDA that regulates new drug treatments for many disorders. Dr. Campbell will provide some opening comments from the FDA perspective. Dr. Campbell, over to you.

Michelle Campbell, PhD (00:16:42):

Thank you and good morning. My name is Michelle Campbell and I am the Associate Director for Stakeholder Engagement and Clinical Outcomes for the Office of Neuroscience and the Center for Drug Evaluation Research. First, I'm happy to see so many patients, caregivers, and advocates on the web today. Thank you all for being part of this meeting and sharing your experiences with us.

(00:17:04):

I would like to also thank that STXBP1 Foundation and all of the staff that was involved in planning this meeting. I know we also have representation from industry, academia and other medical product development stakeholders participating online as well. While FDA plays a critical role in medical product development, we are just one part of the process and I'm glad to see a high level of interest from those of you who also play an important role. Additionally, we have colleagues from various offices and centers from the FDA attending as well. We share the patient community's commitment to facilitate the development of safe and effective medical products for STXBP1.

(00:17:51):

We know when we say medical product development, we mean it in the broadest sense of identifying, developing and evaluating potential therapies or devices that can help patients manage their condition. We are here to learn from you in your experiences with STXBP1.

(00:18:10):

A decade ago, the FDA started its patient-focused drug development program. As part of this program, we began having patient-focused drug development meetings, also known as PFTD meetings. These meetings brought patients, caregivers, and various members of the FDA community together to listen and learn at about a patient's experience with their disease or disorder. Since this program began, we've held roughly 30 PFTD meetings. What we've learned from these meetings is patients are the expert in their lived experience of their disease or disorder. Patients are uniquely positioned to inform regulatory agencies and provide an understanding of the burden of disease in currently available treatments.

(00:18:52):

Another outcome of the PFTD meetings we held was the growth of patient- focused drug development meetings being hosted outside of the FDA, meetings like the one today. A product of these meetings is a Voice of the Patient report, which FDA can reference for future information when providing advice in a specific medical product development program for STXBP1. As I said earlier, this is why we are here today to learn from the experts with a lived experience of STXBP1.

(00:19:26):

FDA promotes and protects the public health by evaluating the safety and effectiveness and quality of new products, but we do not develop medical products or conduct clinical trials. It is, however, FDA's responsibility to ensure that the benefits of a product outweighs its risks. Therefore, having this kind of dialogue is extremely valuable for us because hearing what patients and caregivers care about can help us lead the way in figuring out how best to facilitate medical product development and understand how patients view the benefit risks of therapies and devices for STXBP1.

(00:20:04):

Our commitment to better understanding rare disease drug development's unmet needs and finding opportunities to accelerate rare disease drug development where appropriate is critical to all of our rare disease families including STXBP1. One area I would like to highlight is our funding of the Rare Disease Cure Accelerator Data and Analytics platform. This is an effort that is occurring outside of a specific drug development program and allows for the sharing and leveraging of data where advanced computer analytics can help inform rare disease drug development. This opportunity to share data from various sources will only assist all in learning about various rare diseases including STXBP1.

(00:20:45):

We learn so much from these meetings. We look forward to incorporating what we learn today into the agency's thinking and understanding of how patients view benefits and risks of therapies and devices for STXBP1. We thank you for your participation. We are grateful for each of you for being here and sharing your personal stories, experiences, and perspectives. Thank you, and I now turn it back to Charlene and James.

Charlene Son Rigby (00:21:18):

Thank you, Dr. Campbell. Next up, Dr. Ingo Helbig will provide a clinical overview of STXBP1. This will serve as a scientific foundation for today's discussion. Dr. Helbig is a well-established STXBP1 expert and clinician scientist. He's also the Director of Genomic Science at Children's Hospital of Philadelphia. Dr. Helbig has a deep interest in understanding the biochemical and molecular basis of STXBP1 and has developed a research group dedicated to these efforts. Dr. Helbig, over to you.

Ingo Helbig, MD (00:21:55):

Thank you so much for the kind introduction. What I would like to show you in the next 50 minutes is an overview about STXBP1 related disorders.

(00:22:08):

Let me tell you about what the STXBP1 gene and the STXBP1 protein does. STXBP1 is a rare genetic condition that was first identified in 2008 in people with severe epilepsies, and it is caused by disease causing variants in the STXBP1 gene. It's actually now known to be a very common cause of neurodevelopmental disorders of epilepsy. STXBP1 is really very important in the functioning of synapses, the cell elements that are important for communication between neurons. You can see on the right how STXBP1 is really driving the connection of neurons and synaptic vesicle release.

(00:22:58):

When we think about STXBP1 related disorders, we're dealing with a very complex inborn neurodevelopmental disorders. We have symptoms that are very consistent and we have symptoms that often vary between individuals. We know that almost all individuals have global developmental delay, muscular hypotonia, speech impairments, and often don't acquire the spoken language. We know that the

cognitive impairment can be quite variable. There can be seizure disorders, that I'll comment on on my next slides, that can be very difficult to treat and epilepsy may become intractable in a subset of individuals.

(00:23:38):

A particular epilepsy type that is very common in STXBP1 are so-called infantile or epileptic spasms, and we see a variety of different neurological and non-neurological symptoms. The range of symptoms in our children with STXBP1 related disorders is so diverse that we came up with novel ways of showing symptoms, which you can see here is this radar plot that gives you an overview of what these symptoms look like.

(00:24:04):

What do we know about how common STXBP1 disorders are? Right now, we estimate that one in 30,000 individuals in the US and worldwide will have an STXBP1 related disorder. This makes STXBP1 disorders one of the most common diagnoses found on epilepsy genetic testing, which is performed in thousands of individuals every month in the US. Here at Children's Hospital of Philadelphia, we have seen more than 120 individuals in the last five years. More than 220 individuals have been diagnosed by a single US diagnostic lab only. Right now, the STXBP1 Foundation, the major US-based advocacy organization, connects almost 300 individuals with STXBP1 disorders.

(00:24:52):

Finally, in a recent publication, we collected information on more than 500 individuals with the STXBP1 disorders. On the right, you can see the spectrum of genetic variants that we see of these individuals.

(00:25:05):

What makes STXBP1 disorder so unique? When we first started working on STXBP1 disorders, we realized very early on that we're dealing with a very dynamic and very often difficult to understand seizure trajectory. We know that seizures happened very, very early and happened in more than 90% of individuals with seizures in the first year of life. There are other features that are unique, such as a peculiar subcortical myoclonus, a very marked expressive language delay, and right now we're looking at specific subgroups that may have unique features. What I would like to point out though is that epilepsy and STXBP1 disorders is very, very prominent in the first year of life.

(00:25:51):

What you can see here on the right is a reconstruction, a rebuilding of the patient trajectories of 37 individuals who had seizures in the first year of life, and every bar represents a single month of life. Every little horizontal bar is a single individual. What you can see here is the changes in seizures frequencies in a month by month. Dark red are individuals who have many seizures per day, then individuals who have several seizures per day down to individuals who are seizure-free. If you see a connecting bar in yellow, it means seizure worsening between months. If you see a connecting bar in blue, it means improvement. What I would like you just to appreciate from this graph is how common and how frequent seizures in the first year of life are. This is really knowledge that we created in the last five years, really showing how prevalent seizures are and how urgent the need for treating them is.

(00:26:51):

We know that there's a very complex pattern of seizures over time, which we increasingly understand. Here, you can see now a larger version of what I've shown you previously. This is now from a publication that is accepted in Brain and will come out in the next few weeks. Here we have reconstructed seizure histories in 162 individuals across more than 1,200 patient years. What you can see on the right are the types of seizures and the frequency of seizures in these individuals. Again, in a month by month basis, at the bottom here you can see the cumulative onset of seizures. We know that seizures happen in more than 90% of individuals in the first year of life and that a majority of these individuals may have seizures that resolve, but still a significant fraction of individuals have ongoing seizures.

(00:27:40):

Infantile spasms, a peculiar seizure type, are very common in STXBP1 disorders, affect more than 50% of individuals, and are a major cause of regression and ongoing seizures and contribute to morbidity. What we don't know yet is the seizure burden in later life. Again, we have a very clear subset of individuals who have intractable seizures.

(00:28:07):

We have made significant progress in getting STXBP1 disorders trial ready. We now know that we can overcome the clinical variability which has become a bottleneck in trials. There are some attempts right now to really forecast seizure trajectories. On the right, you can see that we can really predict future seizures very reliably on what is happening in the first year of life. We can use our knowledge base in STXBP1 to really understand what a clinical trial would look like.

(00:28:40):

What you're seeing at the bottom right, down here, is a virtual clinical trial that asks the question, if we had a medication that would decrease seizures by 20%, and we would have this trial last for six months, how likely is it that this trial would show a significant difference? We know that in variable disorders there's a lot of noise and we may not see a difference, but we know that between the age of six months and five years and between seven years and 12 years, we have a very high probability that a trial that only diminished seizures to only 20% would be significant.

(00:29:24):

There are unique implications for STXBP1 disorder, so this is the main reason why I'm talking to you today. We know that a diagnosis of STXBP1 clearly has a choice on how we prescribe medications even today. This is important for screening for infantile spasms, a severe devastating seizure type that typically happens at the age of six months. We know that strategies as the ketogenic diet work particularly well for children with STXBP1 disorders.

(00:29:54):

On the right, you can see the age of diagnosis of the last few years in STXBP1 related disorders. We can make the diagnosis now as early as three to four weeks, which gives us the possibility to anticipate seizure types in the first year of life, such as infantile spasms, and really allows us to identify patients very, very early to enroll them in clinical trials.

(00:30:18):

We know that our patients with STXBP1 disorders need to be monitored for features like spasticity and require specific treatments. We know that they often benefit due to their profound hypotonia with physical therapy, but only really early on. We know that they are really benefiting from assisted devices given their lack of expressive speech. There are other features such as behavioral therapy and feeding therapy that are important, but these are the treatment applications that really improve the lives of children with STXBP1 disorders already today.

(00:30:54):

Where do the needs lie in STXBP1 disorders? We struggle with controlling seizures and we are struggling with finding optimal treatments. Many children still have refractory seizures and epilepsy. Even with therapies that can be very intense, the vast majority of children will have severe intellectual disability. We are not at this point where we can meaningfully affect the developmental outcome.

(00:31:22):

We have a very unique tremor that can really interfere with all the activities of daily life and communication. This has been resistant to treatment and we see a large discrepancy between the receptive ability to communicate and language expression. And then, we have lots of children who have behavioral dysregulation. What you can see on the right are milestones and just an idea on what our individuals with STXBP1 can achieve and what they struggle with. You can see while many individuals can learn how to

vocalize and are good at nonverbal communication, using words, feeding independently, or even using more complex speech is very, very rare in children with STXBP1 disorders.

(00:32:19):

There is rapid research progress. Over the last five years, STXBP1 preclinical studies have really exploded and have taken on their own dynamics. Now, STXBP1 is considered one of the most rapidly developing fields in rare and neurodevelopmental disorders. We have several companies working on gene replacement therapies. We have repurposed small molecule drugs such as 4-Phenylbutyrate, and RNA therapies are on the horizon. This really is a unique opportunity to treat one of the most common genetic causes of epilepsy and neurodevelopmental disorders. How can we put STXBP1 disorders into clinical trials? This year, we've started a natural history study that comprises four sites in the US and is projected to see more than 100 individuals in the first year of life undergoing a very detailed assessment, a clinical assessment with scales at the level of typical clinical trials, evaluating various neurological and non-neurological domains and quantitative EG analysis and analysis of CSF and blood biomarkers. Patients will be jointly assessed by our colleagues in neurology, genetic counseling, physical and occupational therapists, behavioral pediatricians, and neuropsychologists. What we will get from this information from this study that will run over a five-year timeframe is an in-depth view into the outcome markers in STXBP1 disorders that will allow for a wide range of clinical trials.

(00:34:02):

Let me summarize what I was sharing with you. I'm here today for you to talk about STXBP1 disorders, which is a rare genetic neurodevelopmental disorders with very high needs. In the US, a child with STXBP1 disorders is born every third day and we estimate a prevalence of one in 30,000. STXBP1 is extremely complex with many unfilled needs. We increasingly understand the relationship between genotypes and phenotypes. We understand outcomes. We understand how clinical trials would look like. We have a detailed developmental assessment and detailed information on longitudinal outcomes in our natural history study or NHS, and we know that therapies need to treat these complex features. And then, finally, our emerging data really will inform how clinical trials can be designed in the future. We have seen...

PART 1 OF 9 ENDS [00:35:04]

Ingo Helbig, MD (00:35:03):

... how clinical trials can be designed in the future. We have seen some first information from our virtual trials, how a subset of trials may be conducted, but we expect that a wide range of trials will be able to be successful once this data has emerged. With this, I would like to give this back to the moderator, and I thank you for your attention.

Charlene Son Rigby (00:35:26):

Thank you, Dr. Helbig. Now I'd like to welcome our moderator for today's meeting, James Valentine. James has worked for the last 15 years as a champion of the patient voice as part of the regulatory process.

(00:35:39):

He previously worked at the FDA, where he was a patient liaison helping to incorporate the patient voice into medical product review across the FDA's various medical product center and review divisions. There, James helped develop and launch the patient-focused drug development initiative.

(00:35:58):

In private practice, James has worked with many patient organizations to ensure their community voices are heard by decision makers. He has also been involved in helping to plan and moderate many of the over 75 externally-LED PFDD meetings. So, we're in good hands today with James. And now, over to you.

James Valentine, JD, MHS (00:36:19):

Thank you so much, Charlene, for that introduction, and it's so wonderful to be here this morning with this STXBP1-related disorders community. And I really look forward to hearing from so many of you throughout

today's program, as we now shift into the part of the program where we're going to be inviting you to participate.

(00:36:36):

But before we do that, let's cover a little bit of an overview of the meeting. So, now that we've heard a clinical overview from a disease expert, we do turn to that core of today's meeting, which is to hear from you, the people and families living with STXBP1, including parents and other direct caregivers.

(00:36:57):

Patient-focused drug development, or PFDD, is a more systematic way of gathering patients' perspectives on their condition and on available treatments. As you heard from FDA's Dr. Campbell, your input will help inform the agency's understanding of STXBP1 to help inform drug development and review.

(00:37:17):

While FDA has held many of its own PFDD meetings, today marks the 79th externally led patient-focused drug development meeting. As we heard from Dr. Helbig, STXBP1 is quite rare, and with over 10,000 rare conditions alone, this is truly a unique and an important opportunity for this community.

(00:37:39):

Today's meeting is interactive, so let me tell you a bit about what we'll be asking of you and how today's meeting will be organized. So, the day will be organized into two overarching sessions. In our first session, which will be this morning, we'll be exploring the patient and caregiver experience of living with STXBP1, and its impacts on you and your loved ones' daily lives. In our second session, in the afternoon, we'll bring everyone back together to explore the various approaches to treatment including participating in clinical trials, and we'll also be asking you for your preferences for future treatments. So, what will those two, those morning and afternoon discussions, look like? We'll primarily be using three different ways to hear as many voices as possible in this community.

(00:38:25):

We'll start things off by hearing from panels of patient and caregiver stories of those living and experiencing STXBP1. That will set a good foundation for our discussions that will follow, where we invite all of you to participate. And those panels will also reflect a range of experiences to give us that good foundation. Although we know that five individuals can't reflect the full range of experiences with STXBP1, and that's why after those panels we'll be opening it up and we'll have a facilitated audience discussion for all of our caregivers who are tuned in today.

(00:39:06):

We'll be asking you to build on what we've heard from the panel. As the meeting moderator, I'll be asking questions and inviting you to state your name and provide a comment. This can be done in one of two ways. We want you to dial in by phone, or you can submit written comments. We'll also have a Zoom panel on of other caregivers from this community who will be sharing their experiences throughout those sessions.

(00:39:33):

The third way that we'll bring your voices into the discussion is through the use of polling questions. This will give us a sense of the experiences we have represented in our audience, but also it will be important as a way to facilitate our discussions. We'll ask that caregivers only use either your phone or a web browser to respond to the questions. And in fact, you can go ahead and get on this system now, as once you're on it, you'll be able to stay on it throughout the entire day.

(00:40:03):

So, go ahead and pull out your phone, open up a browser, open up a tab on your web browser on your computer, and go to www.pollev.com/stxbp1. Again, feel free to go there now. www.pollev.com/stxbp1. And we'll be getting to polling very soon. We'll be using these polling questions, again, to broaden the discussion to everyone in our live audience, as well as to get you all thinking about topics that you can then share more about by calling in and writing in.

(00:40:46):

I do want to mention, we'll also have the opportunity for you to provide written comments for 30 days after this meeting, whether there's something at the end of the day you just felt like you weren't able to share everything that you wanted, or if you're watching this, the recording, on demand, we want to hear from you as well, and you can submit your comments as part of these next 30 days.

(00:41:08):

All of today's input, as well as that additional written input, will be summarized into that Voice of the Patient report, which will be provided to the FDA and made available to researchers and drug developers.

(00:41:22):

One last thing is, I'd like to cover a few ground rules before we jump into the discussions. We encourage the families of those living with STXBP1, so the parents and other direct caregivers, to contribute to the dialogue through using polling, calling in by phone, and submitting written comments.

(00:41:42):

The discussion today is limited to the patient's family members and other direct caregivers living with STXBP1. Meanwhile, our colleagues at the FDA, at drug development companies, and clinicians and researchers, they're here to listen. I also want to mention that the views expressed today are inherently personal, and the discussion may even get emotional at times, so respect for one another is paramount. And to that end, we ask that you try to be focused and concise in your comments, so that way we can hear as many voices as possible.

(00:42:17):

So, without further ado, let's get into our first set of polling questions, which will give us a sense of who we have in our audience today. So, again, you can go to www.pollev.com/stxbp1. Again, this is for our family members, our direct caregivers of those living with STXBP1. We want you to get into this system and answer these questions, so we can follow along throughout the day and learn about your experiences.

(00:42:46):

So, in our first polling question, we want to know, are you either, A, someone living with STXBP1; or B, a caregiver of someone living with STXBP1? And I'm going to give everyone here a few moments to get into our system. Because again, once you're in it, you'll be able to see new polling questions appear as we go to them throughout the program. And we do want to make sure everyone gets in from the very start so we can follow along with your responses throughout the program today.

(00:43:22):

So, we'll just give you a few more moments, as we're seeing people get into the system and answer this first polling question. And I think as we're seeing our participants today that are responding to this polling question, are the caregivers of those living with STXBP1, as we know that it would be difficult to expect those living with STXBP1 to participate in polling directly themselves.

(00:43:53):

If we go to our second polling question, so here we would like to know where you currently reside. For all of you and caregivers, we expect probably you live in the same area where your loved one with STXBP1 is, but we do want you to answer these questions moving forward for the person living with STXBP1. So, here the options are A, US Pacific Time Zone; B, US Mountain Time Zone; C, US Central Time Zone; D, the Eastern Time Zone; E, US Alaska Time; F, US Hawaii Time; G, Europe; H, Middle East; I, Asia; J, Canada; K, Mexico; or L, Central or South America.

(00:44:43):

So, please let us know where you and your loved one with STX currently reside. I promise these questions get a little harder to answer as the day goes on, so take advantage of these easy ones now where we're just trying to gather a little bit of information about who we have in our audience.

Charlene Son Rigby (00:45:01):

And, James, it's not a surprise that many people are from the US, but I'm really excited to see international participation in Europe and Asia, Canada, Mexico, Central and South America.

James Valentine, JD, MHS (00:45:17):

Yeah. So, this meeting is open to everyone, so if you're joining us from outside of the United States, we want to hear your voices as well. So, when we do get to later in the program where we ask you to call in, write in, please do.

(00:45:32):

Within the US, we have good representation across the different US time zones. Maybe not surprisingly, with a morning start time we have more representation from the Eastern Time Zone. Perhaps we'll see others from Pacific and other more Western time zones join as the day progresses a bit.

(00:45:52):

If we can go to our third polling question here, here we want to know, is your loved one with STXBP1 A, female; B, male; or C, other?

(00:46:10):

So, we'll give everyone, again, a few moments to answer this question. Again, getting a sense of who we have represented living with STXBP1 today. We're seeing results still coming in here. At least as it stands, it looks like we're seeing just over half of our audience is representing loved ones with STXBP1 who are female, we see a little under half represented with those who are male, and we do see some representation of those reporting other.

(00:46:58):

So, we'll go to our fourth polling question. We'd like to know, how old is your loved one with STXBP1? The options here are, A, zero to one years of age; B, two to three years of age; C, four to eight years; D, nine to 17 years; E, 18 to 34 years; or F, if they're 35 years of age or older. And again, this is the age of your loved one with STXBP1 today.

Charlene Son Rigby (00:47:39):

James, it's nice to see that... We just started a census within our community, and these numbers are aligning pretty well with our census numbers. So, exciting to see that the audience today is mirroring our census.

James Valentine, JD, MHS (00:48:00):

Yeah, great to have a good representative group here today. We're seeing that about a third of the audience, their loved ones are between four and eight years of age. You're kind of seeing a bit of a bell curve, so we're seeing next after that, nine to 17 and two to three. We do have representation in the 18 to 34 year of age, and even the youngest living with STXBP1, in that zero to one age range. Nobody reporting today that their loved one is 35 years of age or older.

(00:48:37):

We go to our final polling question for this first set we have this morning. So, we just asked about current age. Here, we'd like to know what age was your loved one diagnosed with STXBP1, and you'll recognize the response options here. It's A, zero to one years of age; B, two to three; C, four to eight; D, nine to 17; E, 18 to 34; or F, 35 years of age or older.

(00:49:12):

So, we'll give everyone a few more moments here to get in your responses. Let us know what age your loved one was diagnosed with STXBP1. We're seeing some of the numbers jump around a bit here, but what's staying pretty constant as our results keep coming in is that around 40% of our audience, their loved one was diagnosed at ages of zero or one. And really, then, we see the next-largest group, about a quarter being diagnosed in the second and third years of life. Just over 10% either between ages four and eight or nine and 17, but even some that weren't diagnosed until they were in adulthood. So, we're really seeing that shift from our last question.

(00:50:05):

Of course, I think we would expect that, but you're seeing the majority of individuals being diagnosed before they turned aged four. So, I want to thank everyone for participating in this first set of polling questions. Again, it's great to just get a sense of who we have in our audience today.

(00:50:26):

Now we get to move into our first session of the day, where we're going to be asking you to share your experiences of what it is to live with STXBP1. And so, to give you an idea of the types of topics and issues we want to explore, we'll pull up some of our discussion questions that we'll be going through over the course of this morning's session.

