



## **Pediatric Low-Grade Glioma Externally-Led Patient-Focused Drug Development (pLGG EL-PFDD) Meeting Transcript**

*The following is a transcript of the Pediatric Brain Tumor Foundation's pLGG EL-PFDD meeting, which took place online on February 23, 2024. For more information about the meeting and to watch the video replay, please visit [curethekids.org/patientfocused](https://curethekids.org/patientfocused). If you have any questions about the pLGG EL-PFDD or the Pediatric Brain Tumor Foundation, please email us at [patientfocused@curethekids.org](mailto:patientfocused@curethekids.org).*

James Valentine, JD, MHS ([00:14:11](#)):

Good morning. My name is James Valentine, and welcome to the Externally-Led Patient-Focused Drug Development Meeting on Pediatric Low-Grade Glioma. I'm joined in the studio by Courtney Davies, the CEO and president of the Pediatric Brain Tumor Foundation, and we're coming to you live from the Washington, D.C. 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 Courtney to provide some opening remarks. Courtney?

Courtney Davies ([00:14:42](#)):

Thank you, James. Hello, everyone. Welcome to the Externally-Led Patient-Focused Drug Development Meeting on Pediatric Low-Grade Glioma. My name is Courtney Davies, and I'm president and CEO of the Pediatric Brain Tumor Foundation. We are committed to leading the way to a future without brain tumors. Our mission is to accelerate the development of treatments to provide educational, emotional, and financial support to affected families from novel research and amplify the voices of patient families through advocacy. A special welcome to the many staff members of the US Food and Drug Administration who are taking the time to be with us today. Thank you for giving us permission to hold this meeting. We are excited to have you with us and hope that you will learn a lot today from the amazing patients, survivors, parents, and caregivers sharing their perspectives.

([00:15:35](#)):

Thank you to our sponsors, DayOne Biopharmaceuticals and the Sontag Foundation, for their generous financial support. Thank you to our supporting organizations, the American Brain Tumor Association, the Brain Tumor Network, Making Headway, and the Children's Brain Tumor Foundation. 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 for joining us today. Most importantly, I want to welcome the members of our audience whose lives have been directly impacted by pLGG. Today's meeting is the result of many months of planning and people working behind the scenes, and I want to extend my deep gratitude to everyone who's had a hand in prepping for this meeting. We are grateful to have the opportunity to ensure that patient and family perspectives are considered in the drug development and regulatory processes.

([00:16:35](#)):

PLGG has a severe impact on quality of life, affecting children, survivors, and their families in ways that can be difficult for people outside of this community to understand. PLGGs include multiple tumor types with few FDA-approved therapies and a tremendous unmet medical need for better treatments. For many people, pLGG is a chronic disease, so the development of new therapies is of critical importance. For some patients, surgical resection is possible, but for others, surgery may only provide partial relief, as you will hear in patient stories today. There are many impacts from these tumors, which can include visual abnormalities, endocrinopathies, motor or sensory abnormalities, vasculopathies, and neuropsychological problems as well. Our work is guided by the experiences of the patient families we encounter every day and by the challenges they face. PLGG has a significant impact on every patient's family that is affected. A pLGG diagnosis affects the health and long-term well-being of the child and impacts the emotional, spiritual, and financial health of every family member. This is a disease with profound and far-reaching impact.

[\(00:17:55\)](#):

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 pLGG. I want to express my appreciation to the investigators working in labs all around the world, striving towards a better understanding of basic and translational pLGG 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 pLGG who urgently need new and better treatment options. For the pLGG families in attendance, we invite you and your loved ones to call in and write during the program. We also ask that you stay on with us, please, throughout the day and participate in remote polling. We want to hear as many perspectives as possible, and we will do our best to get as many calls and comments as possible.

[\(00:18:54\)](#):

When participating, please only use your first name, city, state, or country. No other identification or information should be shared. Be assured that any comments we are unable to share are still very important, and they will be included in the Voice of the Patient Report, a summary of this special day. To begin today's meeting, I'm delighted to introduce our speaker from the FDA. Dr. Elizabeth Duke is a medical officer in the division of Oncology II in the Center for Drug Evaluation and Research at the FDA. This is the part of the FDA that regulates new drug treatments for pediatric brain tumors. Dr. Duke will provide some opening comments from the FDA perspective. Dr. Duke, over to you.

Elizabeth Duke, MD [\(00:19:43\)](#):

Good morning. Thank you for that kind introduction. My name is Elizabeth Duke. I'm a pediatric neuro-oncologist by training and clinical reviewer in the division of Oncology II at the FDA. I'm part of the multidisciplinary review team at FDA that reviews applications for pediatric and adult brain tumors. I've been in the division since 2020 and have a strong interest in the inclusion of patient-reported outcomes in clinical trials. Thank you all so much for being here today, being part of this meeting, sharing your experiences with us. I'd like to thank the Pediatric Brain Tumor Foundation and all the staff involved in planning this meeting.

[\(00:20:21\)](#):

So speaking broadly, patient-focused drug development is a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation. Patient input is very important to our work, and while there are some currently available treatments for children with low-grade glioma, we recognize there's much more progress to be made, more work to be done really to advance the treatment of patients with this

disease. Certainly, FDA plays a role in medical product development, but we're really just one part of the process. These meetings give FDA and other key stakeholders, including medical product developers, healthcare providers, federal partners, an important opportunity to directly hear from patients, their families, caregivers, and patient advocates about symptoms that matter most to them, the impact the disease has had on their patients' daily lives, and patients' experiences with currently available treatments.

[\(00:21:22\)](#):

FDA shares the patient community's commitment to facilitate the development of safe and effective products for pediatric low-grade glioma. When we say medical product development, really, what we mean, in the broadest sense, is identifying, developing, evaluating potential therapies or devices that can help patients across their disease course. Patient input is really important in all stages of development. So from designing the trial to trial conduct and participation to communication of results.

[\(00:21:55\)](#):

What's the history of FDA's patient-focused drug development initiative? Really, there's been sustained research in this area for many years. In the early 2000s, there were working group meetings to start to harmonize efforts around the best ways to communicate patient-reported outcomes in the drug evaluation process. FDA really recognized a need for more systematic ways of gathering patient perspectives on their condition and treatment options. So from 2012 to 2017, FDA conducted 24 disease-specific, patient-focused drug development meetings. You'll see on this timeline, really giving patients and caregivers a platform to contribute input that can inform drug development and evaluation. That number really has only increased from there. We've learned a lot from these meetings. Some of those you'll see on the right-hand side, patients are the experts in their disease due to their lived experience with symptoms and treatment. Patients identify and articulate specific disease aspects, what's important to them regarding treatment benefit, and they can actively participate in the work to develop it and evaluate new treatments.

[\(00:23:05\)](#):

So at the same time, there's been growing external interest in expanding efforts to gather patient input and support of drug evaluation. In 2015, we started welcoming patient organizations to identify and organize their own patient-focused collaborations. So these Externally-Led Patient-Focused Drug Development, or PFDD, meetings provide an opportunity to hear directly from the patients, patient advocates, caregivers about symptoms that matter most to them, the impact on their lives, and patients' experiences with available treatments.

[\(00:23:39\)](#):

What will we do with this information? Many things. Your thoughts can help strengthen our understanding of the disease and treatment burden, what we call the therapeutic or clinical context. It can also contribute to our assessment of benefit risk for products that are under review and then when we're advising drug sponsors on their development programs. It can help identify areas of unmet need, such as aspects of the disease that aren't really being addressed with current therapies. So, as you know, low-grade gliomas can affect all areas of functioning, vision, physical functioning, neurocognition. How do we best capture the impact of a given therapy on all of those areas? And the input can help developers as they identify or create new tools to measure the potential impact of therapies. The deliverable, a summary report from an externally-led PFDD meeting, can be shared on FDA's website. You'll see the link here for that public website.

[\(00:24:43\)](#):

So in addition to agency-wide efforts, we have several ongoing efforts, particularly in the Oncology Center of Excellence at FDA. We have a team devoted specifically to review clinical outcome assessments and trials. We've had several prior collaborations with the external community, including a mini symposium we had back in October of 2022 really to look at the evaluation of functional outcomes as efficacy endpoints in pediatric low-grade glioma clinical trials.

[\(00:25:13\)](#):

We've drafted guidances. Those are public documents that reflect FDA's current thinking on a particular topic. This is just one example specific to oncology patients. This provides recommendations for a collection of a core set of patient-reported outcomes in cancer or clinical trials, as well as related considerations for trial design.

[\(00:25:37\)](#):

So once again, we're all here today to hear the voice of the patient. So thank you for your participation. We're truly grateful to each of you for being here, sharing your experience, perspectives. We know there are many subtypes of low-grade glioma, and we know they affect each patient differently. So we really want to hear from all of those perspectives. My colleagues and I at the FDA are in listening mode, but we certainly look forward to hearing what you all have to say, bringing it back, incorporating what we learn into the agencies, thinking and understanding of how patients view the risks and benefits of potential therapies for low-grade glioma. So thanks again, and I'll turn it back to the moderators.

Courtney Davies [\(00:26:29\)](#):

Thank you, Dr. Duke. Next up, Dr. Jason Fangusaro will provide a clinical overview of pLGG. This will serve as a scientific foundation for today's discussion. Dr. Fangusaro is the Director of Developmental Therapeutics at Children's Healthcare of Atlanta. Dr. Fangusaro has expertise in treating children with central nervous system malignancies, including brain and spinal cord tumors. He's a well-established pLGG expert and clinician scientist. Dr. Fangusaro, over to you.