(00:50:49):

So, in this session, again, we're exploring what it is to live with STXBP1. We want to understand the symptoms and daily impact. So, some of the questions that we want you to start thinking about are, of all the symptoms and health effects of STXBP1, which one to three of those have had the most significant impact on your loved one's life?

(00:51:10):

We also want to know how does STXBP1 affect your loved one, maybe on best or worst days? Maybe some of those symptoms and health effects are present sometimes, some days not, or maybe they're more severe some days versus others, and we want to understand that day-to-day variability that might exist. We also want to know how your loved one's symptoms might've changed over time, as well as the ability to cope with those symptoms over time. So, whether that's over the course of weeks, months, or even years, we'd love to understand a bit about what the condition has looked like for your loved one, how that might have evolved.

(00:51:49):

We know that while there's a lot of symptoms and health effects that are a result of the condition, we do want to hear a lot about those. We also want to hear how those impact your loved one's daily lives. And so, you can think about maybe what specific activities are important to you and your loved ones that they can't do maybe at all or as fully as a result of STXBP1.

(00:52:12):

And finally, knowing that while you've already experienced so much with your loved ones living with STXBP1 currently and in the past, we also know that caregivers in this community are thinking about their loved ones' futures living with STXBP1. And so, we want to know, what do you fear most about as your loved ones get older? What worries you the most about your loved one's condition, thinking about the future?

(00:52:41):

So, to get us started on this topic, it's my pleasure to welcome a panel of your peers from this community who will be sharing some of their experiences on these topics. We have Justin, Elizabeth, John, Leigh Ann, and Raquel. Justin, why don't you get us started?

Justin (00:53:00):

Hi, I'm Justin, and I'm dad to my three-year-old son Reese. As police officers, we see some of the worst things this world has to offer, but nothing has been as traumatic to me as seeing a child struggle the way Reese has. Reese was born on September 9th, 2020, and we were so happy. We had just over a week with him, until we noticed odd behaviors, and we rushed him to the hospital with seizures.

(00:53:35):

After weeks between the NICU and neuro floors at Boston Children's Hospital, we were brought to a conference room where we were told that Reese's diagnosis was a rare encephalopathy. One so rare the doctors themselves aren't familiar with it and didn't even have the correct name for it, which left us Googling afterwards, searching for answers.

(00:53:57):

We confirmed it was STXBP1, and once we had our wits about us, we asked for more information and were told that all they could do was direct us to the information on the STX Foundation website.

(00:54:13):

And by the time we got home, Reese had outgrown most of the clothes he hadn't even worn yet. Reese has had many different complications throughout his short life: focal seizures, tonic seizures, infantile spasms, laryngomalacia, hypotonia, cortical visual impairment. He's legally blind. Astigmatism, cognitive issues, he's nonverbal, G tube, NG tube, learning delays, chronic constipation, asymmetry of the skull called plagiocephaly, and so on.

(00:54:48):

His complications can be made better or worse from the never-ending carousel of medications. Reese continually works his hardest and gains skills only for them to be ripped away by regression from seizures that are still not controlled.

(00:55:02):

I think that's been one of the hardest things for me, is knowing that Reese is just like any typical kid, and that he has wants and needs and has all the ability inside to do things. But because of his condition, it robs him of those skills, skills like communication. At one point he even said "Mama" and "Dada," and now that's gone. It was such a heartwarming time when he was doing that, and it's so heartbreaking to think that I may never hear his voice say my name again.

(00:55:38):

We try to put ourselves in his shoes so that we can empathize with him, try to make it better. Like not understanding why we're not holding him or playing with him while he's on a monitor with short cords in a bed with bars on it; spending hours in a car driving to appointments, or just to medical visits, when he can't keep himself entertained and stares at the back of the seat in front of him; how he's unable to interact with children or socialize because he can't, or doesn't know how.

(00:56:07):

The worst for me in this situation would be not being able to tell us what's wrong. Something as simple as having an itch that I couldn't scratch for hours would be torture. And as a parent, watching a child suffer through all this is stressful. At night, we have free cameras trained on them, all with a different purpose, as well as a heart rate monitor and oxygen monitor, because we're forever terrified of sudden unexpected death in epilepsy.

(00:56:35):

Some of the worst times for Reese and my wife and I is when the side effects from the medications or his condition are so bad that he can barely function, whether it be his saliva from teething, and he can't compensate with the extra saliva, or whether it be choking on his own spit from after having a seizure.

(00:57:03):

He has weekly blood tests at times, where he's brought into a small room with strangers, and they poke him multiple times because the phlebotomists say that he has deep veins, and he doesn't understand why they're holding them down and poking him with needles.

(00:57:16):

The side effects from his medications sometimes are so severe that it turns him into a zombie. No joy, almost no personality. Nights are the hardest because that's when his seizures are activated. He gets the ambulance rides to Boston, which is over an hour away, because no local hospitals handle pediatrics.

(00:57:42):

And while he's at the hospital, he's woken up multiple times, whether it be from seizures, or needle sticks for blood labs, or monitors beeping too loud. And also, just because of something as simple as teething. Because he doesn't eat by mouth, his teeth took longer to break through, and he's unable to sleep through the night for almost three years, because he's had a longer level of teething.

(00:58:11):

Reese is a very happy boy, despite everything, and he keeps fighting through it all and works hard to overcome every challenge he faces. All we want is for him to be happy, and we want to do whatever is humanly possible to improve his quality of life.

Elizabeth (00:58:35):

Hello, my name's Elizabeth, and I am Caroline's mom. Caroline suffered from STXBP1 from the day she was born. In 1997, I delivered Caroline, and at 10 hours old, Caroline suffered the first of hundreds of thousands of seizures that would plague her short but eventful life.

(00:58:56):

We spent three weeks in the NICU trying to get her stabilized enough to get home to join her sisters. When we finally got to go home, we were told to make her comfortable and wait for the milestones. The milestones were delayed... very delayed. She sat up with assistance at 13 months, independent sitting at two and a half, along with combat crawling around that time.

(00:59:21):

Caroline walked at five years old, and soon she was running. She loved to run everywhere, especially places she was not supposed to go. And our daughters loved to snuggle Caroline, and our five-year-old Virginia declared one day how lucky we are that Caroline stayed a forever baby.

(00:59:40):

She was on multiple anti-epileptics to slow the seizures plaguing her life. A feeding tube was put in to help me feed her, as she choked and aspirated. To change her diaper, I needed a suction device to stop her aspirating her saliva. Caroline needed to be watched 24/7 to make sure she did not choke or seize, so we hired a nurse to help. Our entire family became CPR trained and certified. Even our nine-year-old was trained, and it was not uncommon for our girls to come home from school to find that Caroline and I had gone to the hospital, and they would be unsure when we would be home.

(01:00:23):

At age 12, Caroline suddenly, overnight, lost the ability to walk. She had long since lost any language that she had, and we went into the hospital to get MRIs and other tests. And eventually, in that appointment, the genetic testing identified STXBP1.

(01:00:43):

Caroline's genes were important and helpful. She happily donated blood when needed to help the babies. She would smile and put her arm out to let them draw blood. Her goal was to help the babies like herself. She was the oldest STX-er.

(01:01:00):

By 10 years, Caroline, despite all appearances, was quite able to understand, and she could sign "yes" and "no." She appeared to be cognitively impaired, but in some way, she understood very complex things. It's hard to explain, but her EQ was very high. She was empathetic and kind beyond what doctors could assess possible with her IQ. Caroline was eager to have fun. She loved to prank people, and she was popular with neurotypical kids. She was, quite frankly, amazing.

(01:01:38):

Physically, she was deteriorating, and we were all very, very concerned. But Caroline wasn't concerned at all. She never complained about her loss of ambulation, her loss of pincer grasp, her complete loss of swallow at age 15. She took it all in stride, and I explained it all to her along the way. I told her that she was losing muscle tone, that it was affecting her in many ways: her inability to walk, neurogenic bladder, functional obstruction of the bowel, her loss of swallow, and many other things.

(01:02:17):

Her only request at that time was not to go back to the hospital. On that topic, there was no changing her mind. No more hospital. We began palliative care, and then hospice care, which we described to Caroline as hospital at home.

(01:02:36):

Caroline at that time had begun to sleep 18 hours a day, and therefore, at age 17, she could no longer attend school. When awake, she was limp, unable to sit up, unable to use the potty as she had done. We still helped her have a quality of life. We might take her for a ride in her new tricked-out van that she got for her birthday with a 30-inch TV. She might use her pool lift to get lowered into the swimming pool or a snuggle in my lap.

(01:03:09):

She loved the water. She loved the beach. She loved Broadway shows. So, at that time, we snuggled in bed and watched Mamma Mia for the millionth time.

(01:03:20):

I could belabor you with the meds that we tried, the ketogenic diet that had her cholesterol over 800, the ICU visits, the times that she coded and was ventilated. But that is not Caroline's life story.

(01:03:35):

Eventually, she slept nonstop. "Sleeping Beauty," everyone said. And it sounds so comfortable and cozy, but it wasn't. It was hellish and terrifying to me, and to our extended family. We knew what was happening: that STX was taking her.

(01:03:53):

At age 18, just a few months after her huge Mamma Mia-inspired birthday party, Caroline died in my arms, just the two of us, in her room. She left us.

John (01:04:09):

My name is John, and my wife Isabella and I are the parents of Lucas. I have a PhD in molecular neuropharmacology and spent over a decade in early-phase clinical research prior to my son's birth.

(01:04:22):

Lucas is 13 years old, but to us, he still feels like our little toddler, even though he is over five-foot tall. During his first year, we believe we had a healthy child and had cleared any major health hurdles.

(01:04:36):

At 13 months, Lucas experienced this first cluster of seizures. We were led to believe that his seizures would likely disappear. For the most part, he was hitting his milestones. He loved functional play with toys, solving puzzles, and insisting that people greet him. He had learned to walk, and had a few words.

(01:04:56):

But as Lucas approached his second birthday, we saw him becoming withdrawn. He was initially admitted to the hospital for GI issues that led to weight loss and dehydration. After days of testing, it was the neurology team that appeared into our room with the most devastating news of our lives.

(01:05:14):

Lucas had hypsarrhythmia, and a developmental and epileptic encephalopathy. He regressed and lost many skills, including interest, engagement, and motivation. Within a year, Lucas was diagnosed with SDXPP1, and now has profound intellectual disability, autism, and requires our constant presence and help for all daily living activities.

(01:05:39):

He no longer has any words, but his receptive language skills are slowly improving, as is his ability as a teenager to selectively ignore us. We've had very limited success with augmented communication devices, which we believe is due to his lack of engagement and motivation.

(01:05:59):

If we aren't there when Lucas wakes up, he will wet his bed, which immediately adds to our day, as we must change his bedding and wash him. A large part of our day is spent trying to coax him to come. Starts with the toilet. Normally he will void while sitting on the toilet, but we need to ensure he directs his stream appropriately. Can take three to 30 minutes, which often makes us rush the morning routine.

(01:06:25):

We brush his teeth, wash his face, and moisturize his nostrils, as he is prone to severe nose bleeds that he worsens by vigorously rubbing his nose. If we leave his vicinity even for a moment, he'll immediately leave the bathroom, or dining room table, couch, et cetera, and we'll have to coax him back. We need to assist him down the stairs, as he has had falls due to inattentiveness.

(01:06:52):

For breakfast, we have to feed Lucas, then get ready for the school bus. We tend to dress him after breakfast, as he often drools any remaining food in his mouth and rubs it on his clothes. If he hasn't already peed, we need to get him back on the toilet so he doesn't wet himself.

(01:07:10):

Lucas does not sit much, and spends most of the day running around, often over 17,000 steps, stimming and pulling things off tables. Sometimes, he drops things on the floor that makes us think he fell from a seizure and gives us a shock. He always wears a hockey helmet, since we never know when he'll have a tonic drop seizure. He has injured himself in the past, and even losing a tooth that I was luckily able to save.

(01:07:39):

If Lucas has a seizure before the bus arrive, like yesterday, his language, it becomes postictal, and we have to wait before driving him to school. Approximately every four weeks, he has a seizure cluster lasting three to four days, which can affect his ability to walk, forcing us to keep him home.

(01:07:58):

He attends a special-needs school where most children have no communication skills when they start, but we've noticed that after eight years, he hasn't advanced much compared to the other children. We have to be careful because he does not understand danger, especially in the kitchen. We have a baby gate to prevent him from falling down the stairs.

(01:08:20):

Like breakfast, dinner's a slow process. Lucas shows little interest in eating, and we need to constantly encourage him to even open his mouth. He does not like chewing and swallows food whole.

(01:08:33):

He shows little interest in watching TV or playing with an iPad or toys. By the time he goes to bed, we are exhausted. Usually, he falls asleep almost immediately, but one or two nights a week he wakes up again, and then it takes some time to get him back to sleep. Last year we got a dog, but unfortunately, he's mostly indifferent to the dog.

(01:08:57):

Caring for Lucas has been extremely challenging, and we hoped things would incrementally improve. To the contrary, they're becoming incrementally more difficult. Feeding, drinking, going to the washroom are becoming more onerous. Engaging Lucas is challenging, which makes parenting and taking care of him very difficult.

(01:09:19):

Few things motivate him, and he seems to derive little pleasure from activities that even other children with disabilities enjoy. As Lucas gets older, we believe any treatment that could help him do more things even a little bit more independently, or pay more attention, would have a lifetime of benefit and simplify his care. Thank you for your time today.

Leigh Ann (01:09:44):

Hi, I'm Leigh Ann. This is my husband Grant.

Grant (01:09:46):

Hi.

Leigh Ann (01:09:47):

And this is our daughter Lucy. Lucy was diagnosed with STXBP1 at just three weeks old, and she's now two years old. She's our only child. She's the sweetest girl, and she's the light of our lives. Lucy was born August 26th, 2021, and the first-

(01:10:01):

Lucy was born August 26th, 2021, and the first time I held her she had a seizure. In a room full of nurses, no one noticed but my husband and I. And we didn't know what we were seeing. But by the next day when I saw the same full body twitching, we recorded it and we knew something was happening to our baby. The doctors finally took us seriously after seeing the videos, and she got her first EUG and the seizures were confirmed.

(01:10:26):

The neurologist we saw put her on phenobarbital and decided to do a genetic epilepsy panel. The seizures stopped but came back two weeks later and we were readmitted this time with more seizures than ever. During this day, she developed necrotizing enteritis that kept us in the ICU for over a month. We were also trying to figure out her swallowing issues at this time, and because she was aspirating, she needed an NG tube for feeding. During this first long hospital stay is when our genetic testing came back, and Lucy was diagnosed with STXBP1.

(01:10:56):

Throughout her first experience of life we were in and out of the hospital constantly. Lucy's low muscle tone makes her more susceptible to having more severe symptoms from common illnesses. She was hospitalized twice for complications from common colds. One admission lasted a week and required a spinal tap, but nothing is worse than watching your baby have seizures day and night. It feels like your house is on fire and there's nothing that you can do about it. Overwhelmingly stressful is the only way to describe it, but our love for Lucy carried us through the hardest days.

(01:11:27):

Thankfully, her seizures eventually stopped, but the symptoms of STXBP1 still impact every single aspect of her life and ours. From moving from a two-story house to a one-story accessible house after she was born, to her entire life savings plan, every decision has been impacted by her condition and her lifelong needs and struggles.

(01:11:49):

Lucy still struggles with swallowing and chewing, so she's bottle-fed almost all of her nutrition. She's still aspirating with liquid, so even bottle feeding is risky. She also has low muscle tone, which has affected her mobility. She's just started sitting without support but doesn't crawl, stand or walk, and potentially may never be able to do those things despite how much therapy we continuously do. Lucy also does not say any words, so communication with our daughter is extremely limited. Sometimes Lucy will make a sound when we ask her questions, but she's completely unable to tell us what she wants, needs or is feeling. Lucy has been in constant physical speech and occupational therapy since she was just over a month old. She works with all her might in therapy, but nothing comes easy for her.

(01:12:37):

There are so many simple, happy childhood moments that she doesn't get to have. At mealtime, she looks longingly at us eating and tries to pull drinks towards her so she can have what we're having, but it isn't safe, so we can't share with her. When we go to the playground, she's only able to sit in the baby swings and watch other kids run around, climb and slide. At family gatherings with her cousins or at playgroups, she

sees other kids and she's thrilled and she vocalizes and she calls out with so much excitement trying to interact and make friends, but the other kids don't understand her.

(01:13:13):

We see how much she loves life despite how hard hers is, and sadly, from what we know about STXBP1, we don't see it getting easier, we actually see it getting harder. If there was one thing that we could give our daughter, it's communication. We want her to live life without frustration of not being understood, and one day when we're not here, we want her to be able to have her needs met. We've heard so many parents describe all the growing health complications that come with kids with STXBP1 getting older, and we always try to focus on appreciating our time with Lucy right now, because we never know when her seizures could come back or she could permanently regress and all her hard work would be lost. We live in fear for the future of our baby girl for so many reasons. Nevertheless, we have so much more hope and love for Lucy than fear, and we're determined to give her a wonderful life.

PART 2 OF 9 ENDS [01:10:04]

Raquel, (01:14:10):

I'm Raquel and I'm Keyarah's mom. Keyarah's 20 years old and she was diagnosed with STXBP1 in 2017. When Keyarah, or Kiki, as we like to call her, was diagnosed, the doctor told us that there were about 300 known cases in the entire world. We knew early on when she was about one year old that she wasn't developing typically, and we immediately got her into various therapies. Over the years, she received many different diagnoses that described her symptoms, but the genetic diagnosis didn't come until she was about 14 years old.

(01:14:54):

Keyarah suffers from daily seizures that are not controlled by medications, and the seizures are debilitating for her. She has tonic-clonic seizures, partial absent seizures, drop seizures and repetitive episodes. In an effort to control her seizures, she takes multiple medications every day, including Topamax, Epidiolex, Briviact, and Onfi. She also has two rescue medications, Valtoco and Klonopin. It's really hard knowing that the side effects of all of her medications impact her overall quality of life and ability to make progress. We don't really have any alternatives. We tried the keto diets and that didn't work, and her situation is really unpredictable. Whenever she's having a seizure, I feel so helpless, I just can't help her, I just have to wait until it's over. Obviously I have to keep her safe through it, but I can't make it stop.

(01:16:16):

Keyarah also does engage in some injurious self dangerous behaviors. Keyarah also engages in some self-injurious or dangerous behaviors. Lately she does a lot of slapping, screaming, biting herself. She used to do a lot more head banging, and there was one time where she banged her head against the wall and she had to get some staples in her head. She used to run out of the door and down the street if you weren't looking or fast enough. And I kind of mentioned it a little bit earlier, but Keyarah's ability to communicate is very limited, and I can tell that it's frustrating for her. She's completely nonverbal, and I think one of the hardest things as a parent is looking into her eyes knowing that she wants to tell me things, but never being able to know what those things are. And when she was younger, I heard about regression and I always wondered and feared if it would happen to her. And so, I just mentioned that she would run out of the house, and she used to do that a lot. She'd run out of the house, she'd go into the kitchen a ton. I have pictures of her just drinking the Hershey's chocolate syrup. And that type of stuff was dangerous, and it was stressful. I could never... It was really hard to cook dinner because she'd be near the stove. But now it might sound crazy, I kind of miss those days because it's hard to get her... She doesn't stand up on her own, just from the couch. She can't really walk through the house by herself because her balance is really off and the frequency that she has seizures, she can fall. There's been a couple times where she was doing well, so I let her walk around and I stepped into the kitchen and I come back 15 seconds later and she's face down on the floor having a seizure.

(01:18:40):

And she actually, I took her to the dentist recently and I said, oh, it looks like maybe she's getting a cavity. And the dentist said, "No, that's from impact." She has two cracks down her front teeth where she probably face planted during a seizure. One of my biggest fears is, I feel like I could lose Kiki at any moment with the seizures. But then the next biggest fear I have is that she might outlive me and that she would be without the care. Because as I mentioned, I'm a single mom. I'm the one person providing all of her care. I am worried that as she gets older, her seizures are getting worse and that her overall happiness and quality of life consistently seem to be declining. As parents, we all want our kids to be happy and to experience love and joy and excitement. And every day it just seems like those are becoming less and less for her. I'm so terrified that she'll just continue to be sedated by the seizure medications. I'm scared that she'll lose her ability to walk and to feel happiness. If Keyarah was able to have the ability to communicate, it would be life changing. If she could communicate when she was in pain, if she felt a seizure coming on or anything that she needed after a seizure. There's so many things that she can't communicate to us, and I can't explain how much it would mean to hear Keyarah say, "I love you." I've never heard Keyarah say, mom, mommy. I think if there was a way she could communicate, her quality of life would improve so much and our family's lives would improve so much. I wish there was a cure for STXBP1, specifically the seizures. For Keyarah and for all of the kiddos with STXBP1. All of these kiddos urgently need help. Thank you for listening to my story.

James Valentine, JD, MHS (01:21:16):

Wow. Thank you, Raquel, for telling Keyarah's story, and to all of our panelists who were so brave to share first this morning and help us understand a bit about what it is to live with STXBP1. So now we're at our first opportunity in the day to broaden the discussion to all of you, our families living with STXBP1 that are in the live audience today. I'd like to invite you at this time if you would like to share on some of those questions we talked about related to symptoms and health effects that your loved ones have experienced. You can do so now by calling in. You can call in at +1 703-844-3231. Again, that phone number is +1 703-844-3231. As we talk about a number of different topics this morning, you can call in at any time and we'll go ahead and get you into our queue and we'll bring you into the live discussion.

(01:22:16):

I also want to mention that for everyone following along, there's also a comment box under the live stream on the webpage you're at today. You can submit written comments, many have already been coming in, and we'll be reading some of those throughout the program as well. But to get us all thinking about this topic of what it is to live with STXBP1, we're going to start off with a couple of polling questions. So if you can go back to that webpage, if you were with us earlier, or if you've just joined us. If you're a family member or other caregiver of someone living with STXBP1, please go to www.pollEV.com/STBP1. Again, that's www.pollEV.com/STXBP1. Just keep this webpage up throughout the entire day, as we go to different polling questions, they'll automatically appear there.

(01:23:11):

So this first question in our session here, we want to know which of the following STXBP1 one related health concerns has your loved one ever had? And you can select all that apply. The options are: A, fine and gross motor delays. B, speech and communication. C, seizures. D, tremor, including ataxia, unsteadiness and shaking. E, muscle tone, high or low tone or floppiness. F, behavior. G, socialization. H, cognition, including memory learning and information retention. I, gastrointestinal issues, including nausea, vomiting, constipation or diarrhea. J, diet or nutrition, such as poor or restricted appetite or texture or sensory differences. K, respiratory issues, including breathing concerns or infections. Or L, some other symptom or health concern that your loved one has had as a result of their STXBP1, that's not otherwise listed as an option here.

(01:24:17):

And I do want to note, this is the first question we've had today where our audience can select more than one option. So those percentages that you're seeing are the percentages of total responses, not the percentage of total people selecting any one response. So what I like to do, is think of those blue bars that you're seeing as a bit of a relative ranking amongst the different options.

(01:24:44):

So we see a number of responses still coming in on this. Again, we want to know about all of the different health concerns that your loved ones have ever had as a result of this condition. As it stands, it looks like some of our top most commonly experienced health concerns are the fine and gross motor delays, speech and communication related issues, muscle tone related issues. After that, we're seeing tremor, seizures and cognition as some of the top most experienced health concerns. Maybe as a third tier, we're seeing behavior, socialization, GI issues and diet and nutrition. We do have individuals represented who have respiratory issues as well as others. So as you're thinking about these range of different symptoms, we want to hear about how these different things are experienced and how they impact your loved one's life.

(01:25:44):

But if we can move to our next polling question, we're going to ask you to consider these same symptoms and health concerns, but now we want you to select the top three that you would rate as most troublesome, the most troublesome health concerns that your loved one has ever had. So again, the response options mirror the previous question. So: A, fine and gross motor delays. B, speech and communication. C, seizures. D, tremor. E, muscle tone. F, behavior. G, socialization. H, cognition. I, GI issues. J, diet and nutrition. K, respiratory issues. Or L, again, some other STXBP1 related health concern that you would report as a top three most troublesome concern that your loved one has ever had.

(01:26:40):

I promised these questions were going to get more difficult as the day went on. I'm sure it's very hard to narrow this down to just the top three most troublesome. So as you're making these selections, I want you to think about why, what came to mind as I was choosing? For those of you who are rating speech and communication, for example, which is currently our highest reported most top three troublesome health concern. What about that is making you consider that most troublesome? Even for some of you that are selecting some of the ones that are being selected less commonly, like socialization or respiratory issues, we want to hear about those, not just the most commonly selected ones, but even some of those that are being selected less frequently. So, it looks like results are still trickling in a little bit, but we're seeing kind of, again, a little bit of a relative ranking. We're seeing speech and communication as number one. Seizures, and close with that, fine and gross motor delays as two and three. From there, we see a little bit of a drop-off, cognition as number four. But we're seeing every single one of these except for diet and nutrition in some number of people's top three. So, not only from the first question did we see that people living with STXBP1 are living with quite a range of multiple different symptoms and health concerns, but now we're seeing that what maybe are some of the most important things to address vary a bit from person to person.

(01:28:20):

So, I want to thank everyone for participating in these first polling questions. Again, at this time we'd like to have you just weigh in and help us further understand these symptoms and health and concerns. Again, you can call in, that number is +1 703-844-3231. You can also write in using that comment box under the live stream here today. But I'd also at this time like to welcome our zoom panel, some of your peers from this community who will be sharing their experiences throughout the session. And let's maybe get things started off here, a discussion here with our panel. Cristina, maybe we can get started with you. As you're thinking about this wide range of different symptoms and health effects, are there one or two that really come to mind as the ones that are most troublesome? I'd love to hear that from your perspective.

Cristina (01:29:17):

Absolutely. Hi, I am Christina. My son Tristan, who turns 11 on Monday is my STXBP1 child. We come from New York and my son was diagnosed at five years old. The most troublesome, I believe, needs to be the communication, because he can't tell us what he wants to bring him joy, he can't tell us when he's in pain or what hurts or where. He actually fell this morning, face planted on the floor. He was celebrating because he was enjoying a video that he was watching and took a dive into the floor and just looked up at me with terror in his eyes. He couldn't even understand the event that happened to him. So it's hard to deal with the

fact that he can't communicate with us and I can't comfort him all the time. So I'd have to lead with communication.

James Valentine, JD, MHS (01:30:11):

And can you help us understand how he can communicate, and of course, what those limitations are, what ways he can't communicate?

Cristina (01:30:23):

Sure. He does have a communication device, an iPad, but it is extremely limited. He will point to... We're limited to kind of nouns. He can point to what he wants, a Buzz Lightyear, the TV, things like that. But he also sometimes might only be pointing to it in order to get our reaction. And we think that's his way of conversing with us. He hits something that's not relevant and we react. So it's good because he's communicating, but nobody knows exactly what he's communicating. So there's that, he can point. We celebrated when he brought the television remote to us once, which was only about six months ago, which showed us he wanted to watch something on TV, which is his primary activity, sadly. So there's little ways, but there are ways that only we really understand, it doesn't translate out into the real world.

James Valentine, JD, MHS (01:31:13):

Sure. And you also mentioned one of the reasons that communication is so important to you is you're not able to know or understand if he's in pain or why he's in pain. Can you talk about, or maybe share an example of a time that you were trying to communicate with him to understand and what that looked like, knowing that ultimately that's a challenge and something that you're not able to do?

Cristina (01:31:47):

It's hard to come up with an example because it's almost every interaction. Even mealtime, "Do you want what I'm offering? Do you not want what I'm offering? Do you understand what's going on?" It's almost every minute of the day because he does not understand yes or no, and he can't communicate back yes or no. So it's sort of a constant guessing game and it can get pretty exhausting. Even just this morning with the cut on his lip, when he fell down and hit his face, he just didn't understand why I was trying to blot the blood. It's constant.

James Valentine, JD, MHS (01:32:21):

Wow. Thank you for helping me understand that. One last question for you, just again, so we can understand his communication difficulties. Has his level of communication always been at this level? Were there ever times where he was able to communicate more than he does now or has this been the best he's been able to communicate?

Cristina (01:32:48):

This is his best. We get progressively, very slowly, we get improvements. We have yet to experience regression and we count our lucky stars every day.

James Valentine, JD, MHS (01:32:58):

Sure. Well, Christina, thank you so much for sharing that. And very, very illuminating hearing some of those examples. Russ, I'd like to bring you into this conversation as well. Again, there was such a wide range of different symptoms and health effects. Does anything come to your mind as the one or a few that are most troublesome?

Russ (01:33:21):

Absolutely, yes. Can you hear me?

James Valentine, JD, MHS (01:33:22):

Yes, we can hear you.

Russ (01:33:24):

Great. Good morning. My name is Russ. I live in Danville, California, and my daughter, Katie, is one of our older STXers. She's 20 now. I would say my top three concerns would be seizures, cognitive capabilities, and

then motor planning. And I just wanted to spend a minute on motor planning, because that's what's caused us a lot of angst over the years. Katie is a high risk of falling, and there's been two cases where she's fallen at school, face plant, because she has no reaction, no reflex to brace herself. So head first down onto the ground and would jeopardize her front teeth. So it's an emergency, you rush to the dentist, you rush to the oral surgeon, you brace them up. And we have been able to save them, this happened on fifth grade, happened in 12th grade. We have all the systems in place to help protect her, but she can get away from you in a second and boom, she's very unstable and she goes down. So that's a tough situation.

James Valentine, JD, MHS (01:34:41):

Yeah. No, that's really interesting to hear. I'm kind of curious, it sounds like, obviously she has the ability to be mobile and be kind of up on her feet out and about. Can you maybe talk to us a little bit about what she's able to do from a motor function perspective and what activities then she's participating in where this lack of motor planning might come into play?

Russ (01:35:13):

Extremely limited. Her range of motor skills are so, so small. Upper body and fine motor, she can't pinch, but she can grab and drink from a sippy cup or eat off of a fork. But absolutely no way could she use a spoon or an open cup glass, and she's 20. So on the gross motors, like I said, she's very unstable to move. That was our one joy, being able to take her for a walk to the park a couple times during the day, but she's apprehensive to do that now because she's scared of falling. Who wouldn't be, right? So that's playing into it as well

James Valentine, JD, MHS (01:36:01):

Yeah. And have that instability and falling, has that, as she's gotten older, become more of a thing that she was experiencing and therefore becoming fearful of it?

Russ (01:36:15):

Yes.

James Valentine, JD, MHS (01:36:16):

It has been?

Russ (01:36:16):

Yeah. Absolutely. She used to charge around and we would play chase and tickle. And it was so much fun. We can't now. She will not walk on her own. Katie has to have someone holding her hand, and at school or the carer that comes to the house, we have to put a gate belt on her and someone has to be holding on and she wants to hold on for dear life with her hand. So she's terrified of falling. So yeah, we regressed. Katie is no longer able to walk on her own now.

James Valentine, JD, MHS (01:36:49):

And if there is, it may not be, it might be hard to pinpoint a moment in time, but when did that transition happen from that regression to needing so much support just to be mobile?

Russ (01:37:06):

Throughout high school, over the past couple of years. So say from 15 on it got clumsier more awkward. And once she fell again for the second time in 12th grade, then she doesn't want to do anything on her own.

James Valentine, JD, MHS (01:37:26):

Okay. Yeah, so that particular event really made an impact on her?

Russ (01:37:31):

Yeah.

James Valentine, JD, MHS (01:37:31):

Well, thank you so much, Russ, for sharing that. I do see, we have a phone caller that I'd like to bring into the conversation. We have Jason from California who's a parent and wants to share some of the symptoms that

have been most impacted on his loved one's life. So Jason, I'd like to welcome you to the program. Are you with us?

Jason (01:37:52):

Hi, good morning. Are you able to hear me?

James Valentine, JD, MHS (01:37:55):

We are. Welcome.

Jason (01:37:57):

Thank you. My name is Jason. My wife and I live in California with our 17 year-old son who lives with an STXBP1 disorder. Even though seizures are already a concern, most difficult symptoms of STXBP1 for us have been cognitive impairment and communication. With cognitive impairment, the lack of safety awareness, both in our home and in the community, along with the inability to care for himself and provide basic daily living needs such as feeding, dressing, bathing, toileting incontinence, shaving. Essentially, he functions at the level of a toddler. With communication, he has no words and does not respond using receptive communication except at a very, very basic level. He cannot tell us if he hurts, if something is wrong, what he likes, dislikes, or how he feels. We have actually never had a real conversation with our son.

(01:38:58):

His lack of communication leads to extreme behavior issues and prevents him from engaging in meaningful interactions with others. Both his cognitive impairment and lack of communication drastically affect his quality of life and that as our family as all. Anyway, that's what I wanted to share with you and the audience, but thank you very much for the opportunity.

James Valentine, JD, MHS (01:39:19):

Yeah. And Jason, if you don't mind me asking, first, thank you so much for sharing that and being willing to share. I'm just curious to help us understand the safety awareness aspects, you said that has this whole cascading effect on so many different activities that he can't be doing independently. Are there any examples that come to mind that really might help us understand what that lack of safety awareness looks like?

Jason (01:39:51):

Oh yeah, absolutely. Just think of anything in anyone's daily living life. Like I said, he is at the level of a toddler and all of the different things that a child of that age would get into, and anything from being in the kitchen and hot stoves, lack of awareness, situational awareness in terms of if... He's very mobile, so if he's outside not being aware of his surroundings and potentially walking into the street. The bottom line is it requires absolutely constant watching over him to make sure that he's not getting himself into trouble. And again too, not being able to actually explain the consequences of why he shouldn't do something or why we have to stop him from going into an area around the home or whatever.

James Valentine, JD, MHS (01:40:57):

Sure. No, that is very helpful to understand. So Jason, thank you again for so much, for sharing the range of different things your son's living with, but then giving us some idea of what that actually means in terms of the family and what daily life looks like. I see we do have another phone caller that I'd like to bring into the discussion. We have Sam from New York, a father of a three-year-old that would like to share the biggest impacts of STXBP1. So Sam, I'd like to welcome you to the program. Are you with us?

Sam (01:41:36):

Yes. Can you hear me okay?

James Valentine, JD, MHS (01:41:38):

We can. Welcome.

Sam (01:41:42):

So yes, as you mentioned, I'm a father of a three-year-old, Florence. We live in New York. We recently moved from Michigan to New York about a month ago. She was getting ready to start preschool and it was really hard to find resources and support in Michigan. It unfortunately isn't very supportive when it comes to special needs people. So yeah, we relocated to New York to get her in a program and to get the support that she needs. And she just started school and she is in a special needs classroom and she's the most impacted, at least it seems like the most impacted kid in the class, but it's also really inspiring to see her in an environment where she's seen. And so that's been great.

(01:42:36):

But the biggest challenges that we've had has been communication. She actually just got her AC device in the mail yesterday, she's had a loaner for a little while, so we're really striving for communication. She had a moment where she could say maybe two words or so. She could say ball and a couple of things that were close, two words, but she lost those not long after she said it. But she's very vocal, but she doesn't say words. She's not mobile. So every day we're constantly working on getting her to walk, to stand, to communicate, to hold onto things, to eat things properly as she grows. Now that she's three, the amount of things that we're working on is endless. It seems like there's not enough time in the day, in the week, the month to get to all of the therapies, to all of the things we need to work on. And it's constantly stressful feeling like I'm failing and I just want to see her thrive.

(01:43:42):

And hearing everyone's stories today, thank you for sharing those. But as she gets older, we're going to start... Things are going to get more challenging. And so yeah, we're just trying our best and thanks for doing this today and thanks for all the parents out there for sharing your stories.

James Valentine, JD, MHS (01:44:01):

Yeah. Well, Sam, we really appreciate you sharing your and your daughter's story. She's a toddler and you're trying to do so much to help her. I am sure beyond this, but you shared about communication and of course about mobility. If you don't mind me asking, you talked about working on communicating through a device that she doesn't really anymore have, the ability to communicate verbally. I guess, could you describe what level of nonverbal communication that she's able to do today? Just give us a little bit of a better picture of what that looks like.

Sam (01:44:48):

Yeah. So she constantly asks for Miss Rachel on her device. She can navigate two menus [inaudible 01:44:55] Miss Rachel. So, I know that she's got the ability to get things if it's motivating enough. That's the biggest thing I'm sure a lot of other parents...

PART 3 OF 9 ENDS [01:45:04]

Sam (01:45:03):

To think if it's motivating enough. That's the biggest thing I'm sure a lot of other parents can say is too, is just finding the right motivator. If they're motivated enough to want something, whether it's a certain food, or a certain TV show or whatever it is, they will somehow find a way to communicate that. But she has a pointer, and she will point on the device, but she's not always really accurate. You're not really sure exactly if she really wants Miss Rachel, or if that's just a muscle memory thing that she's doing all the time. I know she does want Miss Rachel all the time though. She does a little bit of signs, she asks for more.

(01:45:39):

We had an ABA therapist taught her that. We didn't even know they were working on that. And one day she started doing the thing with her hand, and I was like, "What is she doing?" And I asked her therapist and they're like, "Oh. Wow. She's doing more", which is great. So she tells us when she wants more things, and we hope that she holds onto that. But other science has been really challenging. But yeah, that's kind of where we're at.

James Valentine, JD, MHS (01:46:01):

Sure. Well, again, really appreciate you sharing that and giving us that glimpse into your lives. So important to understand all of these ways that STXBP1 are affecting these little ones navigating life. So thank you again, Sam. I'd like to come back to our Zoom panel here, and maybe what I'll do is see if anyone on the panel, we've talked about a number of different symptoms and health concerns related to STXBP1. Is there something that you all would want share that we haven't hit on yet? You can just give me a little wave of a hand. Yes. Kristen, and then we'll come to Ana.

Kristen (01:46:41):

Hi everyone. My name is Kristen. I have a four-year-old little boy named Elias. He started having seizures at three days old, and then was diagnosed with SDX at five weeks. I always expect that everyone's going to talk about seizures, because it affects our lives so much. So I guess I will talk about seizures. He had just started off with life basically at three days old, before we even left the hospital, having seizures. Went to the NICU, started on phenobarbital. That helped for a little bit, but then by a month of life he had hundreds of seizures a day, which progressed into infantile spasms, and we've never been able to control his seizures. Sorry.

James Valentine, JD, MHS (01:47:28):

It's okay.

Kristen (01:47:29):

He has right now about 15 clonic seizures a day. So seizures of course impact everything. So low muscle tone, every one of those symptoms I clicked on the poll, because seizures really impact everything. So until we can get those figured out, which we never have been able to really everything is affected.

James Valentine, JD, MHS (01:47:53):

Yeah. Well, thank you for bringing up seizures, Kristen. And you know, we saw in the polling that that is something that many people live with and we heard in the clinical overview that as well. So I do want to maybe ask, you said it kind of impacts everything, low muscle tone. Have there been any periods of time, just I don't know if whether it's been in the span of days or weeks, where seizure burden has been a little less than others? Has it been pretty consistent over time for you all?

Kristen (01:48:31):

It changes all the time. So every time we visit with the doctor, it's always something new. But we did have three months of seizure freedom from starting an over the counter CBD oil that I found online. So that was the best three months of his life. It happened around 13 months, I want to say, old. So yeah. We were for three months and we saw a significant change in behavior, just a happy guy. He has very low muscle tone, so he uses a wheelchair.

(01:49:05):

He cannot hold his head up at all. He cannot use his body really at all by himself. So we saw just even change in he was bringing his hand to his mouth, which he's never done before. We had him in intensive physical therapies, because it was the best time for us to really focus on, "Let's use this time right now, we don't know how long we'll have it", to really, really help try to improve some of those motor skills. And unfortunately, his molter started to come in, and that just all the seizure freedom went away, and then basically we progressed into what is called Lennox-Gastaut syndrome, which is just a severe type of seizure disorder.

James Valentine, JD, MHS (01:49:50):

Right. Well, I mean I think it really helps make an impact for me to hear about when there was that period of seizure freedom, what activities, and functioning, and even just quality of life was impacted for him. I guess I'm wondering does he have good days and bad days, even just today versus yesterday versus a few days ago? What does that look like?

Kristen (01:50:24):

Yes. Absolutely. So one of the hard things is kind of how I was saying everything really builds on top of each other. So respiratory issues is a big one for us. So we started him in school because we've never been able to

take him to daycare. We want him to be involved and have that normal kid experience. So he goes to school full-time when he's healthy. But of course with that comes getting viruses, and having such low muscle tone is just so susceptible. And he's never been around other kids to really, really build his immune system. He's our only child. So just when he gets sick, his seizures get off the charts. And so it's not only managing the sickness and respiratory issues, which we've had. We have oxygen at home. We have a number of devices to try to keep him healthy from home, because a lot of times, even just the common cold will send us into the PICU for a week.

(01:51:24):

So we've basically taken the hospital home with us, but with the seizures, it's really up and down. Whenever he's sick, he has a lot more. And then when he is healthy, he's still probably having 10 or so a day, but they don't affect him as much with the postictal stage. Where he's not necessarily knocked out as much afterwards when he's not feeling well. Those seizures, a lot of times we'll just take him out for 30 minutes at a time-

James Valentine, JD, MHS (01:51:58):

Wow.

Kristen (01:52:00):

... and then he'll wake back up and then he's having another one. And so it's just this snowball effect.

James Valentine, JD, MHS (01:52:03):

Wow. Yeah. Thank you Kristen, for sharing. And Anna, I want to bring you into the conversation. You said there was something we hadn't covered yet you'd want to share.

Anna (01:52:12):

Thank you. And really it's piggybacking off of what Kristen was talking about, the rollercoaster of epilepsy management. So my name is Anna, my daughter Ella, she'll be 20 at the end of the month. We live in Pennsylvania and Ella was just diagnosed at the age of 18 with SGXBP1. So we're a little bit newer to the community and appreciate everybody's time today. So Ella's story is a little bit different. She didn't start having seizures until she was 12 years old.

(01:52:43):

She started with tonic-clonic seizures that were fairly well managed by one medication, slowly added a second medication, but still did not have too severe of an impact on her life. And then around the age of 15 started having much more frequent seizures, changes in seizures, and that's when we sort of learned that epilepsy management was not going to be a simple one or two-step process for us. So Ella has been probably on dozens of different anti-epileptic drugs. It's really challenging to determine when things are working, when things are not working. They all have very significant side effects. Some have been pretty adverse. They all require monitoring, frequent trips to see neurology, frequent EEGs. Because the communication being maybe the equal or second most concerned, she can't tell us how they're making her feel. So we don't know is she nauseous? Is she tired? Is she hot?

(01:53:53):

How are these medications making her feel? And is it worth whatever small seizure reduction that we're seeing from them?

James Valentine, JD, MHS (01:54:00):

Interesting.

Anna (01:54:01):

She's been on as many as six at once. So we think about polypharmacy with epilepsy management. That was not a good situation for her. We were very grateful for the SBXBP1 diagnosis, because that got us to the right epileptologist that understood the disorder and had a little bit more knowledge of how to treat it and get her on more appropriate medications. She's been on a classical ketogenic diet, which means that well, every piece of her food is measured down to the gram weight. She was on as low as 11 carbs a day for a 19-year-

old, which really wreaked havoc on her physiological cycles, on her ability to digest food on her, sleep on her mood, on her behavior.

(01:54:51):

Again, she had no agency in that decision. Those are things that we are doing to her, hoping to do something for her, but she can't say if it's worth it or not. So that's a constant roller coaster and a constant task of deciding things for this woman now who's an adult, and can't participate. And that's very challenging. Most recently this year she had a deep brain stimulator implanted, which again was a nine-hour procedure that she didn't get a choice in, but we are trying to help her.

James Valentine, JD, MHS (01:55:33):

Yeah. Wow. Well, Anna, thank you so much for sharing that and helping us really not only understand more about the impacts of seizures, but really how communication and trying to navigate treatment approaches is impacted by the inability to understand the tolerability of these different and burdens of these different treatments. We are going to be focusing a lot on those in the afternoon, but as we're talking about symptoms and health concerns here, I don't think I've heard yet that talking about communication is actually making the autonomy of the person taking the products have a role in making those decisions, and or even being able to communicate the type of information that helps you make those decisions. So really appreciate you adding there. I do see that we have a lot of written comments that have been coming in this morning session. So do want to check in with Charlene to see what are some of those that have come in so far?

Charlene Son Rigby (01:56:39):

Yeah. James. So I'll share a couple here. This is from Sean from Georgia, "My daughter has had intractable seizures since she was a baby. She's now 17 years old, and on seven or more anti-epileptic medications and still suffers from seizures every day. She has now developed drop seizures and has suffered a lot of falls. We have to be by her side 24/7 to catch her from seizures." Should I share another one?

James Valentine, JD, MHS (01:57:09):

Yeah. Please do.

Charlene Son Rigby (01:57:10):

Great. So this is from Kevin in Seattle, "Our son's intellectual disability leads to many secondary challenges. In addition to communication, he'll likely need diapers forever. He'll run away if we don't hold onto him while out. He has no sense of safety whatsoever."