Jason Fangusaro, MD [\(00:27:03\)](#):

Good morning, everyone. Thank you so much for the kind introduction. I'm excited to be with you guys today. Although I'm not right there with you, I'm virtually with you, so I'm excited about that, and I'm always excited to talk about my research and the focus of what I've done in the last decade of my career, pediatric low-grade glioma. So thank you so much for allowing me to join you.

[\(00:27:26\)](#):

So here are some disclosures that I have. So what I want to do today is talk first about a brief overview of pediatric low-grade glioma, and then I want to focus a little bit on epidemiology, some common symptoms that we see in patients. Then have a general discussion about therapy. We'll talk a little bit about the diagnostic criteria and pathway. At the end of the talk, we'll talk more about the molecular and genetic landscape of these tumors. Then we'll end with a few conclusions. So let's dive right in.

[\(00:28:01\)](#):

First of all, pediatric low-grade glioma are classified by the World Health Organization as grade I and grade II tumors. This means that they're low-grade. Now, this classification is ever-evolving, and we'll talk a little bit more about this in slides that come up later. But they are the most common type of pediatric brain tumor. Among them, pilocytic astrocytomas represent the most common histology. But if we look at all of pediatric low-grade glioma, they are very heterogeneous. They can be different in their histopathological nature, their demographic characteristics, radiologically, and their clinical features and behaviors. One thing that's really important to note is, they're very distinct from adult low-grade glioma.

That is a distinction both clinically and biologically. So, for example, pediatric low-grade gliomas are typically very slow-growing, and usually they do not transform to higher-grade lesions. Whereas in adult low-grade gliomas, they often transform to a high-grade glioma.

[\(00:29:04\):](#)

Let's talk a little bit about the epidemiology. So the annual incidence of pediatric low-grade glioma is about 1.3 to 2.1 per 100,000 in the United States. So what does that really mean? So this is actually telling us that in the United States, each year there's about 1000 to 1600 new cases of pediatric low-grade glioma.

[\(00:29:29\):](#)

If we look at a pie chart of all the different types of pediatric tumors in the brain and spine, you can see each of the colors represents a different histology or a different type of brain tumor. If we highlight those where pediatric low-grade glioma fall into, the one circled in red, you can see that pediatric low-grade gliomas represented about 30% to 35% of all brain tumors, again representing the most common brain tumor that we see in children. Now, I mentioned the World Health Organization. In 2021, the World Health Organization changed their classification of brain tumors. Now, there's one huge category that encompasses glioma, glioneuronal tumors, and neuronal tumors. You can see in that large category, there are six subcategories, or six families. The ones I've highlighted in yellow are the areas where pediatric low-grade glioma fall into. So pediatric-type diffuse low-grade glioma, circumscribed astrocytic tumors. Actually, that's the category where the most common tumor, the pilocytic astrocytoma, falls into. Finally, glioneuronal and neuronal tumors.

[\(00:30:45\):](#)

Now, I'd be remiss if I did not talk briefly about neurofibromatosis type 1 when we discuss low-grade glioma in children because they are often linked in many patients. So neurofibromatosis type 1, or NF1, is a progressive genetic disorder that's caused by a mutation in a gene called NF1. There are multiple clinical manifestations, and you can see in that picture on the right side of your screen all the manifestations, which include bony abnormalities, skin abnormalities, seizure disorders, neurologic abnormalities. But the interesting one, and the reason why I'm talking about it today, is that about 15% to 20% of patients with NF1 will develop brain tumors, most commonly low-grade gliomas, and most commonly in the optic pathway or in the brain stem, or very rarely other parts of the brain.

[\(00:31:40\):](#)

The other unique thing about patients with NF1 and low-grade glioma is, we don't always treat them only because they have a tumor present or we identify a tumor. Sometimes we don't even treat them if the tumor starts to grow slightly, because, in general, these patients have indolent tumors. So we more so focus on treating them if they have functional abnormalities like vision dysfunction or motor abnormalities, or, for example, neurologic problems.

[\(00:32:08\):](#)

Now, how about all patients with pediatric low-grade gliomas? How do they present? Now, there's really not one symptom that is representative of patients with low-grade glioma, and it really depends on the size of the tumor, where it's located, and what type of pressure it's putting on the brain. But in general, you can see this list of a lot of symptoms that patients with pediatric low-grade glioma can present with. For example, headache, nausea, vomiting, vision problems, seizures, endocrine problems like weight gain or precocious puberty, difficulty walking or balancing, clumsiness. They can have localized weakness, like weakness in their right arm or their left leg. They can have confusion, sleepiness, or sometimes just general changes in behavior that can't be explained.

[\(00:32:56\)](#):

So let's talk in general about treatment strategies. Ideally, if a tumor that's a low-grade glioma can be resected completely,-

Jason Fangusaro, MD [\(00:33:03\)](#):

Ideally if a tumor that's a low-grade glioma can be resected completely, that's what we try to do. And it can be curative for some patients, but that's not always feasible because of the tumor location and metastatic disease. And for those patients we historically rely on chemotherapy. I've listed some of the chemotherapies there for you to review and there are sometimes in rare situations that we use targeted therapy upfront as well. But because of this understanding of the MAP kinase pathway and mTOR pathway and our understanding of the molecular drivers of these tumors, there are a variety of new therapies that are being tested that I'm sure the next speaker is going to talk a little bit about later this afternoon.

[\(00:33:37\)](#):

Finally, I just want to end in talking briefly about radiation therapy. Although it's a very effective strategy, we typically try to avoid it in children with low-grade glioma because of the risk of late effects like secondary malignancy and neurocognitive decline. So what is the pathway for these patients? Now, first of all, as I mentioned, most of these patients will come to the clinic or the emergency room with a new symptom like a headache or vomiting for example. And that inevitably typically leads to some type of imaging study, a CT or MRI of the brain. And when a mass is identified in the brain, they typically go to have a neurosurgical procedure where a biopsy or ideally a resection of that mass is performed.

[\(00:34:25\)](#):

Now once we get a piece of that tissue, the neuropathologist along with the neuro oncologist review that tissue and come to make specific stains of the tissue and send for molecular profiling to come up with a final diagnosis. And obviously in this situation we're talking about low-grade glioma, so that would be the final diagnosis. And then we decide on the treatment for the patient. As I mentioned, some patients have a complete surgical resection and their only treatment is to be observed and get surveillance MRIs on a periodic basis. Other patients may require chemotherapy or targeted therapy. And then of course, we have to monitor these patients carefully while they're on therapy and when they complete therapy, typically with imaging studies like an MRI and physical exams, and then we follow them long-term and make sure that their tumor does not recur.

[\(00:35:16\)](#):

Now, very interestingly, in pediatric low-grade glioma, there's been a bit of a paradigm shift, and this has come about because we've learned a lot of data about patients long-term. So we've looked at children who have now become adults and those patients that had pediatric low-grade gliomas, we've looked at them 20 and 30 years later and we've come to realize that most of those patients do not die from their disease. In fact, the far majority of patients will live well until their adulthood and it's very, very rare for a patient to die from a pediatric low-grade glioma. Because of this, we've come to understand that we need to emphasize other things, not only tumor response and survival, but also other morbidities like vision, motor outcomes, neuropsychological outcomes, and neurologic functioning. We have to focus on these patients' quality of life because we know that they're going to live well into their adulthood and we want to maximize their functional abilities as adults.

[\(00:36:17\)](#):

Okay. So now we're towards the end of our talk and we're going to take these last few minutes and talk about the molecular and genetic landscape of pediatric low-grade gliomas. So really over the last couple

of decades, there's been a wealth of understanding of biologic pathogenesis of pediatric low-grade glioma, and we've come to learn that the mitogen activated protein kinase and mTOR pathways are key regulators to driving pediatric low-grade glioma development and progression. So in this picture, you can see both of these pathways highlighted. On the right is the MAP kinase pathway, which is far and away the most common abnormal pathway in pediatric low-grade glioma. And on the left you have the PI3-AKT-mTOR pathway, which is less commonly aberrant in pediatric low-grade glioma. You can see here this pink box representing those patients with NF1, which is tied to the MAP kinase pathway.

[\(00:37:15\):](#)

And if you have reregulation or abnormalities at any place within this pathway, you can lead to propagation of the pathway and tumor formation. So the great thing is, now we have new drugs that can target different parts of these pathways. So for example, we can target BRAF directly with BRAF inhibitors. We can target all of the RAF variants with Pan-RAF inhibitors. We also can target something downstream from BRAF called the MEK inhibitors. And then there are mTOR inhibitors and there are even other inhibitors like RK inhibitors, which is farther down in the pathway, which are early in their development and testing.

[\(00:37:57\):](#)

So far in away, the most common mechanism of BAF activation in pediatric low-grade glioma is something called the genetic fusion, which results in the loss of the regulatory domain of BRAF. And this is known as the BRAF-KIAA1549 fusion. If you look at all pediatric low-grade gliomas, it's probably present in about 35 to 40% of cases. But if you look more specifically at the most common subtype that we talked about before, pilocytic astrocytoma, it may be present in up to 60 to 80% of cases. And then the second most common abnormality that we talk about is NF1, and as I mentioned that is present most commonly in patients with neurofibromatosis and seen in about 15 to 20% of patients with low-grade glioma.