James Valentine, JD, MHS (01:57:31):

Great. Well, thank you for everyone who's been writing in. We're going to continue looking at those and sharing those throughout the program here. Know that if we don't get to your comment, we do have that information and we're going to incorporate that into that voice of the patient summary report. So I want to broaden the discussion a little bit. We've heard some of this already about how these different symptoms and health concerns impact what things your loved ones can do in daily life, but we want to more directly talk about that, and try to further understand how activities in daily life and quality of life you are impacted because of STXBP1.

(01:58:10):

And we're going to go to a polling question again here to get us all thinking about this topic. So please go to that webpage, www.PollEV.com/STXBP1. Again, you can keep this up throughout the program. This is for our caregivers, family members of those living with STXBP1. Here we want to know what specific activities of daily life that are important to your loved one are they not able to do or struggle to do because of their STXBP1. And here, we want you to select the top three.

(01:58:49):

So again, as you're thinking about this and selecting, we want you to maybe think a little bit about what about your loved one's STXBP1 makes these activities difficult or impossible, and why amongst all of these

different impacts the ones you're selecting represent kind of one of those top struggles. So the options here are "A, communicating wants and needs. B, self-care, including feeding and hygiene. C, using the toilet. D, engaging and learning. E, muscle tone, including higher low tone and floppiness. E, participating in community outings. G, social interaction and participation. H, regular sleep. I, walking. J, attending school or having a job. K, sitting up." Or, "L, some other activity that's important that your loved one is either not able to do or struggles with due to STXBP1 that represents a top three most impacted activity that's important." (01:59:52):

So we'll give you a few moments here to get your responses in to this question. Selecting your top three activities that are most impacted. As it stands, and we've been hearing this theme already, but certainly want to even better understand what this actually looks like, and how this impacts daily life, which is, "The impacts on communicating wants and needs." We see another top response here is, "Self-care, including feeding and hygiene." Those are I think really clearly the top two. After that, we see, "Social interaction and participation using the toilet." And then pretty much actually every other single thing here is in a number of people's top three important activity that's impacted. Although no one here so far has selected, "Other." Some other activity that represents a top three biggest impact. So I'd like to come back to our zoom panel here now that we've thought about this polling question a little. And Melanie, we'd like to bring you into the discussion here as you're thinking about that range of different activities that are either difficult or impossible, what maybe stands out to you as one of those?

Melanie (02:01:14):

Absolutely. First, I'm Melanie. I live in Pittsburgh, Pennsylvania. We have a seven-year-old daughter, Eva, who presented with seizures within her first hour of life. And we received the STXBP1 genetic mutation diagnosis when she was about four months old. I'm a crier.

James Valentine, JD, MHS (02:01:32):

Oh. No worries.

Melanie (02:01:32):

I feel it coming, just to let you all know. So the three that I chose on the first poll would be, "Speech and communication, seizures and fine and gross motors." Which translates into this question here.

James Valentine, JD, MHS (02:01:47):

Sure.

Melanie (02:01:48):

The three that I chose is again, "Communicating wants and needs, self-care, specifically feeding and hygiene as well as social interaction and participation." And I'll relate those second to the self-care as well as the social interaction back to the lack of fine and gross motor skills.

(02:02:07):

Our daughter is non-ambulatory, so we make decisions for her where she wants to go or whatever she needs to do. She does eat by mouth, but we feed her. So I've been preparing food for about seven years and dicing and chopping. And I'm certain that I'm going to have carpal tunnel syndrome someday with all the knife work that I do in the kitchen.

(02:02:33):

And I think too, that her inability with gross motor and fine motor things, we have three kiddos, Eva's the middle, but it's hard for her to play with her sisters, excuse me. You can tell by the look on her face, her eyes light up. She wants to be around her family, but she can't pick up the toys that her 10-year-old and two year old sister can. She can't interact with them the way that is appropriate or necessary. She brings a lot of things to her mouth, which is fine, but then she just quickly loses interest. Even though you can tell she wants to so badly interact and play with them, she's really unable to, because of the lack of the fine and gross motor skills. So that deeply affects her social interaction and participation. I know it's like that at home and she does attend school, which is one of her happy places.

(02:03:31):

But I know even there, she wants to be around the kids, she wants to interact. She cannot communicate that. She also has a hard time playing with others, playing meaningfully with toys. And I think that kind of excludes her from a lot of things because of that.

James Valentine, JD, MHS (02:03:50):

Yeah. Melanie, I mean, you're describing so well the interplay of all of these things. It's not just one symptom, one health concern that makes socialization and play difficult. It's this combination of communication and fine motor skills and so much more. And likewise with you're describing being able to feed herself and eating and there there's so many different aspects of STXBP1 that makes those things difficult. Maybe just on the topic of playing with whether it's her siblings or her classmates, are there types of play or modified play that where you find she is enjoying that certain things? You said she loses interest quickly, but just maybe to understand where maybe she does find some joy and brings her greater quality of life compared to some of those things that are more difficult.

Melanie (02:04:56):

Sure. So Eva, I think like a lot of our kids, she's best at big movements. Not small movements, but big movements. So you can always tell that she's interested, that she has the desire to play to participate, but if there is a musical instrument that she can bang on, if there's a drum, or something that she can shake in her hand, a tambourine, she can do that pretty well. And she knows that she is producing music sound, which she loves automatically. So I would say those are the better types of play for her. Anything that involves a bigger, larger movement.

James Valentine, JD, MHS (02:05:31):

And so the banging was one example of that. Are there other big movements that you put into that category?

Melanie (02:05:41):

I mean, she loves bouncing. Like if she's on a trampoline.

James Valentine, JD, MHS (02:05:45):

Okay.

Melanie (02:05:45):

She bounces herself on the floor. We are always having to get a dynamic headrest for her wheelchair, because she loves to bounce. She loves that movement. So when she's excited, you can certainly tell-

James Valentine, JD, MHS (02:05:58):

Sure.

Melanie (02:05:58):

... and she does just like to move in general.

James Valentine, JD, MHS (02:06:02):

Well, thank you for sharing all of that, Melanie. I do see we have a phone caller, Jason from Atlanta, Georgia, who's a father that wants to talk about some of the things that make the ability for his six-year-old to participate in activities in life more difficult. So Jason, I'd like to welcome you to the program. Are you with us?

Jason (02:06:29):

Yes. I'm here. Can you hear me?

James Valentine, JD, MHS (02:06:30):

Yes. We can. Welcome.

Jason (02:06:33):

Hi. Thank you for having me. I just wanted to kind of share some of my experiences with my daughter Juniper. She has XTSP1, she's six now. She was diagnosed at six months after a panel was taken due to seizures. So actually it was six weeks old, excuse me, she started having seizures and then we had to go to the hospital and found that she had STXP1. She does take medicine now to control those seizures. She takes on the Topamax and Klonopin for emergencies, but those medications, they worsen or make I think more challenging her other symptoms that she has. Which are global delays in walking, speaking common language, she can't feed herself, she can't dress herself, she can't use the potty.

(02:07:29):

So we all have to facilitate all that for her, it creates a real lack of autonomy for her. That breaks my heart, because she has a twin sister who is neurotypical. It's fraternal, and can see as they grow older, the gap widening. Laurel can run outside and go play on the playground in the backyard. She can ask us to have a friend over. She can play with toys that Juniper can't play with. And Juniper watches all that happen, and can't communicate to us what she wants to do, much less go out and participate herself. So their abilities and their differences as they get older are just getting more and more obvious. We just want her so bad to be able to participate, but we don't know sometimes if we're even projecting our own preferences, right? Like I'll take her on the playground when we go on more of a public playground and try to get her to participate in that.

(02:08:40):

But sometimes I can't tell does she enjoy me kind of holding her body up to make her way around or would she rather just sit there, but when she sits in the swing and watches others, I can see this light in her activating that she wants to go and do these things. So it's all just really hard to kind of watch. And there's just all those social implications as well, where she's not talking common language yet. So she does use an AAC device and she has a couple of words on that device, that she'll kind of go to, it's still very emerging. And we even see situations out in public where people will say hey to her twin sister.

(02:09:29):

But they don't really acknowledge her Juniper, because she's not able to outwardly speak. It just kind of feels like we obviously as her parents, it's heartbreaking. It's also really difficult physically to just facilitate everything by carrying her, assisting her walking, trying to keep her AAC device always, and her access, having to do the guesswork and figuring out what her communication needs are, trying to feed her while we're trying to eat. We go out to dinner. It's hard to even communicate with other people at the table, because we have to really focus on feeding Juniper.

(02:10:09):

We have her toileting how to change her diapers. She has accidents that we have to clean up quite a bit. And then I think a lot of things that maybe haven't discussed yet that kind of come to the parents is just also just like the paperwork. And I know that's not to the kids, but my wife and I both have full-time jobs, and it really is a full-time job to help with Juniper. And we're just overwhelmed, overburdened, exhausted, and I don't feel like we can give her what she needs with what's available today. So I really appreciate you guys setting this up and making this opportunity for us to tell you our story. And I'm happy to answer any questions, but those are kind of the real-

James Valentine, JD, MHS (02:10:54):

No. Jason you did-

Jason (02:10:55):

... high-level things that we struggle with.

James Valentine, JD, MHS (02:10:58):

I mean, you gave such great vivid examples of these challenges, and what those really look like for Juniper and your family. I guess just one question that I do have is those ability to play or engage on the playground, or some of those things that you described as the self-care that she can't even do herself, lacking autonomy,

are those all situations where those are skills that she's never had, or were there any skills that were attained at some point, that were lost for her?

Jason (02:11:43):

Juniper's had occasional kind of mild regression in areas, particularly pertaining to gross motor. But I think that has a lot to do with just sometimes when we have her like go through for an example an intensive, she'll have these gains, and then as time wears while she's in school, sometimes it will regress a bit. But in terms of her overall trajectory, she's done really well to continue to have these slight improvements. I know in our community we kind of call them inch stones. They're like milestones, but smaller. And she's still having her inch stones, but occasional smaller setbacks.

James Valentine, JD, MHS (02:12:24):

I see. Well, Jason, thank you so much for calling in and sharing all of this. It's so important to hear these different experiences. And again, as we're focused on impacts on activities, hearing how the interplay between a lot of these different symptoms and health concerns actually together contribute to some of those impacts. I see we have another phone caller I'd like to bring into the discussion, which is Sarah from St. Joseph, Missouri, who's a parent of an eight-year-old, and wants to talk about some of the impacts on activities that result from different behavior issues and communication. So Sarah, I'd like to welcome you to the program. Are you with us?

Sarah (02:13:08):

I am. Thank you. My name is Sarah and I'm from St. Joseph, Missouri. And I had Kennedy in 2015, and as soon as I had her, she had seizures. She turned completely purple. She was having one to 200 a day. They stopped them in the NICU. She was able to come home and she started walking about two and a half. And as soon as she started walking, I started noticing that her behavior instantly, she would not sit still. She was just go, go, go, go, go, to the point where she would pull everything. We cannot have any decorations at all. She's eight years old now, so our house looks like we just moved in with no decoration. She climbs everything. So our kitchen table, our buffet, anything, she climbs. She doesn't really feel pain like other kids. So she's fallen off, she's busted her tooth-

James Valentine, JD, MHS (02:14:10):

Wow.

Sarah (02:14:11):

... didn't cry. And it's just constant with the movement. So if you put her into her chair, she bangs it so bad that I mean, even with the wheels blocks, she just go, go, goes.

(02:14:25):

She is hand fed. So we have something we call the Kennedy Radius, the baby radius, so we cannot have any food or anything in her vicinity because she will pull it right off. And this goes with communication. She is like an infant baby, so she still puts everything in her mouth. So we've tried the communication device, it was a loner device, and because she didn't make any progress, they took it away from her. So she's eight years old, and she's still putting everything in her mouth. So my cell phone, the communication device, she breaks the glass. If we have anything on the wall, she'll knock it off, and bust a glass and that.

James Valentine, JD, MHS (02:15:02):

Right.

Sarah (02:15:02):

She has no interest in other kids at all. She's just kind of wanting to play with herself. And she does keep herself occupied, she really does. She's really good at that. And so anytime if I have to go to the bathroom, she has to go in her room. So I go into the kitchen to cook, she has to go into her room. We do have a baby gate that keeps her from being able to go into the kitchen, but that's still not safe.

(02:15:26):

She will climb, like I said, anything she can, or pull anything she can over a dresser over on top of her if she could get the chance to. Like we can't have a dresser in her room. Her room just literally has her bed, her toys and a swing in it. And even the swing has become pretty dangerous, because she gets to go in so high on it. And it's not like a swing where you would hold on like you would see at a park or anything like that. It's one that she can sit in and rest her back on, because she does not understand how to hold on at all. So she does not have that cognitive ability.

James Valentine, JD, MHS (02:16:01):

I see.

Sarah (02:16:01):

But she can walk. So she's like a whole whirlwind, just like getting her out of the car. She doesn't want to go into the house. She loves to be outside, and she has no danger concept. So she doesn't know what a car is, or a street is, or how that can affect her. So she will fall to the ground and if you do not have a good hold on her, she will take off running. And she has gotten super fast, and it's really scary. We have an alarm in our house that beeps anytime any doors open, any windows open. Not that she could open a window, but just in case. So we have to take a lot of steps to keep her safe. And I haven't really heard a lot of behavior mentioned, which is kind of shocking to me because Kennedy, she never stops moving. I mean, when I say that, it's literal, never stops moving. So we're always trying to find something to keep her occupied, and it's really hard.

James Valentine, JD, MHS (02:16:54):

Yeah. No, it sounds incredibly hard. And I mean all of this is just within the confines of the home. I can only imagine trying to leave the house and where it's, you have less control over that environment and what that looks like. I guess that might be a good question, does that impact how much or what you do outside of the home as well?

Sarah (02:17:20):

Oh. It absolutely does. We actually don't really go a lot of places with Kennedy. If we do, one of us sits in the car, my husband or I does, because in public settings, she gets overstimulated. Even going to Walmart, going to a restaurant, going to a park, going anywhere, she gets overstimulated, and she just hollers. And it's not like screaming badly. She is just in excitement, top of her lungs, hooting and hollering. And for us, we think it's cute. It's cute to us, because it's nice to see her vocal, I think. But to other people, people stare at us constantly. So it's definitely hard to take her out into a public setting. And like I said, even if I do take her out, she would have to be in her wheelchair because she would never stay with me and I couldn't just hold her hand. She would drop to the ground and roll until I could let go of her, because she was hurting me or hurting herself, and then she would just zoom off.

James Valentine, JD, MHS (02:18:20):

Wow. Well, Sarah, thank you so much for calling in and sharing all of that. Really enlightening hearing that and those examples. I want to come and check in with our Zoom panel here to see if there's some impacts on daily life that maybe we haven't touched on as much, or you have a personal take. Russ, I see you raising your hand there. I would love to bring you into the conversation

Russ (02:18:43):

Just to lighten things for a quick second. I did want to share that I think all of us parents of SXTBP1 kiddos are the world's greatest detectives. Call us all Sherlock Holmes, because it's so hard to figure out what our kiddos want. You got to follow that glance, or watch for that gesture, or listen for the hum versus the cry. So kudos to all of us for being clever and being good detectives. Just to comment.

James Valentine, JD, MHS (02:19:15):

Yeah. I mean, I guess Russ, I think you have a good idea in your mind of what that looks like. Maybe is there a little story that you can tell that shows where you had to put on your detective hat and figure out the answer to the puzzle?

Russ (02:19:36):

Oh boy. Well, occasionally Katie will kind of hoot when she's happy. And at night, at 2:00 or 3:00 in the morning when you get up to go to the hoot and see is she cold and she needs to be covered? Or do you need to change her diaper? Well, where we live, there's some redwood trees in the back, and turns out her hooting sounds exactly like an owl-

PART 4 OF 9 ENDS [02:20:04]

Russ (02:20:03):

He's in the back and turns out her hooting sounds exactly like an owl, and we have an owl back there. So just to figure out that, "Oh, that wasn't Katie calling for us. It was an owl." But you have to respond to any kind of sound, gesture, or motion, whether it's a kiddo or owl.

James Valentine, JD, MHS (02:20:24):

Right. Yeah. Well, thank you so much, Russ. I see another phone caller that I'd like to pull in. In this discussion, we have Elizabeth from Houston, Texas that wants to share some of the impacts of inability to sleep and stimulating seizures. And so would like to... Elizabeth, welcome you to the program. Are you with us?

Elizabeth (02:20:50):

Yes. Yes, I am. Can you hear me?

James Valentine, JD, MHS (02:20:51):

We can.

Elizabeth (02:20:56):

Okay. Well, one of the things that... First of all, my heart goes out to all the parents. I just want to say, I think that STX parents deserve an awards dinner. We deserve the Academy Award for parenting because everything is so difficult. And the parents that I've met so far that they do it with such grace and such kindness and love, it's amazing to me. But one of the things I don't know that we've touched on, are the sleep issues. And it kind of goes to the behavior that this other parent was discussing. It's the... I've heard it described by doctors as excitatory, inhibitory, and I don't know exactly what that means. I'm not a doctor, but we just heard that mother describing how the child gets so excited and the energy level and the running and the nonstop motion and movement. And you would imagine that a child, let's say three to eight years old, gets so excited and they're running everywhere and they literally never stop.

(02:22:08):

You cannot convey to a neurotypical parent what we're talking about. But it is a level of motion and movement and busyness climbing, food seeking, oh my gosh, escaping, running, that you cannot describe. And you would imagine that that child would drop off to sleep at 7:30 or 8:00 in the evening and crash for 12 hours. But they don't. They actually have that excitatory nature. And we see it in a lot of these kids, it extends 24/7, which is hard to understand, but they're up. And I know with Caroline, our daughter, and of course back in those days, we had no diagnosis and I didn't understand. But she would wake up about every other hour in the night, screaming, back-arching-

James Valentine, JD, MHS (02:23:05):

Wow.

Elizabeth (02:23:05):

... unable to be consoled. And at that time, I think she was still in the crib because we had to keep her contained for fear of her escaping her room or her bed and finding I had three other girls... One time we found her choking on a Barbie shoe. I mean a LEGO piece. Any errant toy that my children had was a danger to her. Anyway, I remember nights where I would wake my husband and say, "It's your turn. She's screaming again. It's your turn." And he would say, "No, it's your turn. I think I was just up." And I'm like, "No, I was just up."

James Valentine, JD, MHS (02:23:43):

Oh, my God.

Elizabeth (02:23:43):

We'd be so exhausted and I would hear my other children yelling, "Please make her stop. Please make her stop." Because they just screaming and it's one o'clock, three o'clock, five o'clock in the morning. And I remember falling asleep. I know this sounds shocking in the crib with her trying to console, rub her back because I was so tired. I feared if I were in the rocking chair with her that I could fall asleep and fall out of the chair with her because we were so sleep-deprived.

(02:24:16):

And I would be crying, crying, saying, "Please sleep, honey, please sleep." I never got frustrated with her. And although you could see a parent doing that, easily, see a parent doing that. And I felt, and I see it in these other parents as well, just this empathy for the child, just this sadness that they're so ill and their body, their neurological makeup was just so off that they just couldn't settle or they're seizing and it just... I don't know. I'm probably not making a lot of sense, but the empathy for the child was so strong in me, and I feel it for these other parents that their children as well.

(02:25:04):

But later... Okay, so we wound up, and I think other parents have as well, we find clonidine or other medications to help them sleep, which works really, really well. And some are using melatonin. But I see a lot of the parents sharing back and forth about medications that have helped. But then what I saw, what was almost more frightening was after puberty, I think she started around age 15, she couldn't stay awake. And as frightening as it was to have her so high energy and couldn't sleep, which stimulated seizures, now I was seeing a child who can't stay awake.

(02:25:55):

And we had to take her out of school because she was asleep, and I felt instinctively that she must need to sleep. And so I have had other parents say, "Well, I just get her up, get him up, put them in their wheelchair and put him on the bus." Well, and then the child sleeps all day at school in the wheelchair. If that's what you do, and I can understand that, of course, for me instinctively, I thought she's needing this sleep. But I was going back to the hospital saying, "Something is terribly wrong. Something is terribly wrong. She can't stay awake." And I'm not talking she needs a nap. I'm talking 18, 20 hours straight. And then that proceeded to 40 hours, 45 hours of not waking. You were changing diapers. You are putting in the feeding tube, taking out feeding tube, not waking.

James Valentine, JD, MHS (02:27:02):

Wow, that's incredible to hear-

Elizabeth (02:27:04):

And they [inaudible 02:27:04].

James Valentine, JD, MHS (02:27:05):

... that complete shift from almost never stopping moving, never sleeping, very little sleep to such extreme sleeping all the time, and how during each of those different phases, how that impacted her and the family's quality of life. So Elizabeth, thank you so much for calling in and sharing that. I do see that we've been getting a lot of written comments coming in, talking about impacts on activities in daily life. Charlene, what are we seeing?

Charlene Son Rigby (02:27:35):

Yeah, let me read a few of these. So this is from Allie in Ocean Springs, Mississippi. "My sweet daughter, who is now seven, has just in the last couple of months started having a lot more frequent atonic drop seizures. She fell on her chin and busted it wide open in June, and since then has had drop seizures and reopened the wound two more times, which has made it look a million times worse." And then this is from Alexander in Queensland. "On his worst day, our son is practically catatonic, severely wiped out by seizures and their

systemic effect on him physically and cognitively. A worst day could be compounded by insomnia, choking on food or a foreign object, relentless screaming, unable to communicate his pain." And then this from Gert in Belgium, "When our daughter is feeling good and when she's having a bad day, she can't out of nowhere start crying or shouting very angrily, going somewhere to eat a piece of cake or to have a drink with her remains an adventure. The outcome of which you can never predict in advance."

James Valentine, JD, MHS (02:28:58):

Yeah. Well, I want to, again, thank everyone who's been writing in with comments and we see your comments coming in. We know we can't get to all of them, but again, we will incorporate all of them into the voice of the patient report. And I also want to recognize those if you have been calling, and we'll be coming back to the phones here shortly, but I do want to expand to our final topic of this morning's session. We've heard so much already about what your loved ones have already gone through, what they're currently going through, but we know you as caregivers are thinking about what your children's life is looking like into the future and may have worries about that.

(02:29:35):

And so want to go to our final polling question of this morning here. So you can again open that browser tab, go to the browser on your phone, go to www.PollEV.com/STXBP1, and here we want to know what worries you the most about your loved one's condition in the future. And again, we're asking you here to select the top three greatest worries. The options are A, prolonged seizure activity. B, symptoms will get worse. C, not knowing what is causing pain. D, falling E, loss of current skills and functioning F, social isolation, G, needing extended or long-term care. H, who will care for my child after I'm not able? I, dying prematurely. Or J, some other worry that you have about your loved one's condition in the future that represents a top three greatest worry or concern for the future that you have.

(02:30:44):

Again, as you're answering this polling question, I want you to think about how you landed on the one to three of these that you selected about where your loved one is at in their STXBP1 journey. Is maybe informing what your worries are today. Are these worries that you have in the short term? Are these longer-term worries? Just want to understand what you've selected and why. So we'll just give you just a few more moments here to get your responses in. It looks like what we're seeing is the top greatest worry is a worry of who will care for my child after I'm not able. So we certainly want to hear about that. What is driving that worry for you and for your loved one in particular?

(02:31:42):

We see after that maybe as a second-tier worry that symptoms will get worse or that there'll be a loss of current skills or functioning. And then after that, we're seeing most of the others kind of together needing extended or long-term care, dying prematurely, prolonged seizure activity, and not knowing what is causing pain. Although all of these here except for other, are in some number of people's top three. So if we can come back to our Zoom panel here. Thank you for everyone doing that polling question. Anna, I'd like to perhaps start with you on this topic. What comes to mind as a greatest worry or concern that you and your family have?

Anna (02:32:28):

Thank you. So yeah, I mentioned that my daughter will be 20 at the end of the month. Where I live in Pennsylvania now, 22 is the cusp where they stop going to school. Basically the entire funding system changes for nursing care for any other care. And it's a little bit of a black abyss that is coming towards us that we don't really know exactly what we're looking at right now. But looking at what some other parents of older kids are facing at the moment, it's not looking super promising. So, there's certainly a lot of significant worry right now about what life will look like just in the practical day-to-day of...

(02:33:21):

What will her day-to-day look like? Will she find a meaningful place in the community because that's important to her and it's important to us? Will we have to stop working? What will this look like financially?

How will this impact my other children? That's definitely a significant worry, and I have to think about what one of the other mothers was sharing about that empathy that we have that makes us get in the crib in the middle of the night and deal with the waking up and deal with everything. You don't know who else will have that empathy that may end up being the person that is looking after your loved one.

(02:34:06):

So it's a very challenging time. You want to promote as much independence as possible. We would like to have a break at some point. We would love to know that there's some sort of settling in what life is going to look like, but you can't really, again, hand over this adult who doesn't have agency, who cannot communicate, who cannot tell you how things are going to strangers.

James Valentine, JD, MHS (02:34:34):

Yeah. Wow. Anna, thank you so much for sharing those worries and helping us understand that. Christina, I'd like to bring you into this topic as well. What comes to mind for you as some of those concerns or worries that you have?

Cristina (02:34:52):

Well, Anna hit the nail on the head. Every minute of every day, some part of my subconscious is thinking about, "What if I get into a car accident? What if my husband's plane crashes? Who will care for him the way we care for him?" We have experienced an abuse situation from a caregiver. We are always afraid of who could care for him. It's truly overwhelming and it overshadows everything. We are in a desperate scramble to try to teach him to potty-train so that caregivers don't have to change his diaper and get that intimate with him if at all possible. We're always, I think, inadvertently thinking about the future if we are not there. It's endless.

James Valentine, JD, MHS (02:35:52):

Wow. Christina, thank you so much for being willing to share that. I do see that we have a phone caller that I'd like to bring into the conversation. Steve from Washington State who's a grandparent, an involved grandparent in providing care. And so Steve would love to bring in the conversation here what you have to share about this morning's topics. So welcome to the program. Are you with us?

Steve (02:36:21):

Yes.

James Valentine, JD, MHS (02:36:22):

Hi. Welcome.

Steve (02:36:27):

Hi, my name is Steve. I live in Washington State and I'm talking about my four and a half year old grandson. I'm with him every day, so I know his life. And... Can you guys hear me okay?

James Valentine, JD, MHS (02:36:41):

We can hear you wonderfully.

Steve (02:36:44):

Great. Thank you. Thanks for doing this. This is really important to our family, obviously. I can share that our grandson was diagnosed at about six months. He's now four and a half years old now. Just in order of respecting everyone's time, I won't go through the whole history. His struggles have been very similar to many others that were described by other families in the program. What I will focus on now is similar to what some others have said. It's four and a half. He's in preschool and he wants to play with other kids. He wants to engage with them in the playground at school and so forth. And as others have said, his inability to communicate it just prevents that from happening. Someone has to be with him. Sorry about that. That's grandson number two. Anyway, so his inability to communicate with children at the playground or at school or the teachers or the teaching assistants just makes that impossible. And it's just heartbreaking to watch his sadness when he can't really play with the kid at the playground that runs up to him and wants to swing or climb on a toy or whatever the case may be. Same at school. And so I think amongst the other issues that

he's encountered, as everyone's talked about in terms of daily living, feeding, toileting, seizure activities at birth, and then later when he was about three, that's one of the biggest concerns that our family has, that he just cannot participate in activities that a four or five-year-old is doing every day, including school and friends because he wants to do it, but he just can't.

James Valentine, JD, MHS (02:38:51):

Yeah.

Steve (02:38:52):

Thank you for listening.

James Valentine, JD, MHS (02:38:53):

No, thank you for sharing, Steve. Again, hearing about how the whole constellation of different symptoms and health effects are the things that are driving all of these different limitations in what can be done in daily life, and to hear those examples in your grandson's experience, it helps further paint that picture for us. So really appreciate it. I'd like to bring in one more caller here in this morning session. I really want to thank all of the people who have been calling in as we get towards the end here of the time we have this morning. This community has really stepped up and we're getting so many colors and written comments, and we just hope that you will call back in this afternoon and we can bring you and into the conversation then. But right now, I'd like to bring in Jennifer from Calgary, Canada that wants to talk about some of her son's experiences and perhaps Jennifer, you can share some of if you have any concerns for the future you'd like to share. So Jennifer, I'd like to welcome you to the program. Are you with us?

Jennifer (02:40:06):

Hi, good morning. Can you guys hear me?

James Valentine, JD, MHS (02:40:08):

We can hear you, yes. Welcome.

Jennifer (02:40:10):

Great. Thank you. My name is Jennifer. I live in Canada and I have a 12-year-old son, Miguel.

James Valentine, JD, MHS (02:40:18):

Yes.

Jennifer (02:40:18):

I'm pretty sure he was having seizures even before he was born because I remember on the last two weeks of the pregnancy, he was moving in a way that I knew it was in hiccups, so I knew that something wasn't right. And when he was born, he was having this infantile spasms and I asked the nurse and she said, "He's just been [inaudible 02:40:41] because he's a newborn," but I knew something was wrong. And two days later when we went to see the nurse, I explained to her she saw him having a seizure. And since there we were sent to the hospital, they did a whole bunch of CTs, MRIs, lumbar punctures, any type of tests to try to solve or to answer why he was having seizures.

(02:41:05):

We didn't have a diagnosis until he was around maybe four or five years old. And the reason that we got a diagnosis was because his neurologist here at the children's hospital recommended us to send DNA samples to a research study in Philadelphia. I think, I don't remember. This was 12 years ago.

James Valentine, JD, MHS (02:41:24):

Of course.

Jennifer (02:41:25):

And thanks to that research study, we were able to have a diagnosis with STXBP1. My son, he's nonverbal. He can walk a little bit, but he's most of the time on a wheelchair. He can eat, but with support. So he doesn't have any NG tools or anything. He wears a diaper. But my journey has been the best experience because Miguel came to change my life for the better. I hear other parents and I relate so much, but I used

to tell my son, Miguel, "I love you so much that it hurts. My love for you is so big that it hurts." I think part of my process in accepting was to let go of the child that I thought I was going to have. I grieve that person for around 10 years until I decided to cherish the one the universe gave me. My faith has helped me a hundred percent with this process of accepting and wanting to be the best version of myself. For him, I am not the best, but I try.

(02:42:50):

But when I said that Miguel came to change my life, he did because thanks to him and his diagnosis, I think I am a better person. I am more compassion. I have a better husband, a better family. And my faith has been, like I said, everything. Miguel still have seizures. He's nonverbal. He goes to school on the special education class here. We have an amazing healthcare system here. But still I struggle with trying to understand how is it going to be later on when he's no longer able to go to school or high school or when he's an adult. But during my process in accepting, I allowed myself to process the fact that perhaps he may die of a seizure and what was going to be his legacy in my life because the universe brought him to me with a purpose. And that is something that I want to share with other parents.

(02:43:59):

I know it's hard. I know it's difficult. We don't see the light, but we have to allow them to teach us what is exactly the reason why they came to our life. They came to make us a better people. They came to teach us that life is not as hard maybe as we think. We have to go with their flow. We cannot push them to come or to go with our flow.

James Valentine, JD, MHS (02:44:27):

Sure.

Jennifer (02:44:27):

They are our masters. They are the ones who are going to show us what we have to do. And I know maybe this makes no sense for the parents who just started this journey, but once you allowed to son to teach you or your data to show you exactly what is the purpose in life, everything little by little will start falling into place. I am not saying that we will have a cure tomorrow, maybe, why not? But we do really need, and I appreciate all the doctors, nurses, research, all the people who is behind all of these supporting us, helping us wanting something to change the quality of life of these kids and for the future generations. Because unfortunately, more kids are going to be born with STXBP1, but we are the first generation of parents who are preparing the ways or the past for the next parents and the next kids.

James Valentine, JD, MHS (02:45:24):

Well, Jennifer, that was so beautifully said. I imagine that so many of the other parents in the audience are relating to what you said. And we've focused so much this morning on describing and pulling back the curtain on the hard aspects of living with this condition in hopes that future treatments can help address that. But I am so glad that you recognize the gift that are your loved ones for all of the parents in the audience who are listening and participating as well today. So thank you so much for sharing that very important perspective. I know we're a little over time, I hear, but I do recognize that a lot of you have written in with comments. So we'll give the final word perhaps to a few of those that have come in. So Charlene, what are we seeing?

Charlene Son Rigby (02:46:21):

Great. Thanks, James. This first comment is from Lauren in Australia. "As our child grows, we worry about our ability to care for him as the physical burden of moving him, changing his nappy, and dressing him increases. Our biggest fear is his inability to care for himself and who will be available to care for him once his parents are gone." And this from Jennifer in Marietta, Ohio. "As my daughter gets older, I fear most being forced to watch her slowly slip away, losing everything that makes her her." And this comment from Annie in Marietta, Georgia. "My biggest worry with my son is whether or not he's in pain and can't tell me. He broke his hip in March by simply rolling over the wrong way in his sleep-safe bed. Literally the safest place in our home, and he broke his leg."

James Valentine, JD, MHS (02:47:21):

Wow. We're now out of time for this first topical discussion on what it is to live with STXBP1. I just have to thank all of you. I want to thank our Zoom panel who joined us and shared throughout this whole session to everyone that's called in. Again, if we didn't get to your call this morning, please do call in this afternoon. We'll have another opportunity to hear from you. And then again, everyone who's written in, it's going to take us a lot of time to read through and all of the written comments that have come in, you all have participated so actively here in the morning, and we look forward to having that engagement with you in the afternoon when we shift gears talking more now about the different treatment and management approaches that this community employs. For now, we're going to go to a break. We'll take just a little over a 20-minute break, and we will resume at 1:00 PM Eastern Time. Again, thank you and we'll see you shortly.

PART 5 OF 9 ENDS [02:55:04]

James Valentine, JD, MHS (03:10:59):

Good afternoon, and welcome back to the Externally Led Patient-Focused Drug Development Meeting on STXBP1-Related Disorders. My name is James Valentine. I'm your meeting moderator. I'm here in the studio with my co-host Charlene Son Rigby from the STXBP1 Foundation, and we are eager to get into our second topic of today, which really builds on the morning discussion that we just had where you helped us understand what it is to live with STXBP1. Here, we want to begin to understand your experiences with current treatments as well as your thoughts and preferences for future treatments. So to get us oriented to this topic and some of the things we'd like you to think about and weigh in on, we're going to bring up some of our discussion questions here that we're going to be exploring this afternoon.

(03:11:49):

So first, I want to mention, when we talk about current treatments and treatment approaches, we mean that in a broad sense. We're not talking just about medications or drug treatments or even just medical procedures and surgeries, but we're also including maybe medical devices, more holistic treatment approaches, diet, different types of therapy, even lifestyle modifications. Anything that you are doing for your loved one to make life with STXBP1 a little bit easier can count as a treatment. We're just going to use that term as shorthand as we move through this afternoon session.

(03:12:31):

So we want to understand your experience, your loved one's experiences with what they're currently doing to manage their symptoms, as well as maybe things that they've tried in the past, even if they're not using them currently. We want to get your assessment of how well these treatments are helping with some of the most significant symptoms and health effects of STXBP1. In addition to helping us understand what's helping, maybe what isn't helping that you've tried. We want to explore some of the most significant downsides to your loved one's treatments and how those downsides affect life. So whether that's the side effects of different therapies, the burden of keeping up with a certain treatment approach, really anything that you would consider a trade-off or a downside, we'd like to hear about that.

(03:13:20):

Once we've explored the range of different current treatment approaches, we're going to shift gears towards the end of our session, and we're going to want you to think about short of a complete cure because we all want that complete cure for STXBP1, but thinking about the medical products that might come along the line before we get to that cure, what specific things would you be looking for in an ideal future treatment for this condition? Or another way to think about this is what factors would be important to you in deciding whether to try a new treatment if it were to become available.

(03:13:54):

So to get us thinking about this topic and to start to share some of those experiences, I'd like to welcome a panel of caregivers who would be sharing current and future treatment thoughts and perspectives. We have Jen, David, Yisbel, and Lila. Jen, why don't you get us started and take it away?

Jen (03:14:15):

My name is Jennifer, and I'm a 49-year-old resident of Virginia. I'm married, and I have two daughters. When my oldest daughter, Kaylyn, was born 50 and a half years ago, she made me a mama and in turn made me an advocate, chasing a diagnosis at help for the horrible seizures that racked my tiny baby's body every day, many, many times a day, and we would later realize, tortured her in utero as well.

(03:14:38):

At five days old, she was hospitalized for the first time on the neurology floor at Children's Hospital in DC. We knew something was right and had been prompted by our pediatrician to take her there. We were in the ER waiting to check in. When a nurse saw the weird flapping and contorted body movement she was making, and ripped her from my arms and took her directly to the back. That's when shit got real, and it was a pivotal moment in my life never to be forgotten.

(03:15:04):

Her tiny, seven-pound body was poked and prodded. She had many vials of blood, had taken a spinal tap, and then she was admitted and hooked up to her first EEG. At that time, we were sent home with phenobarbital, an antiquated medication created in the 1950s whose job was just to sedate and make my baby sleep all too much and have a difficult time nursing and drinking from a bottle. We were told many times seizures resolve in infants within six months. That was not true, and at six months old, Kaylyn developed infantile spasms, West syndrome, and we found those seizures did irreparable brain damage. My daughter's suck and swallow were affected. Her ability to smile and be present were forever changed. She's nonverbal, non-mobile, and sadly, I describe her as an infant in a 15-year-old's body. She's unable to express pain, sadness, illness, happiness, anger, and joy.

(03:15:58):

She's developed mobility issues and has been diagnosed with cerebral palsy and spastic quadriplegia. She's 100 pounds, and the only reason I can pick her up and transfer her is because I never stopped picking her up. I'm not a physically fit person, and I'm just three inches taller than her, but I pick her up and transfer her from her wheelchair to her bed, and vice versa. At times, it feels like we're just tigers chasing our own tails. We give her medication to lessen the seizures, and then those medicines sedate her and have caused her to not be able to assist in any activities for daily living. Eating is via spoon-fed, like an infant, or feeding tube directly into her belly.

(03:16:37):

Due to the cerebral palsy and being non-mobile, there have been concerns for hip dysplasia, low bone density, and before the age of 10, she was diagnosed with osteoporosis and osteopenia. She's developed a 49-degree curve in her back due to scoliosis and positioning, that must be watched to see how it's affecting her lung capacity and definitely causes her illness to progress to pneumonia at a much higher rate. Full spinal fusion has been discussed but not decided upon yet.

(03:17:04):

She's currently on three seizure medications, which are her best cocktail to date for controlling her seizures, Onfi, Banzel and the prescription CBD oil Epidiolex. She's also on medicine for reflux allergies, multivitamins, vitamin D, probiotics. She gets regular enemas and suppositories, which are necessary for any bowel movement. Breathing treatments with nebulizers, inhalers, including multiple pieces of equipment which are added into the mix when she's sick, including a cough assist, a cough vest, a suction machine, and supplemental oxygen at home. We have to watch for bedsores and are always on high alert.

(03:17:42):

Hypotonia or low muscle tone, it is another crappy side effect from what's happened to her brain and her body, for this affects mobility and grip, but also her intestines and diaphragm. These are all muscles, and low muscle tone in the intestines causes constipation to be her regular. She has a CPAP for sleep apnea and I was told the diaphragm is a muscle, and since hers is so weak, the air isn't pushed out hard enough even to make a snoring sound. In most cases, the fear, the anxiety, the smiling through tears, the prayers that this

time your baby won't die and hope that you won't go in one morning to find she has passed away in her sleep due to seizures and the evil that is SUDEP, sudden unexplained death due to epilepsy.

(03:18:27):

Short of a complete cure and ideal treatment for STXBP1 would be an easier life for my daughter, with less medical issues and complications and aiding her cognitive ability, communication skills, and overall body function in regard to mobility, less living on the edge of anxiety and rushing off to the emergency room when she develops pneumonia or is just non-responsive and won't wake up at school. Over the past year, we've had three of these instances with ambulance rides, trips to the ER, 12-day inpatient stays in the ICU, breathing tubes, feeding tubes, and it just sucks. My friends with kids her age are starting to drive and looking for colleges and what wonderful futures they have before them. I've come to the realization, I will never be an empty nester, and my biggest hope is that my daughter dies before I do, so I don't have to worry about who will take care of her when I'm gone.

David (03:19:19):

My name is Dave, and my 26-year-old son Blake was diagnosed 10 years ago with a deletion of his STXBP1 gene. We live in Middletown, New Jersey, with my wife Colleen and Blake's younger brother Luke, who is a senior at Rutgers University. Blake is nonverbal. He's physically and cognitively challenged and needs assistance with all activities of daily living. Blake can bear weight and walk short distances with assistance. We get Blake up and walking daily to keep him as strong and healthy as possible. He loves the water, and we take him in the pool often. He goes to physical therapy weekly and has a part-time job that only employs adults with disabilities. His nurse accompanies him to work for safety and assistance.

(03:20:05):

Because Blake is nonverbal, communication is challenging. He understands much of what we say and has his own way of expressing his wants and needs to us. Blake's favorite activity is his participation in marathons and triathlons. For the past 15 years, I have pushed and pulled Blake through these races, and he's loved every minute of it. The most pressing symptom Blake has are his seizures. His seizures began at six months of age, and he was prescribed phenobarbital. His seizures subsided at age two, and he was taking off all medication.

(03:20:41):

From ages two through nine. Blake progressed with some speech and was able to sing songs. He was able to bear weight, and he took his first steps at age five. The seizures returned at age 10, and as puberty progressed, so did his seizures. At one point, Blake was having over 250 seizures per month, and he had lost what little speech he had. For safety reasons, we could not have him on his feet or even leave our home. After many different combinations of seizure medications, a vagus nerve stimulator, and the ketogenic diet, we arrived at his current medication regime of Depakote, Keppra, lamotrigine, and Belviiq. The vagus nerve stimulator, the ketogenic diet, and Epidiolex had little effect on his seizures. Blake's seizures have been reduced from 250 a month to 20 or 30. There's a very consistent pattern of increased seizure activity that builds over two weeks and culminates in cluster seizures of five or more in an hour. We administer a rescue medication of Diastat that ends the seizure activity for a few days, and the process starts over again. Blake also has episodes of hyperventilating that can last 24 to 48 hours, and he will not sleep during this time. It was determined during an EEG that this is not seizure activity, and Seroquel is Blake's rescue medication for these episodes. Due to Blake's seizure activity, he can never be left unsupervised. A major concern is having seizures while he's sleeping, as sudden, unexpected death in epilepsy, or SUDEP, is always a possibility.

(03:22:25):

Colleen and I often talk about what Blake's life would be like if there was a cure or a partial cure for STXBP1. A meaningful therapy would be one where his seizures were completely controlled. He would not need 24-hour supervision and would be able to perform many activities of daily living on his own. Complete seizure control would greatly reduce Blake's risk of injury or death. A complete cure for STXBP1 would have a dramatic impact on Blake's physical and cognitive abilities. He'd be able to communicate with us and

everybody around him. He would be able to walk, feed himself, dress himself, get in and out of bed himself, and take care of his own personal hygiene needs.

(03:23:08):

The marathons and triathlons that I have pushed Blake in all these years, he could do on his own if he choose to do so, and by using his own physical body, Blake would live a much longer, healthier, happier, and independent life. With the elimination of seizures, improved physical, cognitive, and communication skills, Blake could have independent employment and a career of his choosing. He could support himself, be a productive member of society, and have friends and long-term relationships of his choosing. Thank you for listening to Blake's story.

Allison (03:23:46):

Hi, my name is Allison, and I live in Akron, Ohio. Nothing I had previously experienced could prepare me for the life-changing event of my now-five-year-old son Mason when he was first diagnosed with STXBP1 at the age of six months because of infantile spasms, a very terrible, rare type of seizure. Mason began rigorous physical therapy at the Cleveland Clinic two to three times a week since he was about eight months old. We persisted for months on end with minimal progress, tiny steps we had called inchstones. It was disheartening as caregivers and parents to witness such slow improvement, and we struggled to stay motivated. His extremely low tone makes it difficult for him to do very basic tasks, like even holding up his own head.

(03:24:34):

Mason's inability to hold his own head up has far-reaching consequences. Swallowing issues, difficulty chewing, challenges in reaching and playing with toys are just a few examples. Our efforts at the Cleveland Clinic had yielded few gains despite trying every therapist, every piece of equipment, and every technique available. Mason will simply not catch up. Adding more of the same physical therapy sessions alone would not drastically change his life. We had faced a painful realization that, as we celebrated his older sister Harper's first, he might not ever get to experience some of those same firsts.

(03:25:15):

In October of 2020, desperate for hope with the world in the midst of COVID, we sought an alternative type of therapy when we met Darwin. Darwin focused his time and effort with Mason on the basics of motor patterns in the body. Without relying on equipment, Darwin focused on understanding his very specific needs, dedicating hours of therapy each morning and each afternoon.

(03:25:39):

Just after three days, Mason accomplished the remarkable feat of sitting on the floor for the very first time. He was three years old. This began my annual trips out west to Arizona with Mason for the next three years to spend our weeks, mornings, and afternoons with Darwin. While the flights and sleepless nights were very challenging, I became more prepared and hopeful each time. However, I realized I could not do this alone.