[\(00:38:46\):](#)

And then the third most common is something called the BRAF V600E mutation, probably seen in about 15% overall of all pediatric low-grade glioma. And then it's seen to a lesser extent in those patients with pilocytic astrocytoma and more commonly in other rare histologies like pleomorphic xanthoastrocytoma for example. It can also be seen in pediatric high grade gliomas, which we're not talking about today, and are much more rare than pediatric low-grade glioma. And you may have heard of the BRAF V600E mutation because it's also common in adult diagnoses like melanoma and colon cancer for example.

[\(00:39:26\):](#)

So here's just a table view of the most common abnormalities that we see in the molecular landscape of pediatric low-grade glioma. And far and away it's the column on the left that we see the most abnormalities, the MAP kinase pathway aberrations, and we highlighted those in the last couple slides. The KIAA 1549 fusion and F1 and the BRAF V600E mutation. And then you can see in the middle column, the mTOR pathway abnormalities really representing a small fraction of pediatric low-grade glioma molecular drivers. Then one that we really didn't talk about, which is separate from the MAP kinase pathway, but can be seen more commonly in pediatric low-grade gliomas is abnormalities in something called FGFR. And there are actually drugs that target this as well that are early in development.

[\(00:40:19\):](#)

So in conclusion, pediatric low-grade gliomas are the most common brain tumor that we see in children and adolescents. We really consider these patients as now having more of a chronic disease of childhood because now we are focusing on their functional outcomes, their vision, their motor functioning. We want to highlight their quality of life and their neuropsychological outcomes so they can

live the most fulfilling lives as adults. We typically treat these children with surgery. If we can completely resect the tumor, that's ideal. If not, we will commonly treat them with systemic therapies like chemotherapy or molecularly targeted therapy. And I'll just highlight briefly again, remember those patients that do have the BRAF V600E mutant low-grade glioma, we treat them at diagnosis if they need therapy with a combination of the BRAF inhibitor and MEK inhibitor, dabrafenib and trametinib.

[\(00:41:14\)](#):

There really has been a wealth of new information about the molecular landscape of pediatric low-grade glioma, and there are a variety of trials that are ongoing really looking at these targeted therapies. What I think is going to happen over the next decade as the results of these trials become available is we'll better understand how to treat specific types of low-grade glioma with specific types of targeted therapies to result in the best outcomes for our patients, both in terms of response rate, in terms of their survival and their functional outcomes and their quality of life.

[\(00:41:51\)](#):

So that concludes my talk and hopefully it was a good overview of pediatric low-grade glioma. I want to give a big thank you to all of you for listening today. A special thank you to our patients and their families, not only for putting their trust in us, but also for guiding us and teaching us as we learn more about pediatric low-grade gliomas. I want to thank the Pediatric Brain Tumor Foundation. I want to thank the organizers of this meeting, the externally led patient focused drug development meeting, and of course, I want to thank my own colleagues both at Emory and CHOA and the Aflac Cancer Center and all of my collaborators.

[\(00:42:28\)](#):

So thank you again so much. I hope you have a wonderful morning. I look forward to hearing so much more from the patients and their families and those people who have treated patients with pediatric low-grade gliomas. And thank you again for allowing me to join you today. I'll send it back now to the studio for you guys to continue your great morning.

PART 1 OF 10 ENDS [00:33:04]

Courtney Davies [\(00:42:57\)](#):

Thank you Dr. Fangusaro. I now like to welcome our moderator for today's meeting, James Valentine. James has worked the last 15 years as a champion for the patient voice as part of the regulatory process. 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 centers and review divisions. There James helped develop and launch the patient focused drug development initiative. In private practice, James has worked with many patient organizers to ensure their community voices are heard by decision makers. He has also been involved in helping plan and moderate many of the over 85 externally led patient-focused drug development meetings. So we are in good hands with James and now over to you, James.

James Valentine, JD, MHS [\(00:43:47\)](#):

Thank you so much for that introduction, Courtney, and it's so great to be here this morning with the pediatric low-grade glioma community. So now that we've heard a clinical overview from a disease expert, we get to turn to the core of today's meeting, which is to hear from you, people living with pLGG and their parents, family members, and other direct caregivers.

[\(00:44:10\)](#):



Patient focused drug development is a more systematic way of gathering patient perspectives on their condition and on available treatments. As you heard from FDA's Dr. Duke, your input can help inform the agency's understanding of pLGG to inform drug development and review. Today is such a unique opportunity for this community, given that it's one of the less than 100 externally led PFDD meetings held to date, yet we know that there are many tens of thousands of known diseases.

[\(00:44:44\)](#):

So today's meeting is interactive, so I'm going to tell you a little bit about what will be asking of you and how you'll be able to participate in today's meeting, including how it's organized. In our first session this morning, we'll be exploring the patient and caregiver experience of living with pLGG, including the top symptoms and health effects, and how the condition impacts daily life. In our second session this afternoon, we'll bring everyone back together to explore the experience with treatments and disease management strategies, as well as to seek your input on what represents the top treatment goals that you have for new drugs.

[\(00:45:20\)](#):

So what will these two discussions look like? We'll be hearing from this community in a few different ways. First, we'll start each of our sessions by hearing from a panel of pediatric low-grade glioma patients and caregivers who will be setting a good foundation for the discussion. And these individuals were selected to reflect a range of experiences of living with pLGG, but we know that no single panel of individuals can fully represent this community's experiences, which is why after we have those panel discussions, we're going to open it up and have a facilitated audience discussion with all of you, our patients, and our caregivers in the audience. This discussion is intended to build on what we heard from the panel. I'll be asking questions and inviting you to participate in that discussion. You'll be able to participate in one of two ways. First and the best way is to share your experiences by calling in, but we'll also be offering you the opportunity to submit written comments and I'll explain how to do both of those things a little later when we get into those discussions.

[\(00:46:33\)](#):

The third way that we'll be hearing from this community is through the use of polling questions. We'll be using this to broaden the discussion to all of you in the audience, and we'll be asking you, our patients and caregivers, to use your phone or web browser on your computer to respond to those questions. And in fact, we want to go ahead and get you in that system now because once you're in, you'll be able to stay in that polling throughout the entire day.

[\(00:46:58\)](#):

So at this point, I'd ask if you want to pull out your phone and open up a browser or open up a new tab on your computer's web browser. Again, this is for patients and caregivers only. Go to [www.pollev.com/plgg](http://www.pollev.com/plgg). Again, feel free to go there now. That URL is [www.pollev.com/plgg](http://www.pollev.com/plgg), and we'll get to polling very soon. These polling questions will broaden the discussion to everyone, as I mentioned, and will actually be an important part of aiding in our discussion. As you're answering these different polling questions, I'll ask you to think about the selections you've made, why you've made those selections, and then invite you to call in and write in to help us understand.

[\(00:47:49\)](#):

You'll also have the opportunity to provide written comments for 30 days after this meeting. So whether you attend the meeting live today and there's something additional beyond what you were able to share during the live meeting, or if you're watching this program on Demand after the live meeting day, know that your voices are still important and you can provide written comments. All of today's input, both the

live input as well as any additional written input will be summarized into a voice of the patient report, which will be provided to the FDA as well as be made available for researchers and drug developers.

[\(00:48:24\):](#)

Finally, before we get into the discussion, I'd like to cover a few ground rules. We encourage people living with pLGG as well as their parents, family members, and other direct caregivers to contribute to the dialogue. Again, you'll be invited to do so using polling, calling in by phone, and submitting written comments. The discussion today is limited to patients, family members and other direct caregivers with pLGG. Our other attendees, our colleagues from the FDA, drug developers and clinicians are here to listen.

[\(00:48:58\):](#)

And finally, views expressed today are inherently personal and the discussion may get emotional at times. So respect for one another is paramount. And to that end, I'd ask that you try to be focused and concise in your comments so that way we can hear as many voices as possible. Without further ado, let's get into our first set of polling questions. These are a set of questions that will allow us to understand who we have in our audience. So all of you are patients and caregivers. Again, at this time, if you haven't already, please go to [www.pollev.com/plgg](http://www.pollev.com/plgg). One more time. That's [www.pollev.com/plgg](http://www.pollev.com/plgg). Once you're in the system, you can keep this webpage up for the rest of the day. Anytime we go to a new polling question, it will automatically appear there. You'll be able to click and make your selections. There's no need to hit submit. As soon as you click your selection, that response will be recorded for us.

[\(00:49:57\):](#)

So our first question for you today is we want to know, are you either A, someone living with pLGG or B, a caregiver of someone living with pLGG? And we'll give everyone a few moments here to get into the system. Again, we want to make sure everyone has a chance to get into the polling, so that way we'll be able to track your responses throughout today's session. So we'll give everyone a few more moments here to get in your responses. As it stands, it looks like our audience today is made up of our caregivers of people living with pLGG. As if anyone living with pLGG joins the program, we'll be inviting them to participate directly as well.

[\(00:50:50\):](#)

If we go to our second polling question Here, we want to know where do you currently reside? The options are A, the US Pacific Time Zone, B, US Mountain Time, C, US Central time, D, US Eastern time, E, US Alaska time, F us, Hawaii time, G, Europe, H, the Middle East, I, Asia, J, Canada, K, Mexico, or L, some other country or region not otherwise listed in the other response options. And we'll give our audience a few moments here to get in their answers. It looks like we have good representation across most of the US time zones. Not surprisingly, for a meeting starting in the morning on Eastern time, we have a larger contingency from the US Eastern Time Zone, but we hope that as it gets a little later in the morning in other time zones, we'll get greater representation there. And we also welcome those of you who have joined from Europe. This meeting is for everyone around the world, so we encourage you to call in and write in throughout today's program as well.