(03:26:09):

With intense planning, very intentional savings, and support from my friends, we spent an entire month in Arizona in April of 2022. From learning proper sitting techniques to helping him take steps, my family had the time and space in their busy lives to practice caregiving and ended up collectively in over 60 hours of hands-on therapy. This experience surpassed anything we could have learned at an outpatient therapy center.

(03:26:41):

At the beginning of that one-month intensive, my in-laws, equipped with their knee pads, started on their hands and knees, helping Mason move his feet forward, and by that third week, when my sisters joined, we progressed to holding his hands as he took steps forward. He gained a whole new experience of viewing the world upright for the first time at four years old, but we gained so much more.

(03:27:12):

My family gained confidence that they too had what it takes to care for Mason. I gained an understanding that the responsibility of Mason's progress does not squarely sit on my shoulders. That month, we learned all what kind of support system was truly needed to care for someone with such profound disabilities. Fast-forward to today, Mason takes steps with someone holding two hands. He is slow and methodical, but doing something we never dreamed he would.

(03:27:50):

Every area of our lives have been impacted by his disability with STXBP1. Our home, our jobs, our time, our money, everything has a direct correlation to caring for Mason. To ensure his safety and foster independence at home, we have worked with our local county Board of Developmental Disabilities. We installed a chairlift after our caregiver fell, carrying him down the stairs. We redesigned our bathroom to facilitate bathing without causing us back pain. We remodeled our kitchen with his needs specifically in mind and created a bedroom on the first floor for him. Thinking about Mason's future brings a mix of emotions. I find myself going to a dark place when I think of the nevers in Mason's life. He's never told me, "I love you, mom." He's never petted his dog. He's never clapped for his big sister during her ballet performances, and it's still sadder to think he may never throw a baseball with his dad or laugh at his uncle's jokes. These nevers are daily reminders of what my son cannot do. If the treatments we are pursuing would increase even the slightest bit of cognition and increase his ability to communicate the words to say, "I love you, mom." Or for him to eat with a spoon or for him to walk his dog, we would be part of that. The smallest gain to his independence, motivation, or abilities would increase his quality of life and let him be the kid he is to be. Thank you.

Yisbel (03:29:31):

My name is Yisbel, and I'm the mother of my two-year-old Lucas, who was diagnosed with STXPB1 in April 2021 when he was three months old. Lucas started having seizures at six weeks old. Since then, he's been hospitalized many times, and he takes Keppra for epilepsy and Nexium for acid reflux and other stomach issues he has. Keppra has worked well in controlling seizures. He-

PART 6 OF 9 ENDS [03:30:04]

Yisbel (03:30:03):

Keppra has worked well in controlling seizures. His dose has been adjusted as he gains weight. Nexion, he used to take 5mg twice daily before lunch and dinner, which worked for a while, but in January, 2023, he started doing nausea and pain phases every day and after an endoscopy, he was diagnosed with a new condition called eosinophilic esophagitis, which causes inflammation of the esophagus. So he was indicated lansoprazole 15mg twice daily in substitution of Nexion because the nexion dose that is needed for this condition is not yet approved by the insurance. We haven't experienced not any size effects from Keppra or Nexion so far, although it's hard to tell with Keppra because he's been on it his entire life since he was six weeks old. He needs help in every aspect of his life from brushing his hair teeth or get dressed. He cannot chew for all solid foods since he needs daily feeding therapy for this.

(03:31:20):

He does not have a G tooth at the moment and has made slow progress chewing, but he still cannot chew his entire meal, so we have to blend the food for him to get him good nutrition. He is non [inaudible 03:31:36] and does not know how to spread his needs, frustrations, desires, so it's even more challenging to help him with his needs and his daily necessities. In speech therapy, they try to show him different animal sounds and teaching how to use face words such as no, yes, by pushing a button. They recently ordered an AC device, but it has not arrived yet, so they are still waiting for this tool to arrive to incorporate it into his speech therapy.

(03:32:14):

His struggle with gross and fine motor skills since he was the baby, therapy is his whole life, both occupational and physical as well as feeding and speech. We also do other complementary therapies to this one like horse therapy that helps started with his core strength and balance, of course, in combination with

everything because none of these therapies by itself works, but the combination of all. We also try to do intensive therapies every year, which consists of three weeks of three sessions daily, including new techniques such as DMI, neuro suit. DMI is dynamic movement intervention and is a therapeutic technique to improve automatic postural responses and provoke a specific active model response from the child in response to the fine dynamic exercise prescribed by the therapist. On the other hand, the neuro suit is one for two hours under the supervision of a trained physical and occupational therapist. He now can sit and play. His progress is very slow, but he cannot crawl, stand or walk yet. His low tone or hypotonia causes many other struggles besides the motor delays such as acid reflux, constipation, and scoliosis. There are many days that he's in pain because of the reflux. We know this because of his nausea, faces because he cannot talk or communicate his pain. Equipment such as the standard and gait trainer are used daily to help him gain strength, but the impact of this equipment is still not enough to improve his quality of life. We need to constantly watch him too, to make sure he's not having seizures and not to be confused with other movement disorders caused by this condition. And as he grows, I feel like it's even more challenging to take care of him. He also has more stomach issues such as acid reflux.

(03:34:35):

More problems at the eating time, is also more challenging for him to do some exercises during his PT or OT times. It would be easier if he could communicate his necessities, gain independence on daily routines. I would love to see changes in his muscle tone. He has severe hypotonia. I would like to have a therapy that at least could help him have more energy, strength, and engagement in his daily routines improving his communication and motor skills, changing diapers, carrying him have become very difficult now that he is getting bigger.

(03:35:17):

I haven't been able to enter any trials yet, but I'd be more than willing to participate in any research to help my child and the STXBP1 community. I believe the risk is worth it when this condition causes so many different struggles for the entire family. It's a very low quality of life. While other children attend to school and do normal toddler activities, we have to go to therapies, more therapies and doctor appointments. And even the doctors are clueless about what to do next because they don't know enough about the condition or have no tools or anything else to do this. Suffering is daily and our only hope for the better future is the treatment that can cure our children. Thank you for listening.

Lila (03:36:13):

Hello, my name is Lila, and I am the mother of this fabulous 16 year old young man Rowan, lovingly nicknamed Mr. Mayer because of his desire to fist bump everyone he sees. He was diagnosed with STXBP1 when he was 12 years old. Rowan has been homeschooled for the last eight years. When I left my research scientist career to be his sole caregiver and parent handling his day-to-day needs, I have the time and the ability to do anything he needs, but as perfect as that sounds, there are challenges. There are no targeted treatments or therapies for STXBP1 and traditionally prescribed therapies were undertaken for years, occupational therapy, physical therapy, speech and language therapy, behavior therapy, all producing only mild to moderate progress for Rowan and his youth. I also had him participate in other treatments to see if there would be positive results to no avail. Special diets, adaptive group sports activities to encourage exercise and socialization.

(03:37:18):

We have also tried every adaptive communication style out there. Sign language, picture cards, assisted communication devices. Nothing to this day has taken hold. I've had to resort to medications and herbal treatments to modulate his behavior, aggression, anxiety, and his related sleep disorders. I have taken him to the best doctors with the most current innovative ideas as well. Music therapy, five days a week with one hour sessions daily has changed his life for the better, is the newest recognized clinical therapy. And Rowan has approved across the board. Using specific targeted goals, he has increased verbal skills, found ways to create coping skills for his anxiety with instruments and songs, and made progress in the preschool level, academic skills with songs uniquely written to motivate Rowan using his specific interests. Now this panel

remembers the year 2020 for the pandemic of Covid-19, but for us it was a quite different experience with a known rare disease as a risk factor and an unknown virus.

(03:38:29):

We stopped living out in the world for 774 days in the hopes of just keeping Rowan alive. It was also at this time that Rowan entered puberty. He was 13 years old. He felt the anxiety and fear in the household and saw his daily routine come to a full stop. He didn't sleep for four months. Lots of medication changes occurred in this period because my happy child was now an anxious and depressed teenager losing every life skill he worked so hard to achieve. There's not a single skill that has not had some level of regression since 2020. Walking, eating, sleeping, behavior, learning, desire to interact with others, personal care. These declines are noticeable every day. His status as of today has him recovering from two major surgeries done August the 9th of this year, both caused by the STXBP1 gene mutation.

(03:39:32):

The first surgery was to insert a feeding tube due to regression by increased refusal to eat or drink, causing dehydration and loss of more than 30 pounds in less than eight months. Generally, this happens because of the body's instinctual need to protect the airway from choking and aspiration of food or fluids when consumed by mouth. So he now receives all of his nutrition and hydration from tube fed formulas. Secondly, a spinal fusion surgery of nearly his entire spine was done due to neuromuscular scoliosis on that same date in August. Rowan was increasingly unable to maintain proper muscular strength in his trunk and core to maintain the spine in its proper alignment. Due to the neuromuscular losses caused by STXBP1. Untreated, it would lead to a lifetime of worsening curvature and internal organ damage. These surgeries were medically necessary to save his life and his quality of life long-term.

(03:40:35):

We need so many things while we are waiting for the science to catch up. And there is an effective gene therapy treatment for Rowan that targets the protein deficiency caused by the STXBP1 mutated gene. Innovation and change within the educational training programs of all types of therapies must include techniques on how to communicate and manage the challenging behaviors with patients like Rowan and understand what their needs are in the teen and adult years.

(03:41:05):

Better diagnostic modalities need to be used to determine what areas of the brain each STXBP1 patient has neural deficits in maybe through functional MRI. They can also test treatments like neurofeedback or biofeedback to see if they can aid STXBP1 related brain function deficits. These treatments are not currently recognized and therefore a potentially untapped resource worth exploring. More research also needs to look into the regression effects that seem to begin in puberty and see what can be done to stop, slow or reverse them. We treat the symptoms until we have a cure for STXBP1. Hope never fades and advocating for Rowan is the most important unpaid side hustle I have ever embarked upon.

James Valentine, JD, MHS (03:42:00):

Wow, thank you Lila for sharing Rowan's story and his experiences with treatments and really to all of our panelists who helped us really understand so many of the different, not just treatments, but kind of symptom management and other management strategies that you all employ. So we're now come to the second opportunity that we have today to broaden the discussion to all of our caregivers and other family members that are in the audience to share your experience with different treatments and again, other management strategies with us today. We encourage you to call in now or anytime this afternoon. You can do so by calling in at +1 703-844-3231. Again, that number is +1 703-844-3231. If you call in, you'll be able to get into the queue and we'll be bringing colors into the discussion throughout the afternoon. Also, there is that written comment box that you'll find under the live stream on the webpage that you're following along today.

(03:43:08):

But to get us started on this topic, first around current treatment approaches, we're going to go back to polling. So if you've been with us, you can open up that tab in your browser or the browser you've opened on your phone. If you've just joined us, you can go ahead and go to this webpage, www.pollev.com/STXBP1. Again, it's www.pollev.com/STXBP1.

(03:43:37):

Keep this webpage up throughout our afternoon session as we go to new polling questions, they'll automatically appear there. So our first question for you here is we want to know what medications or treatments has your loved one used either currently or previously to treat the symptoms associated with STXBP1 and you can select all that apply. The options are A, anti-seizure medications, B, rescue medications, C corticosteroids, D ACTH, E, pain medications, F, bladder medications, G, bowel medications, H, sleep medications I, antidepressants or anti-anxiety medications, J, C, B, D, K, some other medication or treatment that your loved ones used. Here we really are focusing on those medical treatment approaches. We'll ask about some of the other types of management strategies here shortly, but other medications or treatments that they've used either in the past or currently. And then there's an option L if your loved one has not used any medications or medical treatments to date.

(03:44:47):

As a reminder, this is our first question in the afternoon where our participants can select more than one response option. So you're seeing on the right hand side percentages that represent the total or the percentage of total responses, not the percentage of people who have selected any individual response. So again, you can think of these blue bars as a bit of a relative ranking of different responses to one another while final results or responses are coming in here. One thing I think we're clearly seeing is that the top medication and treatment approach that our audience has experienced is anti-seizure medications. And after that, we see rescue medications, bowel medications, and other medications as kind of the next three. We do have a good representation of experience with all of these different medications for the many of the different symptoms and health effects of STXBP1, and we do have some representation from those who have not yet used any medications or medical treatments.

(03:45:54):

We want to hear from those of you that selected that as well, whether that's just based off of where your loved one is in their journey or if there were made to be medications that were an option to you, but you've chosen to forego those for any kind of ways you've evaluated whether those products might be helpful or the trade-offs of those.

(03:46:21):

If we go to our second polling question, so we've got a good idea of some of the medications that are experienced here. So moving beyond that, we want to know what has your loved one used to help manage the symptoms of STXBP1? And here you can select all that apply. The options here are A, gastric tube, B, physical or occupational therapy, C, dietary modifications including the ketogenic diet, D, speech therapy, E behavior therapy, F, equine therapy, G, epilepsy surgery, H, skeletal surgeries I, any other surgery, J acupuncture or K something else. Give some examples like, music or aquatherapy, but any other kind of therapy that we haven't otherwise listed on as a response option for this question. And then L, if your loved one has not used any different strategy or approach to manage their STXBP1 symptoms, and again, please select all that apply. So we'll give everyone a few more moments here just to make sure we get in everyone's responses so we get a good sense of the experiences of our audience. As I mentioned, we want to hear about these types of treatment approaches as well, as well as anything that we might've missed that wasn't included in either of these two polling questions that are things that you all have tried or done. Just one example that we've heard earlier today is modifications to the household, whether that was moving from a two-story house to a one-story house or needing to put in place alarms or gates or things like that.

(03:48:14):

Those are the kinds of things that make living life with the condition a little bit easier. And so count on our fair game for discussion this afternoon is treatments. What we're seeing in the responses here is the top types of therapy or different management approaches that are experienced by our audience are physical and occupational therapy as well as speech therapy. After that, we see a lot of others being mentioned here as well as dietary modifications. But we do see a good experience with pretty much every other type of management approach. No one noting acupuncture and no one is reporting that they're not doing anything to manage symptoms.

(03:48:59):

I have one more polling question here before we go to the live discussion and bring you into that. And so I want you to think about everything over the course of those last two questions that we listed. And I want you to think about how well does your loved one's current treatment regimen treat the most significant symptoms of STXBP1? And so here the options are A, not at all, B, very little C, somewhat, D to a great extent or not applicable because your loved one's not using anything. And again, this encompasses everything that we've listed over the last two in the last two polling questions.

(03:49:40):

So as you're making your response here, I want you to think about why you're making this selection. If you're reporting that it's helped to a great extent, what treatments and in what ways have those had that great impact? If it's about the 50% of people who are saying very little, what's your metric for what counts as the little bit that's helped? Help Us understand that selection and what more would you have been looking for in terms of treating most significant symptoms? We're seeing close to 50% also saying somewhat. Those two very little and somewhat are going back and forth a little bit here, but we do have people reporting, some saying that current treatments aren't helping at all and some saying to a great extent. And again, no one is saying not applicable because they're not using anything. So with that, I want to thank you all for participating in polling.

(03:50:39):

Again, you can call in now if you'd like to share some of your experiences with those different treatment approaches. That number is +1 703 844 3231. Or you can use that written comment box to submit written comments we'll be sharing. But now I'd like to welcome our zoom panel for this afternoon discussion. Some of your peers will be sharing their experiences throughout the time we have together this afternoon. So I'd like to maybe start our discussion here on maybe the things that have been most helpful of those treatment options. Again, we're casting a really wide net on what counts as a treatment. And so maybe Melissa, we can start with you thinking about this across that wide range of things. Is there anything that you view as being particularly or most helpful?

Melissa (03:51:30):

Yeah, so my name is Melissa. My STXBP1 child is Alex. He's almost 18 years old, so we've been at this for quite a while. We live in California and we have done so many things over the course of his life. So we've had experience with pretty much everything that was listed here. So thinking back over his, like I said, almost 18 years, I would say there has been very little that has provided improvement for him. So we have been able to have some seizure control for short periods of time depending on the medication that we were using. We also currently tried the ketogenic diet for the second time, and this second time we actually had some pretty good seizure control for almost two years. Unfortunately though we're losing that seizure control now. So I would say typically what we would see with medications, any control that we had was for a short period of time and we often refer to that as a honeymoon phase.

(03:52:49):

And I would say that that's something that a lot of the kids in our community see as far as seizure medications. The other thing I would say is behaviors have been a huge challenge for us. And so we've done ABA therapy, which is common with kids with autism, and that did help also with some of his behaviors. But

things are always changing and we're always trying to stay one step ahead of all of the symptoms and it's difficult. So I would say there's been very little that has helped to really continue to improve his symptoms.

James Valentine, JD, MHS (03:53:31):

Yeah and I really appreciate you being honest about that. We know that don't necessarily expect that the things that are helpful will have stayed helpful permanently, that they might've only helped for some period of time. But I do want to explore some of the things that you said about where there was even some help. Maybe we'll start with the ABA therapy and behaviors. You said it helped a little. Can you maybe just give us a little context? What did that look like, that little bit of help?

Melissa (03:54:04):

Right, so ABA therapy helps with not only behaviors within the home, but also behaviors in the community. And I would say as we've heard, we've made a lot of modifications to our home to make it safe and so that he's able to function within our house. But going out in the community is a whole different ballgame and it's very difficult to go out in the community. He is mobile, but he has no safety awareness whatsoever. So ABA therapy helped to a certain extent for him to be able to function within the community. So that's even just going to the grocery store, being able to do these things that most people take for granted. But we can't do that because we never know what that environment is going to present to us that could pose a safety risk for him. So we've tried a therapy, which to some extent has provided us with the ability to take him out to certain places and allowed us those opportunities to be able to help him to function out in the community. Even at school-

James Valentine, JD, MHS (03:55:21):

And Melissa, can you give an example of that just because for those of us who aren't close to it, being able to go to the grocery store or what was the difference maker that made that possible because of a therapy?

Melissa (03:55:38):

So we had to train him. We really had to train him to hold onto the cart. If I could get him to hold onto the grocery cart that was keeping him focused on what he was supposed to do. And if we can keep him focused on this is what you do when you go to the grocery store, you hold onto the cart, and if I can keep him holding onto the cart that prevents him from running off, that prevents him from grabbing things. So we literally were just going and trying to train him to hold onto the cart or to hold my hand, hopefully have that cart which kept him focused on something as opposed to acting out in a way that wouldn't be acceptable or trying to get away from me within the community.

James Valentine, JD, MHS (03:56:30):

Yeah, that's incredible. I'm glad that you shared that. Something so you might think is such a small difference opened up so many opportunities for where he could go and what he could do with you. So really appreciate you sharing that. Alicia, I want to bring you in on this topic as well as we're exploring of all these different approaches or management strategies, even lifestyle modifications, is there anything that has been most helpful in your family's experience?

Alisha (03:57:08):

Yeah, my name's Alisha and my daughter is Charlie. She turned one on September 23rd. So we are kind of on the opposite end of the spectrum in regards to Melissa's experience. We are just a little over a year in our journey in finding what works for Charlie and aside from anti-seizure medication, which has helped, we're doing physical therapy and occupational therapy and feeding therapy. But in regards to what we're thinking about long-term to make life easier for Charlie and as well as us, we're considering moving to a single story home. Charlie has very low muscle tone and of course she's only a little over a year, so carrying her is definitely manageable right now but we are thinking about the difficulties that will present itself as she gets older and needs more support physically. So definitely thinking about moving to a single story home or.

James Valentine, JD, MHS (03:58:16):

Right, one thing that you started with was mentioning that seizure medications, they've helped some... I am always curious, when you say that, what did that mean? One could wonder is that full seizure holiday or is it just a reduction in seizure burden? Can you kind of describe when you get a benefit or Charlie gets a benefit, how much of a benefit is that and how does that benefit translate to quality of life?

Alisha (03:58:53):

So as most people know on this call or maybe don't know, we're constantly, I could say chasing seizures, so I don't want to jinx it here, but we've had seizure freedom for the last several months, and as you could imagine, it impacts all of Charlie's entire life. She can participate in the different therapies in a better way because she is not so exhausted from having her seizures. And I think obviously aside from just not having a seizure, just being able to participate in life is the most positive outcome we could ask for in regard to the seizure medication.

James Valentine, JD, MHS (03:59:39):

Yeah, and do you find that when Charlie's able to participate in those other therapies more, is that making those more helpful or useful or is it just really getting to have that experience and not be so exhausted and going through those therapies that is the benefit?

Alisha (04:00:03):

I think it's a little bit of both. I think that unfortunately just not having seizures isn't enough to make the therapies as beneficial as they should be, but like you mentioned, it is just being able to participate is important to us and I have a feeling to Charlie as well.

James Valentine, JD, MHS (04:00:27):

Right, well, Alisha, thank you so much for sharing on that. Just kind of as we want to keep exploring different treatment experiences here. Danielle would love to bring you in on this topic as well, anything that you'd like to share that maybe has helped your family?

Daniele (04:00:46):

I'm Daniele and our STX'r is Cece she's eight, soon to be nine, and she's a twin and we had a pretty normal pregnancy. She had a pretty normal entrance to the world and has not experienced seizures, but she's very globally delayed. And because she's a twin, we saw her brother Marshall hit his gross motor milestones. So we entered Cece into early intervention when she was about six months old. And for her treatments. Her therapies right now are her physical therapy, occupational therapy, speech therapy that have all helped her tremendously, but she does not walk without assistance.

(04:01:44):

We actually go on Monday to get her first gait trainer that she'll have at home to help her take some assisted steps. And Russ mentioned earlier in the day that we're all detectives, and I 100% agree with that, but I'd say that we're also MacGyvers because we have to be very, very creative with the things that we feel will work for us. I remember when Cece was barely able to kind of get up into Quadripad into that crawling position, and we tried everything. And I know other parents here have too, where you put a blanket under them and you pull up straps and you start thinking and Googling and ordering random things on the internet that you think you could kind of rig some sort of device. If that device doesn't exist, you're going to create it.

(04:02:40):

Not only are we the MacGyvers, but all those therapists that surround us in our orbit are extremely helpful. So we rely very, very heavily on therapies for walking. She also has very limited communication, both receptive and expressive. She does have a device that she's still kind of grasping the concept of, but we know she is so desperate to be able to express what she's feeling, what she needs.

James Valentine, JD, MHS (04:03:15):

Right, yeah. Well, thank you for sharing those different things and also the idea of being a MacGyver on top of a detective. I guess one thing that I'd maybe like to hear a little bit more about is whether it's the combination of the different therapy and therapists and also what you're doing individually at home, trying

to find ways to help figure out crawling or whatever, as I heard it described earlier, the inch stone, maybe not the milestone. Next inch stone might be for your loved one. Can you give examples of where those inch stones were able to be achieved and was there anything you can attribute to that?