[\(00:52:09\):](#)

We go to our next polling question. So here we want to know, are you, if you're living with pLGG or for all of our caregivers, your loved ones who are living with pLGG, are they, A, female, B male, or C other? This is the, you're answering for the person that is living with pLGG, or I should say for those of you who are caregivers of someone who has passed away living with pLGG. We do encourage you to answer these questions as well, not as relevant for this question, but as we get to other questions that maybe are asking about a certain period of time, we'd like you to think about perhaps the final year of their life

as you're answering some of those other questions. But you can still participate in all of these questions as well. So responses are still coming in, but as I think we're seeing, there's a pretty even split depending on every vote, having female and male jumping slightly ahead of one another. But we're seeing that there's a good mix of people living with pLGG represented today that are both female and male.

[\(00:53:27\)](#):

Go to our next polling question. Here we want to know how old are you or your loved one with pLGG? So the options here, this is for, again, we're answering about the person with pLGG. So for our caregivers, answer this on behalf of the person that you care for with pLGG. The options are, A, zero to two years of age, B, three to five years of age, C, six to 12 years of age, D, 13 to 18 years, E, 19 to 35 years, F, 36 to 50 years, G, 51 to 60 years or H, 61 years of age or older.

[\(00:54:17\)](#):

I promise, as the day progresses, these questions will become a little bit more complex, even perhaps even difficult to answer. But these first batch of questions again, is really to get a sense of our audience. And as it stands, it looks like about 1/3 of our audience, the people living with pLGG represented are between 6 to 12 years of age. We're seeing good representation across all of the pediatric age ranges, including that first two years of life. And then we do have representation in adulthood in that 19 to 35 year age range.

[\(00:54:54\)](#):

We can go to our last polling question here for this first batch of polling questions. Here we want to know, unlike the question before, which was about current age, we'd like to know what age were you if you're living with pLGG or your loved one diagnosed with pLGG? The options are, A, prenatally, B, between birth to 12 months of age, C, 1 to 3 years of age, D, 4 to 5 years, E, 6 to 10 years, or F, between 11 and 18 years of age. Just give you a few more moments, make sure everyone can get in their response. So as it stands, it looks like the largest age ranges that represented in terms of age of diagnosis is between 6 to 10 years of age. And then in those years, basically between 0 and 3 years of age, no one is reporting diagnosis prenatally or in the 4 to 5 year age range, but we do have some that were diagnosed a little later from age 11 and older.

[\(00:56:24\)](#):

So I want to thank you for participating in this first set of polling questions. It's just valuable to get a sense of who's in our audience today, but at this point, we're going to move into our first discussion topic for today, which is really for you all to help us understand what it is to live with pLGG. So here you'll see on the screen some of the questions that we want to explore with you in this morning's session. We'd like to hear from you about the different symptoms and health effects of pLGG, including which one to three of those have had the most significant impacts on you or your loved one's lives. We'd like to hear about how pLGG and its symptoms maybe vary from day to day. So if you could share how pLGG affects you on your best day versus worst days, it's a good way to help us understand that. Also, we want to know how these things have changed and your experience with the disease has changed over time, whether that's week to week, month to month, or over the course of years, and how your ability to cope has changed as those symptoms have changed over time.

[\(00:57:29\)](#):

In addition to wanting to understand these direct symptoms and health effects, we want to know how living with pLGG actually impacts your daily lives, and so are there specific activities that are important to you or your loved one that you or they cannot either do at all or is fully because of pLGG? And then finally, recognizing that in addition to everything that people with pLGG have lived with and what they're going through currently, that you also have to worry about their futures of living with this

condition. So we'd like you to share with us some of your greatest worries or concerns or fears for the future.

[\(00:58:06\)](#):

So to help us get started in understanding your experiences on these different topics, we have a panel of your peers. We have Sam, Cynthia, Kadeja, Stephanie and Katie who are going to be sharing their experiences. Sam, why don't you get us started?

Sam P. [\(00:58:25\)](#):

Hi. My name is Sam. My wife Amy, and I have three children, Blake, Maddie, and Benjamin Maddie's our middle child, and she lives with a low-grade glioma. About three and a half years ago when Maddie was three years old, she wasn't gaining any weight. She seemed to be struggling to thrive. She had headaches. She laid down a lot to rest and sometimes couldn't keep food down. She would also wake up upset at 4:00 or 5:00 in the morning saying things like, "I have to throw up and I don't feel good." As a result, her pediatrician did some lab tests and ultimately determined that the issues Maddie was experiencing might be psychological and therefore we should take her to a child psychologist. She usually had been a very talkative and happy child, so this didn't seem to totally make sense.

[\(00:59:04\)](#):

A couple of weeks later, Maddie woke up in the middle of the night screaming that her head hurt. She vomited a little while later and then became unconscious and unresponsive with her eyes rolling around in the back of her head. As a result, we rushed Maddie to the ER thinking it might be a concussion because she had said she'd hit her head at school the previous day. However, within 20 minutes of being at the ER, the doctors did a CT scan and found a giant mass in the middle of her head, which ultimately ended up being pilocytic astrocytoma without the BRAF mutation. The mass was causing extreme hydrocephalus. Maddie was then transferred to another hospital and had an emergency shunt placement to relieve the pressure. She woke up afterwards from that surgery surprised and said, "My head doesn't hurt anymore."

[\(00:59:49\)](#):

Three days later, Maddie had another surgery to resect as much of the brain tumor as possible. The surgery was tricky and therefore only removed part of the tumor as the doctors wanted to avoid damaging critical areas like her memory banks and her pituitary gland. A few weeks later, she started chemotherapy at Lurie Children's Hospital, but the hydrocephalus returned, which resulted in a shunt ultimately being placed in her head.

[\(01:00:12\)](#):

Since Maddie's diagnosis and the shunt placement, we've had several surprise surgeries to deal with shunt malfunctions and the related headaches and pain that go along with those. More recently, after finishing her first course of chemotherapy, which was a year long by the way, her MRI showed slow tumor progression. After several stressful weeks, my wife and I made the decision to have another surgery, this time out at Boston Children's that ended up being nearly 20 hours long.

[\(01:00:40\)](#):

All things considered though, Maddie's doing okay. She's in kindergarten now, and when we ask her teachers how she is doing, they don't notice anything significant. The headaches are the biggest question that come up, and she deals with really bad sinus pressure. If you look closely, one of her eyes is droopy, especially if she's really, really tired. Despite all this, Maddie is cleared to do things like bike rides and skiing. However, we really don't want to risk a head injury, so contact sports are out. Although,

to be honest, I never really envisioned her being much of a linebacker anyway, so I guess I'm okay with that. She does ballet. She's an actor. She's all sorts of other stuff.

[\(01:01:17\):](#)

With all that said, Maddie also is more mature for her age. Her kindergarten teacher has shared with us that she helps get in the class organized, and when one of her classmates cries, Maddie runs right over to them to try to comfort them. She's very empathetic. She really likes to help and support other children. Perhaps after all that she's been through, Maddie has accelerated her emotional development on some levels. My wife and I, we worry constantly about what's going to happen to Maddie today, and as she grows older. Her specific tumor type is relatively new, so it all feels like a bit of a guessing game, and Maddie's health could truly change in an instant as we've now experienced several times over the past couple of years.

[\(01:01:54\):](#)

When she has a headache or feels under the weather, we always wonder if it's a cold or a medical emergency related to her tumor. It's in the back of our mind at all times. Looking back, our sweet little Maddie has been through so much over these short six years of her life, and yet her strong spirit has helped her become much more empathetic and always be loving towards other people. She truly is a survivor, but I really wouldn't wish this journey on anyone.

Cynthia H. [\(01:02:22\):](#)

My name is Cynthia, and I'm writing this statement next to my 2-year-old son, Grayson, while he lies in the bed in the ICU at Boston Children's Hospital. He is in pain, afraid and angry because he doesn't know why he is here, but I know why. Grayson has a diffuse low-grade glial with an FGFR three mutation that just hours ago was debolt by Dr. Baird on December 11th this year. His tumor burden was large and his two high dose seizure medications were failing. He was previously on trametinib trying to shrink the tumor before surgery, but scan after scan showed no change in the tumor. Prior to surgery, I sought four neurosurgery consults to ensure we gave Grayson the best outcome possible. He was in surgery and under anesthesia for 10 hours, but even then, they were unable to resect all of the tumor.

[\(01:03:19\):](#)

Let's back up a bit. In February of 2023, Grayson had an episode where I was playing patty cake with him on the couch. In mid-clap, he stopped moving. I thought I heard gurgling noises, and it seemed like he had stopped breathing. I put my ear to his chest to listen if he was breathing, but within 30 seconds, it resolved. I called the pediatrician to let him know what happened and was referred to neurology. While waiting for a neuro consult, one day I picked up Grayson from daycare and he had unexplained leave vomited on himself.

[\(01:03:54\):](#)

One weekend in April, he had two staring episodes and breath holding, and by Monday we went to the ER. He had three more seizures in the ER and vomited after them. A video EEG showed focal seizures, so he was started on Keppra. He was then ordered to have a brain MRI. After the MRI, a straight face neurologist came out and took me and my husband into a private room. We were tightly holding hands and felt anticipatory, dread and terror. Our worst fear had come true. Brain images showed that Grayson had a large diffuse brain tumor. I was eight months pregnant at the time, about to give birth to her second child, and I tore the mask off my face and screamed and cried.

[\(01:04:45\):](#)

At first, the neurologist said it was good news that the tumor was low-grade, but not so good because it was very large and diffused throughout his brain. His case was presented in front of the hospital's tumor board because the diagnosis was unsure. One physician thought it might be extreme focal cortical dysplasia, but eventually a brain tumor was diagnosed. This diagnosis led to the eventual surgery that was performed on December 11th.

[\(01:05:13\)](#):

As I record our story, we are now home with Grayson. After discharge, Grayson screamed and cried much of the day until he was exhausted. We had to travel home with my infant. We named Graham, my husband and Grayson, flying the long flight together from Boston to California. The incision on the side of his head was left open to air. The flight was not easy, and at one point I lost it and yelled at someone that my son had just had brain tumor surgery. When we got home, we started his treatment regimen, giving him antibiotics to control post-op infection, two medications for seizures, BRIVIACT and Lacosamide, steroids to reduce brain swelling and oxycodone, Tylenol and Motrin for pain. We are constantly monitoring...

Cynthia H. [\(01:06:02\)](#):

... for pain. We are constantly monitoring Grayson for seizures and we try to manage his pain. We are gradually trying to increase his activity, at the same time, trying to keep him calm so he can rest. He is getting speech therapy, which seems to be helping him relearn words again. We are planning to get PT as well because he is showing signs of left-sided weakness and asymmetry in his gait. Sleeping has become a problem. He seems to be afraid of the dark for the first time in his life. He wakes up at 2:00 AM every day screaming and won't go back to bed. The steroids have made him very hungry and he is eating a lot, but he's not eating healthy things like broccoli, which he used to love, and now, he prefers Cheez-Its.

[\(01:06:49\)](#):

It is still hard to tell how the surgery has affected Grayson, so we are giving him time. It seems like he is struggling to make decisions and he is frustrated by that. It is also starting to look like he might have cognitive and developmental delays. To help with this, he has started developmental play therapy for four hours a week. It is too early to see if this therapy is helping. Grayson loves his little brother and gives him kisses. He is a sweet soul and very loving.

[\(01:07:24\)](#):

During Grayson's surgery, they were able to resect the whole hippocampus and the right temporal lobe and chase the tumor back towards the thalamus, but some tumor remains. I fear what Grayson's future will be and how long it will be. I fear what his quality of life will be if the tumor invades other critical areas of the brain. Currently, it is pressed up against his basal ganglia and around his optic tract. I hope this surgery buys us time as we wait for an FGFR inhibitor to become available for his FGFR3 mutation. I hope that Grayson doesn't have to feel the fear of another seizure. He is aware of them and comes to me crying before it happens with eyes wide, terror on his face. He stops breathing and gags all the while looking at me with fear. It crushes me I can't take his pain away. All I can do is advocate for him and hope there's more time for my son.

PART 2 OF 10 ENDS [01:06:04]

Khadijah H. [\(01:08:51\)](#):

Hi. My name is Khadijah and I live in New York. October 25th, 2015, a day that I will never forget, a day that would change my family's life forever. That evening, I made another trip to urgent care with my three and a half year old daughter, Anaya. I had taken her there previously for morning vomiting and was told she had a stomach bug. My spunky energetic child was not herself. She began to vomit in the mornings, mostly on her way to her daycare in Columbia, South Carolina. Her behavior began to change where she would get very agitated and sleep more often than usual. On the evening of October 25th, I knew something wasn't right. My husband and I would return to urgent care with my daughter. When we saw the doctor again, they thought it was something minor, but after I kept voicing my concerns, they decided to do a CT scan.

[\(01:09:41\):](#)

A short while later, the doctor rushed into the room and told us that the scan results were not good and we were going to be transported via ambulance to the hospital. We arrived at the hospital and met with a pediatric neurosurgeon. They informed us that my daughter had a massive brain tumor and would need to have surgery. My daughter underwent surgery on October 27th. We were relieved when she awoke and began to talk and answer questions. Unfortunately, our relief only lasted a short time, as she became mute and lost her ability to walk and move. She developed posterior fossa syndrome. My youngest child who was always singing, chatting and running around was now like a newborn child, unable to speak or hold her head up, stand.

[\(01:10:28\):](#)

A few days later, we were transported again via ambulance to Levine Children's Hospital in North Carolina to be admitted to inpatient rehab. I would soon be notified that the results of her biopsy were back with a diagnosis of a low grade juvenile pilocytic astrocytoma. Due to the location of her tumor, it was not possible to remove it entirely. She began receiving physical, occupational and speech therapy. She completed a swallow study and it was recommended she receive a feeding tube. I then asked the doctors to allow me to try feeding her without giving her a feeding tube. I was allowed to feed her liquids through a syringe and her weight was closely monitored by the doctors. I did my best to keep her off of a feeding tube and I was successful. We would spend Thanksgiving in the hospital with a visit from my husband and my two other daughters, who were elementary aged. Since Anaya was not able to eat, we did not celebrate Thanksgiving that year. She was discharged December 10th, 2015, still unable to speak or walk, but she had made improvements.

[\(01:11:33\):](#)

In the next few months, she would slowly regain her ability to speak and would continue to receive outpatient speech, physical and occupational therapy. In 2016, our family was transferred through the military to Los Angeles, California. Anaya would undergo shunt replacement due to hydrocephalus, a shunt revision due to a shunt malfunction and another tumor debulking surgery. I was not given many options for treatments for her and was told chemotherapy was the only thing available. I did some research and decided to seek treatment at Memorial Sloan Kettering in New York City. My family and I was soon transferred to the East Coast. Memorial Sloan would submit for molecular pathology testing that was never completed before. Between 2020 and 2021, she would undergo another tumor debulking surgery, numerous shunt redirections, shunt revisions, shunt externalizations and plastic surgery for her wound closure. She was put on mechanist and she experienced severe diarrhea and rashes throughout her body.

[\(01:12:39\):](#)

Her treatment was unsuccessful and terminated. In late December 2021, she would undergo surgery for an endoscopic third ventriculostomy. Her shunt would be tied off in case she would have any

emergencies in the future. She began her treatment of carboplatin that same month. She completed her treatment and undergoes routine MRIs to monitor the tumor and check for any concerns of hydrocephalus. At this time, her tumor is stable. Today, Anaya is 12 years old and still unable to walk on her own, but she has made major improvements. She's dependent on me for bathing, transporting, and many other things as she still has problems with balance and coordination. She continuously asks me when she will walk again, so she can be like all the other kids. Anaya goes to school with a one-on-one aid. She can feed herself and write with a pencil and stand, but needs help. As birthdays pass, Anaya throws coins in the wishing wells, hoping that she'll soon walk again.

Stephanie V. ([01:13:43](#)):

Hi, my name is Stephanie and I am an adult oncology nurse. But four years ago, my own son was diagnosed with brain cancer. My son, Declan, started having freezing spells when he was three, where he would grab his chest and kind of wince in pain. And originally, the pediatrician thought that he might be having some type of constipation. We were given a post-it note on how to mix MiraLax for a 3-year-old. And then our second visit, we were sent with a referral for a GI specialist. And it wasn't until our third visit when I was begging for answers in the Boston Children's Emergency Room where we learned that those freezing spells were seizures and he was having up to 15 of them a day when we brought him in. We were about to leave with a diagnosis of epilepsy when one doctor said, sort of as an afterthought, "Why don't we get an MRI?" I'll never forget asking the doctor if they were ruling out a brain tumor and him laughing it off as if that never happens. While we were sitting there watching our limp three-year-old wake up from anesthesia after his MRI, we were told that our son had a very large brain tumor. I stared blankly at that provider who told us that that would never happen as the news set in, and it felt as if all of the air had escaped not only my lungs, but my entire body. And at that point, we knew that our world was changed forever.

([01:15:20](#)):

Our journey's been marked by the highs of celebrating the people that we've met along the way and our strength and the work that we do to find a cure for Declan. But man, the lows of dealing with the debilitating side effects of this tumor are very prominent in our life. Declan's had 18 months of chemotherapy, seven surgeries, 21 sedated MRIs, thousands of seizures and numerous side effects. To me, the words benign brain tumor feel like a way of gaslighting us into thinking that these side effects are minor. Chemo led to a low immune system, platelet transfusions, increased seizures, nausea, vomiting, and multiple hospital stays. After debulking and seizure control surgery, Declan was left with left-sided weakness and speech issues, which meant PT, OT, and speech therapy. And as soon as he regained most of the strength back from the second brain surgery, he had a laser ablation because the seizures were back.

([01:16:25](#)):

Four years later, we continued to bring Declan to intensive therapy. This has led to a revolving door finding the perfect medications for Declan's seizures as well as behavior and possibly a medication for the tumor. But we've had no success and the side effects that they cause are still there and they definitely decrease Declan's quality of life. Declan's behavioral challenges are equally as difficult. The challenges of getting him into a doctor's office or a hospital are exhausting. We know that he's going to struggle. We've watched him be restrained with a sheet to get an IV in his arm, and it's heartbreaking.