Daniele (04:04:04):

Sure, so funny enough, during the pandemic when unfortunately she's very social, she likes to interact with others, and she was stuck here with all of us. The silver lining to that for us was that she spent more time on the ground than she would have if she were at school, either in a chair or in a stander, which there's time and place for all that as well, but because she was able to be down and explore her environment a little bit more, that's where we saw her pull up to her knees for the very first time. We celebrated those little tiny things, and her therapists have been building upon all of that for us and thinking very creatively about how to support her and being able to make progress in those-

PART 7 OF 9 ENDS [04:05:04]

Daniele (04:05:03):

... How to support her and being able to make progress in those areas.

James Valentine, JD, MHS (04:05:06):

Great. Well, thank you so much, Daniele, for sharing that. Great to hear some of that type of specific example to give us, again, those of us who aren't as close with the condition an idea of what that can look like. I do see we have a phone caller. We have Erin from Philadelphia who's a parent that wants to share some experience with the keto diet as a treatment approach. So Erin, I'd like to welcome you to the program. Are you with us?

Erin (04:05:36):

Hi, yeah. I'm here.

James Valentine, JD, MHS (04:05:40):

Hi, welcome.

Erin (04:05:40):

Thank you. Like I said, I'm Erin. I'm from Philadelphia. My daughter Lucy, she's five years old and she's been on the ketogenic diet since she was about seven months old. So, I thought I would bring a perspective on keto for you guys today and just share a little bit about that. So, Lucy was born and had seizures on day three. She went to the NICU and her seizures evolved over time. They went uncontrolled for the first couple months of her life. They evolved into infantile spasms, so she had that diagnosis by two months old. She was having probably 20 to 100 cluster seizures several times a day, and her EEG background was hip rhythmic. We tried all the frontline defenses, phenobarb, Keppra, ACTH, Sabril, ONFI, I think maybe seven or eight different types of anti-epileptic drugs, and then our neurologist recommended the ketogenic diet for epilepsy. And she's been seizure-free for almost five years, knocking on wood right now. And I would say that's not-

James Valentine, JD, MHS (04:06:44):

Complete seizure freedom?

Erin (04:06:47):

Yeah, so it took about a month and a half. She was still having seizures and it took about a month and a half, I guess, to kick in, and then one day she just didn't have any. And I was like, "Well, maybe this is a fluke, or maybe I missed one, or maybe I wasn't quite..." It was around the holidays. I was like, "Maybe I wasn't quite paying attention," but then a couple of days went by, and then a week went by, and a month went by and I think after three months my husband and I were like... I didn't want to talk about it, but I didn't want to jinx it, but I don't think Lucy's had any seizures.

(04:07:19):

So we both noticed, but neither of us were discussing it. So, she has been seizure-free and has since been able to wean off of all of her medications. So, that's been incredible for us as a family. I think seizures are debilitating both for kids and for families. So, it's a really tough one to stomach and watch your kids seize over and over again several times a day. So, I feel for parents that are out there right now dealing with that, and I'm sorry, I wish I could do something to stop it.

James Valentine, JD, MHS (04:07:53):

I wonder, Erin-

Erin (04:07:55):

Sorry, go ahead.

James Valentine, JD, MHS (04:07:56):

Just as you're describing, it kind of took a couple months and then there's kind of almost at some point a switch that turned off. Was there anything you noticed in terms of energy levels, behaviors, other aspects of quality of life that changed when that switch got flipped off and there wasn't those seizures happening? Was there anything else besides obviously not having to experience seizures that you would describe as a benefit of having that relief from seizure?

Erin (04:08:34):

Yeah, of course she just came back to life. She wasn't on as many drugs. She started making eye contact. She wouldn't look at anyone. We called it her seizure side eye. She would just kind of stare at people and call it like her stink eye that she would look at people, but she just wasn't happy. You could tell she was uncomfortable in her own skin when she was on a ton of different medications, very refluxy, couldn't quite ever really be comfortable as a baby. I remember on Halloween, she finally was able to snuggle me a little bit and I'd never had that before and she'd been alive for seven months or so. She just was never quite comfortable, but she started more eye contact, more engagement, and then slowly and surely the inch stones came being able to... She sat up I think by 13 or 14 months, but she had very [inaudible 04:09:27] neck control, body control. So, I think the more we started weaning further medications, the more light came back into her and more engagement for sure.

James Valentine, JD, MHS (04:09:40):

Wow. Well, Erin, thank you so much for calling in and sharing some of your experiences with keto and what seizure relief can mean for patients that are able to experience it, so really appreciate that. I do see that we've gotten a lot of written comments, no surprise after how engaged everyone was this morning. So Charlene, I want to check in with you, what are we seeing in terms of treatment successes?

Charlene Son Rigby (04:10:08):

I'll share a few of the comments. So, this one is from Evelyn in the Netherlands. "Lorazepam is working well for now to control our son's seizures. Physical therapy helps his tremors and his ataxia is more steady. He has more strength and core stability. Speech therapy helps to find the best way to communicate. We just started the Tobii." And here is a comment from Kevin in Seattle. "Our son recently started being able and willing to bend his knees in order to go downstairs. He spent several years working on this skill." And then this one from Ashley in Portland, Oregon. "My son takes four medications daily for seizures: Keppra, ONFI, Epidiolex, Fintepla, and he has a VNS implant. He currently has between zero and three seizures most days. This is some of the best seizure control he has had."

James Valentine, JD, MHS (04:11:12):

Wow, I want to thank everybody who's been writing in. Again, we'll continue to read out quotes throughout the session, but know that if we don't get to yours today, we will have that to review and include in the Voice of the Patient report. So, I want to broaden the discussion a little bit. Of course, if you have a treatment success story you want to share, please do share that, but we know that there's a lot of things that are tried that maybe it's unclear whether they've helped or maybe it's very clear that it has not helped, as well as the fact that whether or not something's working for you, it might come with certain downsides

like side effects or burden of keeping up with the treatment. And so, I do want to broaden our discussion of current treatments to include some of those experiences with treatments that maybe haven't been as helpful or do come with those downsides.

(04:12:04):

So to get us thinking on this topic, we're going to go to a polling question. So go back to that webpage, www.pollev.com/stxbp1. Here we want to know, what are the biggest drawbacks of your loved one's treatment approaches? And here you can select up to three of the greatest drawbacks. The options here are: it's not very effective at treating the target symptom, B is it only treats some, but not all of the symptoms of the condition, C, it has limited availability or accessibility, D, the side effects, E, the route of the administration or how it's taken, F, that it requires too much effort and/or time commitment, G, some other drawback that represents one of the biggest drawbacks of your loved one's treatment approaches, or H if not applicable because you have not used any treatments. And again, we're thinking about all of the different treatment approaches and management strategies that we've been covering since the beginning of this afternoon session and thinking about what are the drawbacks.

(04:13:17):

Give everyone a few moments here. We have lots of responses coming in on the top three biggest drawbacks of treatment approaches. It looks like the one that's coming in as number one right now is that it treats some but not all of the symptoms. So, we heard about so many of the different symptoms and health effects this morning. So, we're hearing that treatments maybe target just one of those things, but not the others that are important. We do see after that, number two is that the thing that it is trying to target, it's not very effective at treating that symptom. We see as number three, side effects followed closely behind the requiring too much effort or time commitment, as well as limited availability or accessibility, but even route of administration is in the top and others are in the top biggest drawbacks of some number of people.

(04:14:17):

So, I want you to think about what treatments were you thinking of as you were saying it treats some but not all or it's not very effective. We'd love to hear your experiences with that. Again, you can call in at +1 703-844-3231. You can also fill in that written comment box and we'll share some of those, but I'd like to start here with our Zoom panel. And Souha, I'd like to start with you on this topic. Is there a treatment that you all have tried that maybe has not been as helpful or has come with some important downside or trade off?

Souha (04:14:54):

Hi, this is Souha. My son Jude was diagnosed with STXBP1 almost three years ago. We live in Orlando, Florida. I apologize for the voice, recovering from a flu. So, we actually started Jude on multiple therapies even before he got his STXBP1 diagnosis. So, it has been like now almost four years since we have been doing speech therapy, occupational therapy, physical therapy. We kept increasing the number of hours he's doing therapy, so now we are at three hours a day for each therapy. So we do one hour speech, one hour occupational, and one hour physical therapy three days a week.

(04:15:42):

The only thing that I see improvement with is the balance, so the physical therapy is kind of working for Jude. So he's getting a better core balance, better gross motricity, but for the OT and the speech therapy, I don't see any improvement. Now after almost four years, Jude is able to sign only more, that's the only thing that he can sign for. He babbles some words, but I cannot tell you he's saying them because he was trained or he got the speech therapy. It's more because he's just grown and that at his age he would be able to say some words. So, after three or almost four years of therapy, Jude can sign one or two words and he can say maximum five words and it's not a consistent thing.

(04:16:32):

So, you can see how time-consuming these kind of therapies can be because for someone who's working, what kind of job will let you, let's say, be off for three hours a day to drive your kid and then go back? So,

literally there is no job schedule that will allow this kind of commitment. It also takes a lot from our family routine. Jude has a sister and also she needs someone to take care of her. So, staying with Jude during the therapies and being committed to drive him to the therapies takes a lot from our time, and also change the decision we need to make for our family and how we manage our time.

(04:17:18):

I have been in a waiting list for behavioral therapy for six months now and still don't find any spots. We started the therapy, I think it was 2020, so it was during COVID and it was even so hard to establish these therapies, so hard to find people who can go to the place like the school or the house. I think, yes, it's may be working for some symptoms, but maybe 2% of the symptoms that the disease is causing, and it's very, very time-consuming for someone who wants to do a lot of therapies.

James Valentine, JD, MHS (04:17:57):

Well, it's valuable to hear that. I'm very sorry to hear that, so much time and effort for 2% of the benefit that you might hope for. I guess one question then is, can you tell us a little bit about your thinking of why you keep up these therapies? Four years, as you described it's helped about 2%, but clearly it sounds like it's still something that's important that you all prioritize. Can you tell us a little bit about your decision to keep up those therapies and keep doing that?

Souha (04:18:41):

I can tell you that sometimes I ask myself the same questions, do I really need to keep going? But I can tell you that the day when we visited the expert in Philadelphia and he was saying, "We know there is no treatment for STXBP1, but the only thing we can do now is therapy and therapy and therapy. And I said, "He's happy going to these therapies," and for STXBP1, the way that the brain works is going to take way longer for let's say the thing to develop. So for a normal person, maybe it will take you to repeat two or three times for STXBP1, you need to repeat the same thing 100 times, 200 times.

(04:19:23):

So, I said maybe in 10 years I'm going to see a difference, maybe, I don't know. So, I want to give him that opportunity. I want to give him the best he can have, and maybe at some point, one of the therapists actually tried to stop the treatment and she said, "It's not working, we are not going anywhere," but what I was trying to explain to her that with STXBP1, we don't have the same linear trajectory where you train them to do something and in six months they'll be better. It doesn't work that way unfortunately. So, we have to be patient and we have to stay hopeful that one day I will see an improvement.

James Valentine, JD, MHS (04:20:04):

Well, that's super helpful. Thank you so much, Souha. I want to bring Matt, you into this discussion too as we're exploring different current treatment experiences and on this particular topic, maybe things that you're doing or have previously done that either aren't working or have come with some downsides that you want to share.

Matt (04:20:25):

And good afternoon. I feel it's important for me to begin with actually thanking our FDA partners who have chosen to give us time this afternoon, and that really means a lot to me and my family. So, my name is Matt and my wife Heather and I have three children. Our youngest Camden was diagnosed with an STXBP1 gene disorder shortly after his birth six years ago. I can tell you that Camden is completely and totally affected by his disorder. He can't talk or walk, he can't crawl, swallow, or eat properly, he can't play, have friends, or really have any typical childhood experiences that we took for granted six years ago before receiving this diagnosis.

(04:21:14):

So, I'm grateful for the opportunity today to join the other panelists and share my perspective on living with this disease. And when I think about the question about the trade-offs with the therapies and the help that we're seeking, my mind goes to two things specifically. One, and it's super obvious, the seizure medication. I

think we've heard a lot about that. So, we've gone down that path and it's a heartbreaking path to go down where it's just two bad choices, watching the seizures happen, accepting the risks or I guess not accepting the risks with the seizures by giving medicine that has these terrible side effects which result in this trade-off where we are seeing a lesser version of our son, where Camden can't do... Even though he can do very little in the first place, he can do even less, and so that's a terrible position to be in.

James Valentine, JD, MHS (04:22:23):

And Matt, can you give an example-

Matt (04:22:24):

We've also [inaudible 04:22:25] a lot about-

James Valentine, JD, MHS (04:22:25):

Can you give just quickly an example of that to help me understand when you say there's something that he might be able to do less, what that looks like?

Matt (04:22:34):

Absolutely, so when I say that it is literally everything, everything in his daily life. So, Camden eats pureed, spoonfed food, and so he struggles through that, and so mealtime is very difficult. So, when he's on more of the anti-epileptic medication, it drools out of his mouth, he can't swallow, he can't consume as much of it from being able to... So eating, to being able to sit, and sit up and maybe play with some toys with his hands, there's less of that going on. It interrupts his sleep, so he can't sleep properly or as well as he could otherwise.

James Valentine, JD, MHS (04:23:25):

Oh, wow.

Matt (04:23:26):

And I could go down with other examples the more I thought about it, but I hope you get the sense here of it's really everything.

James Valentine, JD, MHS (04:23:34):

No, absolutely, and I know you said you had another thing beyond the seizure medicines that your mind went to. So please do, I'm happy to hear what that was.

Matt (04:23:42):

And just agreeing with the other panelists around what we heard around therapy, so there's a huge cost to us to do therapy. We don't get a lot of results from it, like we heard from Souha, how it's these incremental challenging situations to do a lot of work with very little results, but you can't give up. It's your child. They deserve you to keep trying, and so we do. And so I think Heather and I have... We've really reorganized our lives around providing whatever that opportunity is for Camden, providing that opportunity for him.

(04:24:24):

So, we've moved to a home that has more space for us to actually have therapy equipment. We're fortunate enough to have an au pair now that lives with us who is a physical therapist, and also we go to three weeks of therapy twice a year, or Camden and Heather do. So, they're actually separated from our family. Our family is separated. It's probably a better way to put it. So, the cost there is huge and the reward is very, very small. So it's challenging, but it's essentially as a parent, you'll do whatever you can and that's in front of us, and so that's what we're doing.

James Valentine, JD, MHS (04:25:15):

Well, Matt, thank you so much for helping us understand some of those things and really the sacrifices that you all as families are making to give your children that opportunity. I do have a phone caller that I want to bring into the conversation. We have Jason from Georgia who's a parent. I think, Jason, we might've spoken to you earlier today, but wants to talk about anti-epilepsy drugs. So Jason, I'd like to welcome you to the program. Are you with us?

Jason (04:25:45):

Yes. Hi, can you hear me?

James Valentine, JD, MHS (04:25:50):

Yes, we can hear you. Welcome.

Jason (04:25:51):

Awesome. Hi, thank you very much and thanks for having me back on again, and thank you so much for putting this on. As others have stated, this is so important to all of us and to the lives of our children and our loved ones who are impacted by STXBP1 deletions. So Juniper, as I'd mentioned earlier, she is six. She is currently on seizure medications with reduced seizure activities, so she has breakthrough seizures every few weeks, sometimes every few months. It's relatively controlled compared to what it used to be. She started on phenobarbital when she was just six weeks old. Since then, we've experimented with a number of drugs that have worked often temporarily, like you mentioned earlier, there's kind of that honeymoon period.

James Valentine, JD, MHS (04:26:38):

Right.

Jason (04:26:38):

But she's been on Topamax and ONFI for about a year now, and we've had good success with those meds, but I have kind of four really major concerns about the medication that she's on and has been on. One is the side effects, these medications cause drowsiness, like the sweats, constipation. Some of these actually worsen her seizures. Each one of those I mentioned, she overeats easily, she gets constipation, she's often drowsy, those cause seizures. So, the very things we're giving her to help her seizures actually could be causing more problems. And they do introduce internal side effects that I can't see, like bad taste in the mouth and nausea and depression and headaches. If she's experiencing those things, I honestly wouldn't know because I have trouble with the communication aspect of it. Those side effects, like some examples of them affecting her behaviors as well are like these things can cause drowsiness, lack of coordination, trouble sleeping, slurred speech.

(04:27:37):

All of these things are directly correlated to her motor planning, her ability to sleep, her communication. If she's taking medicines that are impacting coordination and speech, it's just like, how do I know what the medication is causing a problem with versus just her STX diagnosis. So, we just don't know what we're doing to help and hurt sometimes. She's not able to communicate to us directly, so as easily, and so we don't know what's impacting her and none of the meds help anything really but the seizures. All of our medical interventions or neurology is focused on seizures and any other intervention for her other symptoms are through therapies that are completely siloed from the broader medical community. So when we see those therapists, it feels like we're kind of meeting them in a vacuum. So, that's kind of what I wanted to lay out is just I have really concerns about the current meds and they're not really covering even a fraction of what we need them to help with.

James Valentine, JD, MHS (04:28:41):

No, we hear you loud and clear, Jason, and also on the impacts that the side effects are having on the disease and being able to even distinguish what's STXBP1 versus the side effect and the complex interplay of all of that. So really appreciate you calling back in here, Jason, and sharing some of that. I do want to check back in with the panel and Melissa, we can start here with you, something you want to add to this discussion of treatment downsides?

Melissa (04:29:13):

Yeah, so just a couple of things that I was thinking about as I was listening to everybody. I mentioned before the ABA therapy, which was helpful to a certain extent, but there came a point where he stopped making progress and when he stopped making progress, they will not continue with the therapy. They have to show

that he's making progress, so it broke my heart, but we had to stop at a certain point. And I will say though, unfortunately he has regressed because he didn't have that continued repetition that he really needs.

James Valentine, JD, MHS (04:29:46):

Right.

Melissa (04:29:47):

So, there's this double-edged sword where you don't make much progress and then they stop approving the therapy. The other thing that I wanted to speak to are the side effects of the medication. And so as I've shared, Alex has had seizures since he was just a baby, and I've never known my son not on medications. I truly do not know my child. I don't know what he's like because the medications hide who my kid actually is. And the other part of it is that twice in his life, medications have almost taken his life.

(04:30:25):

He had a medication toxicity that put us in the hospital where he was in a catatonic state and I thought we were going to lose him, and that was all because of a medication to treat his seizures. So, these medications sometimes cause more harm than good and in some cases could even put them on the edge of losing their lives. And I just want to be clear that he has to take the medications to control the seizures that we're so afraid could take his life, but in the same place we're having to treat him for the seizures with medications that could take his life. So, there's this very constant battle within us where we're trying to decide what's worse, the seizures, the side effects? It's a really hard place to be.

James Valentine, JD, MHS (04:31:24):

And so Melissa, just to unpack that a little bit, it's this tension of trying to treat what could be really serious or life-threatening consequence of the disease, the seizures versus the side effects, and even potentially life-threatening at times risks of the treatments themselves. Does that need to weigh those two things constantly lead to you changing treatment regimens, changing doses? Can you just tell us a little bit about that? Because it sounds like it's a terrible place to be in to have to try to balance those two things, but at least what tools do you currently have in terms of making treatment decisions?

Melissa (04:32:18):

I would say that that's been our entire life since we've known that he's had seizures and also his entire life, just trying to help him with all of the symptoms. We've really tried so many things over the course of his life and it's always a battle in trying to balance those positives that could help him, versus those risks that we're having to take as far as medications, especially as far as medications are concerned.

(04:32:50):

But we've even gone as far as we've done the ketogenic diet as well, which is extremely difficult. It's extremely challenging for the family and for Alex who doesn't understand that he can't have certain foods. Cognitively, he is impaired to the point where he doesn't understand why he's so limited. We cannot let him grab a single piece of extra food, otherwise that could cause him to have seizures again. And I will echo Erin who called in that the ketogenic diet was one of the more effective treatments that we've seen for seizures. Unfortunately, we were never able to wean medications though. So, it's always this balancing act of trying to figure out what is better, where is this place where we can feel comfortable with a medication? But you have no choice. You've got to be able to help your child, and if that's a medication that you've got to try, then you've got to try it.

James Valentine, JD, MHS (04:33:52):

Right.

Melissa (04:33:52):

You've got to do it. You've got to be able to help them in one way or another. So, I'll just say one last thing. We also now have done a VNS, so Alex as an implant that will stop seizures or that's the goal at least, is to stop the seizures. And I will say that it is somewhat effective and I am thankful, but that was one of the hardest decisions that we have ever made because here you are putting your child through surgery and you

don't even know. There's a 50% chance if it's going to be effective. Are we going to be in that 50% that it works or the 50% that doesn't work? But we had to see, we wouldn't know. So, we had to put him through it. And I am thankful that we did now, but that was one of the hardest decisions, and again, he had no say in that as we heard earlier. He's not able to communicate with us, so these are decisions we have to make and we have to hope for the best.

James Valentine, JD, MHS (04:34:50):

Well thank you so much, Melissa. I'm glad that you shared that. I do see that we have a lot of written comments that have come in. I do want to give voice to those of you who've been sharing some of your experiences with treatments that maybe haven't been so helpful or different treatment downsides. So Charlene?

Charlene Son Rigby (04:35:11):

I have a comment from Adele in Leeds in the UK. "Our son has already failed a handful of medications, the side effects of which were devastating. We are currently treating him with a mixture of the keto diet, sodium valproate, and carbamazepine. While these treatments seem to help decrease the number of seizures at the start, over time they have become less effective." And this comment from Shannon in Cibolo, Texas. "My daughter is on multiple medications for seizures, dystonia, chronic pain, dysautonomia, GI motility, and respiratory medication. She requires regular breathing treatments. She uses a BiPAP machine while she's asleep and as needed when she's awake, and is a TPN and IV fluid dependent. Because of her medical complexity, she requires 24/7 nursing."

James Valentine, JD, MHS (04:36:13):

Wow.

Charlene Son Rigby (04:36:16):

And this third comment from Denise in Coram, New York. "My son is sleepy most of the time. I believe the medications for seizures cause GERD and lead to recurring aspiration, pneumonia, and hospitalizations."

James Valentine, JD, MHS (04:36:32):

I want to thank everyone who's been writing in, again, such valuable comments. And just to continue to reiterate, we know that a lot have been coming in and we'll be making sure that we incorporate all of them into the Voice of the Patient report. So, I do want to make sure that we have time to explore the last topic for this afternoon session, which is shifting us a little bit from talking about current treatments, but really looking at what this community is looking for and needs from future treatments. And while we all do want that cure for STXBP1, we're really going to be thinking about the treatments that might come before that cure comes along. So for the last time today, we'll ask that you go to that polling webpage, www.pollev.com/stxbp1, and here we want you to think about short of a complete cure, what specific things would you look for in an ideal future treatment for STXBP1?

(04:37:33):

And here you can select up to three, your top three. So the options are: A, reduced seizures, B, greater ability to communicate, C, improved cognition, D, improved muscle control and coordination, E, improved ability to self-care, F, improvement in difficult behaviors or safety awareness, G, improved sleep, H, reduced pain, I, maintaining current skills or functioning, J, longer lifespan, or K, some other specific thing that you would look for in an ideal future treatment for STXBP1, something that would be short of that complete cure. Perhaps the hardest question of the entire day to narrow this to just the top three, but again, these polling questions, we want you to think about why you're making your selection, and we want to invite you to call in and write in to share and explain what you chose, why you chose it. So as you're answering this, think about the why behind your selections, and please share that with us.

(04:38:45):

As it stands, it looks like our top kind of treatment goal for a future treatment is the greater ability to communicate. After that, we're seeing improved cognition and then reduced seizures. Maybe as number

four, we're seeing improved ability for self-care, followed by improved muscle control and coordination, and improvement in difficult behaviors and safety. Everything here is in somebody's top three. No one has listed any others. So whichever of these you selected, we do want to hear about what this would mean. And as you're looking and maybe if a new treatment were to become available that is intended to help, what questions would you have? What would go into your consideration of whether or not you'd try a treatment that might have this type of effect? So, I'd like to come to our Zoom panel to get us kicked off on this topic. And so Alisha, maybe we can start here with you. What's top of your list of what you would want from a future treatment for STXBP1?

Alisha (04:39:57):

It's hard to even verbalize one, but I think-

PART 8 OF 9 ENDS [04:40:04]

Alisha (04:40:00):

... but I think... I'm a crier as well. I'm sorry.

James Valentine, JD, MHS (04:40:09):

It's okay.

Alisha (04:40:13):

Just the ability to communicate. I just would like to know when she's happy, or when she needs something.

James Valentine, JD, MHS (04:40:24):

Yeah.

Alisha (04:40:26):

I think the thought of her not being able to do that is, I think, something that's most painful for me.

James Valentine, JD, MHS (04:40:37):

Yeah.

Alisha (04:40:37):

I'm sorry. I'm a crier.

James Valentine, JD, MHS (04:40:40):

No need to apologize. Thank you, Alisha, for sharing that. It is important to hear, not only what it was, but just being able to communicate some of those very, very basic things that could mean so much to her, and to you. Matt, we'll kind of just go around here. I want to hear everybody's thoughts on this topic. What would you describe as your top treatment goals?

Matt (04:41:10):

Yeah. My first election was improved cognition.

James Valentine, JD, MHS (04:41:16):

Okay.

Matt (04:41:16):

But I guess, in my mind, the communication kind of goes along with that. So I definitely agree with what Alisha just expressed, and Heather and I were fortunate enough with a repurposing treatment of 4PB for Camden. Where Camden actually demonstrated some improved cognition, and in a way, it almost makes it harder to understand that, "Hey, there's a little boy in here that we didn't see before." And to see that change, and think about, "Wow, is there more? What would more look like?" Right?

James Valentine, JD, MHS (04:41:57):

Yeah.

Matt (04:41:58):

And it's very difficult to not recognize that there's probably a typical little boy in Camden that's just buried beneath all of these challenges. And so, when I think about this, my mind does go back to cognition, and just his ability to really actualize what I believe is right underneath the surface.

James Valentine, JD, MHS (04:42:24):

Yeah, and Matt, since you mentioned that you did have a treatment experience with the repurposed product, and that you saw something that was a benefit. If you're thinking about the next future treatment, what would you describe as... What would be meaningful if it were an improvement in cognition that you could see? Is there some minimum amount of improvement? What would your... It's hard to say because I don't want to say, "What would your metric be?" And you might not think of it that way, but can you put some words to what that goal might look like?

Matt (04:43:00):

Yeah. I think a more abstract way for me to describe it would be... So we... So Heather and I have two older children that are absolutely exceptional, and emotionally, physically, socially, academically in every way, and Camden has none of that. And so, it's important for us to understand that there's a really broad range of what success looks like.

James Valentine, JD, MHS (04:43:25):

Right.

Matt (04:43:26):

And so, we don't need to be the exceptional, right? Minimally sufficient, for Camden to have a life. Where he can contribute, where he can have relationships, where he can maybe have a job, and sort of take care of himself. To me, that's what we're shooting for. That would be good enough, and certainly more than that would also be good enough, or better as well. But it doesn't have to be that sort of bullseye, but just some level there where Camden can actually have a life.

James Valentine, JD, MHS (04:44:03):

Yeah. Well, thank you, Matt, so much. Danielle, again, just kind of going around here. What is your top treatment priority, or goal?

Daniele (04:44:15):

Definitely communication. We really dare to dream that there's a future for Cece where she can express to us what her needs are. Even for her to... I would love to hear her voice. I would love to hear her voice tell me, "Mommy, I love you." She tries so hard, and the therapies have incrementally gotten her so much closer. She opens her mouth, and makes that, "Ha," sound. And more recently, is trying to use her tongue, which is kind of blowing our minds. But I would trade all the, "Mamas, I love you," for, "My tummy hurts."

(04:45:11):

I'm scared. I'm still hungry for her to really be able to communicate those things to us. There's only so much that detective work can get us, and there's only so much that the therapies are going to be able to get us. We feel like there's just... No matter what, I feel like there's a brick ceiling over her progress. No matter how hard she's going to try, and she does. Everything is very, very incremental, but I think we are dreaming of that. Whatever those treatments, or cures are that are going to help us blow through that bricked off ceiling.

James Valentine, JD, MHS (04:45:46):

Right.

Daniele (04:45:47):

And even if it's just to get us right on the other side of it, we don't have to go all the way to the stars. She doesn't have to be singing. Although, I know she would if she could, but for us, to be able to just-

James Valentine, JD, MHS (04:46:01):

Yeah.

Daniele (04:46:02):

... have her be more independent in her ability to share those needs.

James Valentine, JD, MHS (04:46:05):

Yeah. Thank you. Melissa?

Melissa (04:46:12):

Oh, this is so hard. So I agree with all of my fellow [inaudible 04:46:19] parents here. I think Matt touched on it that, if we had an improvement in cognitive abilities, I think it could improve his quality of life in so many areas. We've talked about behavior today. We've talked about taking care of your daily living skills. All of these things impact his quality of life, and impact our quality of life as a family. And if we could just have an improvement in cognitive abilities, his quality of life would be substantially better, our quality of life would be substantially better. And then, if we could add that communication piece in too, I would love that.

(04:46:59):

We've never had a conversation with our son. We don't know what his voice says. We don't know what his voice sounds like. We don't know what he would say to us. I will say that he's actually regressed as far as communication is concerned. And I hate to say it, Daniele, but I think we hit that brick wall. And I don't think that he can go any further. In fact, I know it because he's gone backwards. So communication would be amazing. I worry about his safety. I want him to tell me if something's wrong. My biggest fear is that somebody's hurting him, and he can't tell me. And I think that those two things, the cognitive abilities, and communication would be my ultimate goal.

James Valentine, JD, MHS (04:47:47):

Absolutely. Thank you, Melissa. And Souha, to finish us off here on Zoom, we very much want to hear what would represent a top treatment goal for you all.

Souha (04:47:57):

It's going to be definitely cognition because I know that an IQ of 20 is not the same thing than an IQ of 60. I'm not asking for an IQ of 100, or 120, but we need the minimum. A minimum where Jude can understand that shoes don't go into your mouth. You wear shoes. You don't put them in your mouth. I want him to understand that you don't open the door, and you try to run away, and your parents are not watching. I just want him to understand how to be safe if I'm not around him.

James Valentine, JD, MHS (04:48:28):

Yeah.

Souha (04:48:28):

If I'm not around him, if daddy is not around Jude, Jude may starve because he cannot say that he's hungry. He cannot say that he's thirsty, and he wants to drink. That minimum of cognition can make a huge difference for Jude. For his safety, for his future, for my family future, too. So for me, if he can understand things, I'm kind of confident that he can use an AC device. He will find a way to communicate with me, but if he doesn't understand how to operate the machine, how can he communicate anything? Now they're trying to teach him how to use the button, but he has intellectual disability. So it is not working. So for me, that's why recognition is the most important thing that, hopefully, one day a treatment can give me some of it.

James Valentine, JD, MHS (04:49:17):

Yeah, beautifully said. I just want to thank all of you so much here on our Zoom panel for everything you've shared, and contributed throughout today, and rounding us out on this final topic here. Really appreciate it. We do have some phone callers that I'm going to get to on this topic. I'd like to start with John from Canada who wants to talk about what some treatment goals would look like for him, and his family. So, John, we'd like to welcome you into the program. Are you with us?

John (04:49:52):

Yes, I am.

James Valentine, JD, MHS (04:49:53):

Welcome.

John (04:49:56):

Thank you. So I did have an opportunity to present my story about Lucas this morning.

James Valentine, JD, MHS (04:50:01):

Yes.

John (04:50:05):

And what I want to say, and I've had an opportunity to say this at an FDA meeting before, is that even incremental improvements in cognition, in motivation, in communication, and the ability to do some self-care will be a lifetime of benefits. It's not just that day, but it's every single day of our children's lives, and it will have an impact on caregiving. Right?

James Valentine, JD, MHS (04:50:32):

Mm-hmm.

John (04:50:33):

If I could spend an hour less feeding, taking him to the washroom, doing all of those things a day, that's an hour that we as caregivers could do other things with our children. Whether it's advocating, or working with them directly. And I think that's really important for everybody to realize that even these small improvements, or in stones as some of the other rare diseases refer to, they have a big impact because relative to your own family, they will make the burden less.

James Valentine, JD, MHS (04:51:07):

Yeah. John, I really appreciate you sharing that, and the point that you just made that there's improvements on cognition on a number of these function that reduces the amount of time caring to help them since they're not independent in those activities, or functions. But that actually has a direct translation then to other things you could be doing with them, with that time, that could improve their quality of life. So thank you so much for sharing that perspective. I'd like to bring in Jen, another caller. Jen from Northern Virginia who is a parent, and caregiver, to speak to some of what she would be looking for. So, Jen, I'd like to welcome you to the program. Are you with us?

Jen (04:51:57):

Yes. Hi, so my video was the first one at 1:00. We've been discussing things on Facebook behind the scenes, and I really wanted to reach out for the parents who have kids who are so much more medically complex. There's a huge spectrum in regards to how STXBP1 affects people, and a communication behavior? Yes, important. But on our end of the spectrum, the more medically complex kids, I want my kid to stay alive. I don't want to have to worry like my friend Becca's parents did.

(04:52:27):

That when her kid goes to sleep, she's not going to wake up because she had seizures, and died from [inaudible 04:52:32]. I don't want to have to worry like Holly, and Marilyn, who recently, in the past month, lost her daughter from pulmonary respiratory issues because of all these effects of STXBP1. So I just wanted to make sure that we're capturing that there is severe life, and death issues along with communication. Yes, I'd love Kaylyn, for me, to be able to speak to me. I've told her multiple times that if her first word is a four letter word, I A-okay with that, but I really just want her to stay alive.

James Valentine, JD, MHS (04:53:02):

Yeah. Well, Jen, I really appreciate you calling in to share some of the treatment goals where there's additional medical complexity. And so, value that perspective. So thank you so much. I do know that we're now at a little overtime here on this afternoon, too. We've just been getting so many callers, and written comments, and have been having such a great discussion. I've been remiss. I don't want to cut it off, but I do, before we conclude here, recognize that there's been a number of written comments that have come in. So, Charlene, would love to hear what kind of our written commenters are saying about what they want from future treatments.

Charlene Son Rigby (04:53:45):

So this is from Jim, and Margie in Decatur, Alabama. "Our son passed away at the age of 14. Any type of experimental treatments would have been welcomed. When you're dealing with children that have such a low quality of life to begin with, the risks are certainly worth any possible gains." And this from Chris in Pennsylvania, "If our daughter is sad, or upset, we have no idea what is wrong. And that, as a parent, can be very despairing. She has spent countless hours of therapies trying to improve her abilities. Anything that could help with these conditions would vastly improve her life." And then, this from Michael in Royal Oak, Michigan, "Our hope for our granddaughter is that in the future, with medical breakthroughs available to the entire STXBP1 community, she will be able to communicate her needs, and possibly find a path to more independence."

James Valentine, JD, MHS (04:54:46):

Wow. So I just really want to thank everybody so much. Everyone who's called in, even those of you that we maybe weren't able to get to either on the phones, or read out your written comments. If you were one of those people on the phones that we couldn't get to, please, please, please still submit your written comments, or for anyone who's here today, if you walk away. Whether it's an hour from now, or you wake up tomorrow, and you're saying, "Oh, I wish I had shared this." You still can. You come back to this webpage, and provide that written comment. We'll be collecting those for the next 30 days. But as we now conclude the part of the program where we're having you all share your experiences, and your views.

(04:55:29):

As your meeting moderator, I just want to personally thank everyone. Today has been tremendous. You all have been incredibly brave, incredibly vulnerable in sharing what your children are going through, what you all as caregivers, and parents who want nothing more than the best for your children, what you're going through. And today, that's what we needed to hear, and it's been a hard discussion at times. I know. I've seen that in our participants, how emotional it's gotten at times. And so, just as your meeting moderator, I want to thank you from the bottom of my heart for being so willing to do this on such a public scale. So now, we're going to move to the part of the meeting where we're going to hear a summary of today. That is surely an impossible task to try to summarize everything that was captured over the hours we've been talking together, but we will hopefully hear some takeaways. Know that the full summary will be in the voice of the patient report.

(04:56:36):

To give some remarks, it's my pleasure to introduce my friend and colleague, Larry Bauer. Larry's the perfect person to do this. He's a nurse by background, worked at the Cleveland Clinic, spent 17 years at the National Institutes of Health in clinical research, and then went to the FDA where he co-founded the Rare Diseases Program within the Center for Drugs where he worked for 10 years as a regulatory scientist. And Larry has been an essential member of the planning team for this externally led PFDD meeting. So, Larry, take it away.

Larry Bauer, RN, MA (04:57:11):

Thank you so much, James. And like James said, this is a high-level overview of the day. It was such a rich day with so much that... The details will be in the voice of the patient report to come. So our meeting today was opened by Charlene Son Rigby who's the president, and co-founder of the STXBP1 Foundation, and also mom to her daughter Juno who's living with STXBP1. This was followed by a presentation from Dr. Michelle Campbell from the FDA's Division of Neurology products in the Center for Drug Evaluation and Research. Dr. Campbell shared that these patient-focused drug development meetings, they're valuable to the FDA to learn from the experts, the caregivers of people living with STXBP1. To help them facilitate treatment development, design clinical trials, and review new drugs for STXBP1.

(04:58:04):

Next, we heard a clinical overview presented by Dr. Ingo Helbig who's the Director of Genomics, and Assistant Professor of Neurology [inaudible 04:58:11] at Children's Hospital of Philadelphia. He gave us a disease overview saying STXBP1 is a rare genetic disorder first identified in 2008 in people with severe

neonatal epilepsy. The US prevalence is about 1 in 30,000. It causes global developmental delay, hypotonia, speech impairment, seizures, and a range of other neurologic, and non-neurological symptoms. Many children still have refractory seizures. Most have severe intellectual disability. Tremor interferes with activities of daily living, and behavioral dysregulation leads to safety risks. Current treatments are limited to medical management of seizures, and supportive therapies. There is a natural history study that's ongoing, and hopefully, will inform future clinical trial design. We then moved into our panel presentations. In the morning, we focused on health effects, and the impacts of STXBP1.

(04:59:11):

We first heard from Justin who spoke to us from his police car. He's the dad to his three-year-old son, Reese. Reese has symptoms... He had symptoms just after birth, and has experienced focal seizures, tonic seizures, infantile spasms, hypotonia, and cortical visual impairment. He's legally blind, and has astigmatism, and cognitive issues. The most challenging has been that he loses his abilities as the disease progresses. We heard that over, and over today. And not being able to say what is wrong is the hardest. Next, we heard from Elizabeth who is mom to Carolyn, who also began with STXBP1 at birth. She's had thousands of seizures, and aspiration has been a problem requiring a G-tube for feedings. She was able to run, actually, when she was younger, and she seemed to understand things, and had a good spirit. But sadly, at age 15, she began sleeping most of the day. And eventually at age 18, she died from complications of STXBP1.

(05:00:13):

Then we heard from John, and his wife Isabella, who are the parents of Lucas who's 13 years old. Lucas first experienced a seizure cluster at age 13 months. By age two, he became withdrawn, and was eventually diagnosed with STXBP1. He requires constant care, as do most of these kids, and help with all daily living activities, and he's nonverbal. If he has a seizure before school, he needs to recover at home, and then be driven to school. He gets severe nosebleeds, and Lucas does not always understand danger. And because he runs a lot, he needs to be watched carefully. Leanne, and Grant shared that they're parents to Lucy who is now two years old, and was diagnosed at birth. Lucy has low muscle tone, which has contributed to poor mobility, difficulty feeding, and having worse problems with things like common colds. She can't walk, and she's nonverbal.

(05:01:07):

Her symptoms impact every aspect of life. She really wants to be social with other kids, but cannot fully engage with other children. Then, we heard from Raquel who is mom to Keyarah who is 20 years old. She wasn't diagnosed until she was age 14. She has daily seizures, and self-injurious behaviors like slapping, screaming, and biting herself. She has poor balance, and she's at risk for falling, and has injured herself from falls. Being nonverbal is actually incredibly challenging, and her condition is regressing over time. Her mom worries how she'll be cared for as she gets older. So from the morning, we heard that STXBP1 is challenging. Children often lose their abilities over time. We heard from caregivers as well about how painful this disease is for the entire family. It's a multi-system disease, and affected people are nonverbal. They're affected by multiple seizures. They have challenges with hypotonia, and daily living activities, and social isolation.

(05:02:08):

Most need constant supervision, and help throughout the day. And almost everyone expressed the challenges of lacking communication, and not knowing what their child needs, and desires. In the afternoon, we shift gears a little bit to perspectives on treatments for STXBP1. We first heard from our panelist, Jen, who is mom to Kaylin who's 15 and a half years old. She said, "Caring for Kaylin is like caring for an infant. She needs to be lifted to move from the bed to the wheelchair. She's on three seizure meds, meds for reflux, and seasonal allergies, multivitamins. She takes multivitamins, probiotics, and bowel meds. She also needs nebulizers, and inhalers, a suction machine, and O2 at home." They would like a new treatment that helped with cognitive abilities, and communication.

(05:02:58):

Next, we heard from David who is dad to his 26-year-old son, Blake. Blake loves the water, and has a part-time job. He has a nurse that accompanies him to his work. He's on a medication combination of Depakote, Keppra, lamotrigine, and Belviq for seizure control. This reduces his seizures, but he still has about 20 to 30 a month. His parents wish there was a medication that would completely control the seizures, and also help with communication would be incredibly impactful. Then we heard from Allison who is mom to Mason who's five. Initially, traditional PT did not do much to help him. He eventually went to a specialized PT clinic in Arizona, and has made some gains in his muscle tone. Including the ability to sit on the floor for the first time. They would enroll Mason in a clinical trial if there was any hope of improving his cognition, and his ability to communicate.

(05:03:53):

We heard from Yisbel, mom to two year old Lucas who was diagnosed at three months old. He takes Keppra for seizures, and Nexium for acid reflux. He has eosinophilic esophagitis in addition to STXBP1. He can't chew solids, and he needs feeding therapy, and he gets blended food at home. Horse riding therapy has helped him with balance, and core strength. And then, dynamic movement intervention, or DMI, stimulates neuroplasticity, and helps develop motor milestones. But even with therapy, he cannot crawl, stand, or walk. He can sit, and play a bit. They would participate in research, and would like a therapy once again to improve communication. We heard this again, and again throughout the day. Lila is mom to 16-year-old Rowan. He lost the ability during COVID. A lot of his abilities during COVID, combined with hitting puberty. He has needed to have a feeding tube inserted, and a complete spinal fusion because of neuromuscular deficits. Music therapy five days a week has changed his life. Helping with coping skills, and anxiety. And Lila expressed that various types of therapists would benefit from special training in working with nonverbal teenage kids.

(05:05:06):

So overall, in the afternoon, we heard about the tremendous unmet... Excuse me. Unmet medical need in the STXBP1 community with no FDA approved products yet. Treatments are not always effective, including the anti-epileptic medications. Treatment can include PT, OT, speech therapy, housing modifications, keto diet, and many other things. Many of the medications though have serious side effects that limit their usage. New therapies really need to be developed to treat the complex disease features of this condition, and many patients expressed willingness to participate in research. Especially hoping for new treatments related to cognition, and communication. And it was brought up that even inch stones of improvement instead of milestones would be meaningful. So on that note, I'd like to now close the meeting, and turn it back over to Charlene in the studio. Thank you.

Charlene Son Rigby (05:06:07):

Thank you for your thoughtful summary, Larry. This has been a truly incredible day and has helped us all better understand STXBP1. The impact on our patients, and their loved ones, and the need for therapeutics for this debilitating disorder. Thank you to the FDA staff who tuned in today, and thank you to Will Lewallen, Ethan Gabor, Karen Jackler, and Lena Marzo from the FDA's patient-focused drug development staff who guided us through this process over the many months of planning. Also, thanks to Larry Bauer, and James Valentine. From Hyman Phelps, and McNamara, whose assistance in planning, and moderating today's meeting has been invaluable. Thank you to the Deadly Digital Works media team for the production planning, and all the behind the scenes work that they have done today. A big thanks to the STXBP1 board members team, and volunteers who have given many hours to the planning and execution of today's meeting. Including, but not limited to, James Goss, and Jackie Steinberg.

(05:07:13):

And finally, a huge thanks goes to you, my fellow community of STXBP1 caregivers. Thank you for honestly sharing your lived experiences of STXBP1. This meeting could not have been as impactful, or enlightening, without each and every one of you. In the coming weeks, we'll compile all the information from today. Including polling data, and comments, into a voice of the patient report, which will be available on the STXBP1 Foundation's website. The form to submit comments for the report is going to be open for another

30 days. So please consider submitting additional comments, which will be added to the Voice of Patient Report. A recording of today's program will be available on-demand immediately following this meeting. Today's meeting will have a lasting impact on the future of STXBP1 research, and medical product development. So once again, to the entire community, thank you for making your voices heard...
PART 9 OF 9 ENDS [05:10:35]

This transcript was exported on Oct 23, 2023 - view latest version [here](#).

Externally-Led Patient-Focused Drug Development ... (Completed 10/23/23)

Page 1 of 2