([01:17:10](#)):

We're very anxious before any appointment, whether it be our fear for Declan or our fear for what we're going to be told at that appointment. And Declan's been diagnosed with anxiety, PTSD from medical trauma and ADHD. He is highly dysregulated, has very intense feelings, and those come out in the form



of shutting down or yelling, throwing things, sometimes physical aggression. His eight medications that he's on cause low appetite, insomnia, anxiety, mood swings. I mean, he's got behavioral outbursts that ended him crying and apologizing profusely about something that he has no control over. It's heartbreaking.

[\(01:17:54\)](#):

We will never leave his providers in Boston or the school system where he has a 30-page IEP and they focus on a trauma-response teaching method. He's got a 504, a one-to-one at all times for seizure safety as well as social cues. And we continuously advocate for the rights that Declan has as a student. Although there are days when we see small results of medications and therapy, Declan's angry. He knows that he's different. He knows that he has a disability. He knows that he's not neurotypical. I mean, he's unable to gain the skills that he needs to cope with a brain tumor, skills that no child should have to learn. I mean, he has really have tough time making friends. It's impossible for us to find childcare, and we've spent three years looking for a child psychologist for Declan with no success.

[\(01:18:48\)](#):

Crisis mode is our norm. The reality is that Declan's living with a tumor the size of a lemon in his child-sized brain, and there's no meds to shrink it, there's no surgery that's going to remove it, and this monster will continue to grow. And our biggest fear is that it's always a chance that it can grow into a higher grade cancer. Ever since Declan was three, he's wanted to be a police officer, and we haven't told him yet that he would never pass medical clearance. It's not even an option. I dream of a day where Declan can say, "I want to be a police officer when I grow up," and have it be a true possibility. But his brain tumor, a tumor considered benign, has taken away his ability to live the life that he dreams of. Let's change that now.

Katie B. [\(01:19:44\)](#):

Hi, my name is Katie and I live and work in Calgary and Canada. I'm British and my son Alexander, lives in London in the United Kingdom. Alex is 22 years old and was diagnosed with diffuse leptomeningeal glioneuronal tumors, also known as DLGNT in October 2021 after 12 months of terrible migraines, vomiting, papular, edema, seizures, and eventually the loss of sight in his right eye. In July 2021, Alex had a brain biopsy, but nothing was found in the tissue sample taken. At the end of August 2021, he was diagnosed with hydrocephalus and had a ventricular peritoneal shunt put in. Shortly after, in September 2021, Alex had another biopsy, this time, on his lower spine. This biopsy led to the diagnosis of a rare cancer called DLGNT, which was only classified by the World Health Organization in 2016, and is seen as being a very rare pediatric low grade glioma, which affects the brain and spine.

[\(01:20:52\)](#):

We learned that before we could progress any form of treatment, we needed to analyze the molecular makeup of the tumors in Alex's brain and spine. The issue was that there was not enough tissue from the spinal biopsy to do further molecular analysis and the surgeons did not want to do another biopsy of the spine as it was considered very dangerous. In November 2021, a further MRI showed that the cancer was spreading quickly and the surgeons were able to do another biopsy of the brain. At the same time, Memorial Sloan Kettering Cancer Center carried out a liquid cerebral spinal fluid biopsy. Both the tissue from the surgical biopsy and from the cerebral spinal fluid biopsy were analyzed. And the conclusion was that Alex has a BRAF KIAA1549 fusion with a 1P deletion and a 1Q gain. The doctors agreed that the best course of action was to put Alex on a targeted MEK inhibitor rather than general chemotherapy or radiotherapy.

[\(01:21:54\)](#):

Alex started trametinib in December 2021 and it had an immediate effect with subsequent MRI scans showing a regression of the tumors in both the brain and the spine. He had some problems with his skin, but these were managed by a dermatologist and the use of some antibiotics. In the summer of 2022, Alex started to have seizures and it took until June 2023 trying different medication to get them under control. In March 2023, the MRI scans started to show signs of tumor progression again. We had been following the progress of clinical trials for the drug tovorafenib and Alex's neuro oncologist agreed that the new trial combining tovorafenib, a BRAF inhibitor with pimasertib and a MEK inhibitor would be the best course of treatment for Alex. With no clinical trials in the UK, we made all the arrangements to start the clinical trial in Barcelona and travel to Spain in May 2023, Alex was taken off of trametinib and underwent a week of tests at the hospital, only to find out that he couldn't start the trial as the pimasertib had not yet been cleared for European import.

[\(01:23:05\):](#)

We flew back to the UK and put Alex back onto trametinib and steroids, which stopped the vomiting and headaches that had been escalating. However, over the course of the next few weeks, he would completely lose his short-term memory as the tumors were growing around the brainstem. In desperation, we searched for other ways to access tovorafenib. Our only remaining options were a clinical trial in Toronto, which would mean flying to Canada for a week each month on an Expanded Access, or an Expanded Access program in the United States, which would also require travel to the US each month. We quickly found out that the Expanded Access programs were not an option, as they are restricted to pediatric low grade gliomas, and despite DLGNT being classified as pediatric low grade glioma, Alex's histopathology report says that his tumors have characteristics of a high grade glioma.

[\(01:23:57\):](#)

The trial in Toronto stopped being an option as well as Alexander became too ill to travel. After eight weeks, on 22nd of June 2023, we managed to get tovorafenib prescribed for Alex on compassionate grants in the UK. Tovorafenib is sent from the USA to Alex's hospital, Charing Cross Hospital in London every month. Alex has responded really well to tovorafenib and the latest MRI scans show a dramatic reduction in the tumors in his brain. His short-term memory has returned, and so far, the only side effect he's experiencing is at the age of 22, his hair has turned white. We are determined to leave radiation to a last resort. Alex says he feels like a lab rat, but that he is certain that he is still alive because of the targeted treatments that he has taken.

Alex [\(01:24:52\):](#)

The generosity has not gone unnoticed at all. So thank you so much, and yeah, I think we'll really reach our goal. So thank you.

James Valentine, JD, MHS [\(01:25:09\):](#)

Wow. Thank you Katie for sharing Alex's journey with PLGG and really to all of our panelists who were so brave to be the first to share today, helping us understand the symptoms and health effects that your loved ones are living with, as well as how that's impacting your lives. So now, it's our first opportunity to bring the rest of you into this discussion. All of our people living with PLGG and your caregivers who are in the live audience today, if you would like to share some of the impacts that PLGG has had on you or your loved one's lives, I'd like to invite you to call in. You can dial in now at +1 703-844-3231, and that phone number is +1 703-844-3231. When you call in, you'll talk to our operator and we can get you into the queue to be brought into the discussion. Don't worry, you'll be able to hear the program. We won't miss anything while you wait. But we'd love to hear your voices and your stories.

[\(01:26:15\):](#)

So to get us thinking about this topic, just a little bit more of some of the impacts of PLGG, we're going to start off with some polling questions. So if you were with us before, you can go to that same webpage you had up. If you're just joining us, this is for our patients and caregivers only. You can go to [www.pollev.com/plgg](http://www.pollev.com/plgg). Again, [pollev.com/plgg](http://pollev.com/plgg). Just keep this up throughout the entire day, and as we go to different polling questions, you'll be able to see them appear automatically and answer those. So here, we want to know which of the following PLGG-related health concerns have you or your loved one ever had? And you can select all that apply. The options are A, loss of balance or motor function problems, B, headaches, C, speech problems, D, vision problems, E, nausea or vomiting, F seizures, G, fatigue or sleepiness, H, weight loss or gain, I, anxiety or depression, or J, other, some other PLGG-related health concern that's not listed in any of the other response options.

[\(01:27:29\)](#):

I do want to point out, this is our first question today where our audience can select more than one option. So the percentages you're seeing on the right side of the responses here are not the percentage of people who have selected any one option. It's the percentage of total responses. So probably the easiest way is just to kind of look at those yellow bars and view them as kind of a relative ranking to one another.

[\(01:27:58\)](#):

So we'll give everyone here a few more moments to make sure as our first polling question of this topic one discussion, you have a chance to log your answer here. As it stands, it looks like some of these are some of the most commonly experienced health concerns in our audience today. We're seeing loss of balance and motor function problems, headaches, nausea, vomiting, fatigue and sleepiness and anxiety or depression, it's kind of a first here, followed very closely by speech and vision problems. However, we're seeing everything here being reported by a number of people, including other things. And so we'd really like to hear what those are. If there's something that isn't listed here, if you could call in, write in, help explain what that is. But of course, we also do want to hear about some of those more commonly experienced things as well.

[\(01:28:49\)](#):

We can move to our next polling question. So the response options here will look very familiar. They're the same as our last question, but here, we want you to select the most troublesome of those PLGG-related health concerns that you or your loved one have ever had. And here, you can select up to the top three. So the same options, A, loss of balance or motor function problems, B, headaches, C, speech problems, D, vision problems, E, nausea or vomiting, F, seizures, G, fatigue or sleepiness, H, weight loss or gain, I, anxiety or depression, or J, again, some other PLGG-related health concern that's not listed here that represents what you would report as one of the top three most troublesome of those concerns.

[\(01:29:40\)](#):

So as you're making your selections, I want you to think a little bit about the why. We saw in the previous question that seemed like there's quite a burden of multiple different symptoms and health effects of PLGG. We saw a lot of those bars quite far to the right. So now that you're having to narrow this down to the top three, what came to mind as you made the selections that you're making here? And so what we're seeing is it looks like the top most troublesome symptom being rated by our audience is loss of balance and motor function problems, followed by anxiety or depression. After that, it looks like vision problems or even some of the other PLGG-related health concerns are up there.

[\(01:30:26\)](#):

What really stands out to me is that every single one of these things is coming up in some number of people's top three. So if everything that's in their top three most troublesome PLGG-related health concerns, and so we really do want to hear about this diversity of these different symptoms and health effects and help us understand why these represent the ones that are most troublesome for you or your loved one. At this point, I want to thank you for participating in these polling questions. Like I said, we'll be coming to some others throughout the program, but I want to dig into this topic and to help us do so, welcome our zoom panel, some more of your peers in this community who will be with us and sharing some of their views and perspectives throughout the morning.

[\(01:31:16\)](#):

Before we get into that, if you'd like to maybe share some of the answers you chose in those polling questions and maybe describe that why you made those selections, I would like to let you know you can call in, you can do so again at +1 703-844-3231. Again, that's +1 703-844-3231. You can call in now and any point during our discussion this morning and we'll be eager to have you join in the conversation. So Janet, maybe we can start with you first on this topic of thinking about that wide range of different health concerns that relate to PLGG, what maybe represents a top one or two of those for your family?

Janet H. [\(01:32:11\)](#):

Well, I agree with those top three, and definitely the loss of balance. My daughter lost her ability to walk after a very aggressive surgery. So having to go to PT and OT five days a week to learn to re-walk was pretty substantial.

James Valentine, JD, MHS [\(01:32:37\)](#):

Sure. And Janet, could you just tell us a little bit about who you and your loved one are to help us understand this?

Janet H. [\(01:32:48\)](#):

Sure. So it's a 34-year history, but I'll be brief. My daughter is now doing well, but she was diagnosed as a newborn with hydrocephalus, and then with the brain tumor at age three. She's had four recurrences, 24 surgeries, most of which were for shunt-related issues. She's had four recurrences and four resections. It's completely changed who she was. She was a very happy, well-adjusted three-year-old, very, very bright. And after the (carbo and Kristen protocol, which when we started that in 1994, it was already a 25-year-old protocol and it was the only protocol, and that is still the first to go. So that's kind of frightening. Chemo put her in the hospital number of times, her IQ significantly dropped. Just social issues as well and concerns.

James Valentine, JD, MHS [\(01:34:09\)](#):

Yeah. Well, thank you for sharing that, Janet. Kind of given that, and circling back to where you started, which was agreeing that for your family, that mobility and some of the physical limitations that came as a result of one of the resections has been one of the biggest impacts, can you maybe tell us when did that procedure occur and how did you start to notice those impacts?

Janet H. [\(01:34:41\)](#):

My daughter's symptom was never seen before, and I've not heard of anyone since. She had audio hallucinations at age three, and by this point, she already had a shunt. So when they did an MRI to take a look at how the shunt was functioning, that's when they realized she had a slow growing brain tumor.

She tends to break molds. When she was young, we were told if kids get to be five or six, they tend to do well if they can reach puberty. She broke that mold, then it was 21, she broke that mold. Her recurrences have been at ages 4, 5, 17 and 22, not what we expected. Needless to say, having loss of function, she went through periods of depression, anxiety, the body hallucinations were terrifying to her. They sounded like lions growling. She was three. She couldn't explain it to us. And then there was just all the years of school with being socially different, maturity issues, just a struggle all through school.

James Valentine, JD, MHS ([01:36:00](#)):

And so talking about the hallucinations and starting at such a young age, how long did it take to get to a point where you were able to understand that that was something she was experiencing, and is that something that she still experiences to this day?

Janet H. ([01:36:24](#)):

Fortunately, she doesn't experience anymore, but it did happen for quite a while. I mean, when it first started happening, we realized that it was a brain tumor that was causing the audio hallucinations. We told her she was going to have a surgery and she was going to get her head fixed, and she had the surgery and they weren't able to remove very much. So it continued. It would happen at night. It would happen many times in a day. She literally would stop eating, playing with her toys. Her personality completely changed, and it wasn't until she had another resection where more of it was removed that it stopped. But she had post-traumatic stress disorder for a very long time after that.

James Valentine, JD, MHS ([01:37:06](#)):

Wow. And then in terms of being different than her peers and difficulty and the social dynamics at school in childhood years, was that directly related to that or were there other things you think that contributed to those difficulties?

Janet H. ([01:37:30](#)):

Well, she just experienced so many years of exhaustion, so she wasn't able to function academically well, socially well, every year we had an IEP. There was just a lot of battles with the school systems trying to figure it out, knowing most teachers have never had a child with cancer, let alone a brain tumor. So that was really, really challenging. We were fortunate to be in a good school system, and she was in a good transition program, but we were always battling.

James Valentine, JD, MHS ([01:38:13](#)):

Right. Wow. Well, thank you so much, Janet, for sharing all of that and being willing to let me explore some of those experiences with you. Joseph, I'd like to bring you into this discussion as well. Again, thinking back to such a wide range of different health concerns that can result from PLGG, are there any kind of one or two that stand out as most troublesome for your family?

Joseph D. ([01:38:40](#)):

Hello everyone. My name is Joseph. I live in Washington DC and my son, also named Joseph, was diagnosed with an optical pathway glioma in March 2021 when he was one year old. And the most significant impact or symptom that we've had throughout this process has been vomiting. We noticed when he was about six months old, he started vomiting more and more often.

Joseph D. ([01:39:03](#)):

When he was about six months old, he started vomiting more and more often and by the time there was doctors kept thinking it was gastroero... I'm sorry, I can't say it, issue for the longest time. And finally, we voluntarily hospitalized him and finally at the end of a two-week hospitalization, they noticed that they did an MRI and discovered the brain tumor. It is in the two years since then, or two and a half years since then, he vomited almost every day, often multiple times a day. And it's only been in the last month or so where that has started to become less frequent.

PART 3 OF 10 ENDS [01:39:04]

James Valentine, JD, MHS ([01:39:46](#)):

Wow. And has there been anything that has changed in the last month or so that may resulting in that lessening of vomiting? Glad to hear that, but just curious. Is it treatment related?

Joseph D. ([01:40:02](#)):

Yeah, it's hard to tell exactly what the source is. I think one of the things is he has such a low threshold for vomiting now, that anything can cause it. And so we started him in school earlier this year and we asked for an IEP originally, and he's done well. He presents pretty well, but once he was in school, he would throw up every single day. And so they brought someone in and started in IEP because it was becoming very difficult for the teachers to manage. That happened in the middle of class, but he was finally got about six months into a regimen of trametinib, which did cause a little bit of shrinkage. Hopefully that may be partially the result of it, but we also know that he's got issues from the biopsy, how it was performed, it had to go in through his nasal cavity, which there's scarring up there, which makes it very hard for him to breathe. And he's constantly has sinus infections.

([01:41:05](#)):

So there could be multiple reasons, but it's something that we have dealt with almost every single day, every single night he wakes up in the middle of the night or he did it for the longest time, and so he's asleep with us every night because we have to be aware that he's about to throw up and be ready for it. So that has been the most significant symptom or the one we deal with every single day since the diagnosis.

James Valentine, JD, MHS ([01:41:32](#)):

Yeah. And you said that it has been every single day. Are there good days or bad days when it comes to the vomiting, even when it is still daily?

Joseph D. ([01:41:45](#)):

It's hard to say. Yeah. Any day that we don't have vomiting is a good day and the stretches that we have where he's not throwing up at night are good stretches, but they can come back up at any moment and then it's back to us being on guard at all times where basically where one parent has to be next to him at all times because it's very traumatic waking up and throwing up at two or three years old and being covered in your own vomit and not knowing really what's going on. And he's not able once it starts, he's really has a difficult time stopping.

James Valentine, JD, MHS ([01:42:22](#)):

Yeah. And one last question if you don't mind is you mentioned that it could be triggered at basically any time of day like during the school day, in the middle of the night. Is there anything in the environment that triggers or makes it more likely that at least you all can tell in terms of vomiting, whether eating or any other stimulus, or is it really just unpredictable?

Joseph D. ([01:42:50](#)):

So it's a little bit unpredictable. We've gotten a little bit of a better sense recently when it's coming. Because he's older, he's able to communicate more when he has a stomach ache and so we can stop feeds. Although he also uses it as he's a smart 4-year-old who likes to use it to leverage, try to negotiate TV time. So he'll sometimes complain he has a stomach ache. He says, "I think maybe a TV show will make me feel better." But at the same time, there are oftentimes when he'll get so worked up either us leaving school and dropping him off or something and he just can't work himself back down and that'll trigger vomit. So we've learned to manage, but it has been the most omnipresent symptom for us.

James Valentine, JD, MHS ([01:43:36](#)):

Sure. Well, glad to hear that Joseph is still up to normal 4-year-old antics, but appreciate you really sharing that experience. Shelly would like to continue this discussion, the things that maybe are most troublesome or bothersome of the symptoms that have been experienced as a result of pLGG. What comes to mind for you all?

Shelley K. ([01:44:02](#)):

Hi, thank you. My name is Shelley and I'm in Ohio. My son is nine now. He was diagnosed at age seven. He has a brainstem tumor, so obviously resection was not really a possibility and the biopsy reproduced just a very small amount of tissue that was inconclusive. But his biggest top three I think would be he has vertigo episodes and he has low grade dizziness, so he didn't actually lose the ability to walk, but he has very changed motions. The way he moves his body, he holds his neck very stiff and he turns his body like this instead of just freely looking. He can't look up, he can't lay flat, so that impacts his sleep, but also obviously largely impacts how he plays at recess with friends, they're all running around playing soccer and he just doesn't have that ability to join in. So he often feels isolated because of that.

([01:45:07](#)):

He has hiccups that sometimes last literally for days. He'll hiccup all day long, all through the night, all day long, all through the night and big deep ones. So his muscles and his rib cage and everything gets really sore. It impacts his appetite, so he doesn't want to eat. He's lost a lot of weight through treatment, but he had lost weight before diagnosis and he ended up having a G-tube put in just to maintain weight because it impacts his appetite. So hiccups, vertigo, and he does have the nausea. All of that heat. He doesn't actually vomit, but he has a lot of he calls them spiderwebs, like a sensation of gagging in his throat, that after he eats, he feels like stuff is still there, and it impacts his speech as well. But the top three are vertigo, hiccups, and nausea spider web situation.

James Valentine, JD, MHS ([01:46:05](#)):

And just in terms of understanding his experience with that, was there one of those that appeared first in terms of those top symptoms and for whichever that was, how did you really first notice that? Was it ahead of before getting a diagnosis or was that something that really happened after that initial understanding what was going on with him?

Shelley K. ([01:46:41](#)):

Yeah. He actually probably went through a very different path than most kids due with diagnosis. He got diagnosed from a sleep study actually because he was doing these big huge gasps in, it sounded like he was resurfacing after being held underwater while he was sleeping. And I had reported it to the pediatrician a lot of times, but they were like, "Well, he's growing on his curve and he doesn't seem to be having any issues and if it is apnea, we don't usually put a CPAP machine on a kid. But he had been to ENTs and people looking into that gagging sensation that he was having and why he was doing all of that because he would sound like he'd throw up, but nothing would come up after eating and while eating. Actually, the vertigo and the hiccups have come since. He had one episode of vertigo before diagnosis and I attributed it to a cold or jumping up off the couch too fast because it was really brief. It gotten worse over time, but that's his main. ENT or not ENT, the ear, nose and throat doctors were the people that we were seeing the most at the beginning. They were looking into like does he have some kind of EOE problem with his throat? Just trying to figure that out. But the other symptoms have come since diagnosis.

James Valentine, JD, MHS ([01:48:10](#)):

And then for the vertigo, it sounds like given that he's had to modify even how he can move and be mobile like playing at recess, does it really come in waves or is it almost something that he's always experiencing?

Shelley K. ([01:48:30](#)):

He has this low grade dizziness and he seems to have a combination of motion positional sort of thing. If he tries to lay down for his MRI or to sleep for example, he can't lay down to sleep anymore. So this backwards motion just instantly starts that vertigo. But the rest, he'll have these cycles where he'll have low grade and he'll sense that it's getting worse. Almost like people go through migraine cycles and then he'll have what we call an attack or an episode, and he'll need lots of medication to calm that and it'll take him out for the day kind of thing. He'll be in bed, but he has always a low grade dizziness.

James Valentine, JD, MHS ([01:49:17](#)):

And how often do those big attacks happen for him?

Shelley K. ([01:49:23](#)):

They happen, they can happen up to twice a month lately, but sometimes it's more like probably about twice a month, it's been happening lately. But he'll also have days where he just pretty much every day he wakes up and says, "I don't feel good." That's his reality. It's a combination of dizzy and nauseous and I feel like he's a little old man and he's only seven or nine. But some days are better than others, but probably the big ones are more like twice a month or so.

James Valentine, JD, MHS ([01:50:05](#)):

I see. Well Shelley, thank you so much for sharing that. So I do see that we have a phone caller that I'd like to bring into the discussion. We have Jerilyn from Utica, New York who's a caregiver of her daughter living with pLGG, and so would like to share some of the experiences they've had with this condition. So Gerilyn, I'd like to welcome you to the program. Are you with us?

Gerilyn ([01:50:34](#)):

Thank you.



James Valentine, JD, MHS ([01:50:36](#)):

Welcome.

Gerilyn ([01:50:36](#)):

Yes, can you hear me?

James Valentine, JD, MHS ([01:50:38](#)):

Yes, we can.

Gerilyn ([01:50:42](#)):

Hi, yes. I'm a mom of a pediatric brain tumor survivor. On March 14th, 2014 at the age of 14, my daughter, Anna, was diagnosed with a brain tumor and obstructive hydrocephalus. When we arrived at the hospital, Anna had an emergency insertion of a cranial shunt to relieve the extreme fluid in her brain and surgery the following morning for a resection of a posterior fossa brain tumor, which was the size of the lemon. My daughter, I have to say, the color for brain tumors is gray and Anna's forever altered life is in a constant state of gray.

([01:51:41](#)):

My daughter is 24 years old now. The impact the disease has had on Anna's daily life, no one prepared us for. No one prepared us for this. Upon discharge, no medical doctor prepared us. We didn't realize, I guess at the time, and I'm a registered nurse, I was really not prepared for any of that. That they had to remove, of course, good brain tissue to ensure all the margins were clean to save her life. However, then came the aftershocks, the sadness over what was lost to impact her low grade astrocytoma would have on her daily life. And some of what was not mentioned is my daughter, due to the injury to her cerebellum, left her with fine hand tremors and at times, full body tremors. She tried, but she was not able to play softball in high school anymore because she was actually ridiculed by her gym coach. So it's a rollercoaster ride for my daughter. She starts her day off gagging every morning in the bathroom. She moves like a unit, her head and neck, she moves as a unit, but the fine hand tremors had made it difficult for her in many ways. And also, besides having neuropathy, she has brain fatigue, neck pain, which now we just found out is due to arthritis in her neck due to the posterior fossa resection. She rocks her nephew, she feels sick. So she has chronic nausea, migraines that last two to three days caused by vestibular symptoms with certain movements. But also, my daughter's pituitary gland was affected, which we didn't find out until later. And this is a deep concern for me as a mom. She has her high school sweetheart and they will get married in a couple years and I worry about her being able to have children someday. She is on a hormonal pill right now. She tried to get off it, but it was not good. She was so symptomatic, it was not good. So we don't know if that it was just her pituitary gland or her hypothalamus or both that were damaged. And I don't think that the hormone problems are really addressed and for girls, it was a big problem for her.

James Valentine, JD, MHS ([01:55:12](#)):

Well, I appreciate you sharing.

Gerilyn ([01:55:15](#)):

Our hope is that it just will be researched and hopefully something will be developed for a drug.

James Valentine, JD, MHS ([01:55:27](#)):

Yeah. Well, Jerilyn, I appreciate you sharing a number of things that we haven't heard much about yet. But on your concerns, given the pituitary gland impacts and the hormonal issues and the impact that might have on her ability to have a family. In terms of those hormonal issues, when did you all first notice that? I think you said it was something that wasn't picked up right away in terms of the pituitary gland impact. Could you just share us with us a little bit about the timing of that and how you noticed that?

Jerilyn ([01:56:10](#)):

Sure. So at the age of 14 when Anna had the tumor, she was not getting her menstrual cycle all of a sudden. And we just thought that was now just part of the regulation of her hormones. The day after her tumor was removed, she got her menstrual cycle and it was just a normal menstrual cycle. However, she was on a high dose of steroids. And then when she was about 15, her cramping feeling, throwing up, it's like a week before her menstrual cycle and just continued during it as well and just really just feeling so sick. So a friend of mine had mentioned it to... She works in labor and delivery. She mentioned it to an OB GYN because I had mentioned it to her neurosurgeon, her pediatrician, and they didn't have much to say about it. And he said, "Have her mom call me."

([01:57:42](#)):

And he met with us just to talk, just a meeting, and he said, "Anna, I thought your tumor was tapping at that pituitary gland." And he was absolutely right and she was so debilitated, she couldn't go to school. She would be in school and the nurse would call me and I'd have to go pick her up. She tried to get off it, but she can't at this time.

James Valentine, JD, MHS ([01:58:17](#)):

Yeah. Well, Jerilyn, thank you for being so willing to call in and share your daughter's story and really your family's journey with pLGG and your being willing to share some of these other effects that we haven't heard about so much yet. So really appreciate it. I do see that we've been getting a number of written comments coming in as well, so I want to check in with Courtney, what are we seeing?

Courtney Davies ([01:58:43](#)):

Yeah. Thank you, James. I'm going to read first from Lacey and she's writing in from Pittsburgh, PA. The symptoms that have most significantly impacted my son are the side effects from the chemotherapies currently offered to treat pLGG from cognitive delays to physical and occupational therapy delays as well as pain in the body. He had to fight every inch to have some semblance of a normal life.

([01:59:12](#)):

I'm also going to read, there's a comment here from Carlos in Texas and Carlos writes, my daughter, Isabelle, had experienced occasional migraines for a year and a half leading up to her diagnoses in the months immediately preceding diagnoses was also developing a loss of balance. Our family pediatrician attributed those both to growth, body changes, hormones, and recommended physical therapy to develop strength. We were a few weeks into physical therapy when she was diagnosed.

([01:59:47](#)):

And I think there's another one here I'd like to read. Let's see here. Carly Ann from Washington has written, she struggles a lot with impaired vision and is not able to drive. Her cognitive, excuse me, her cognitive decline and slow processing speed are a challenge for her. She's dependent on her feeding tube, uses a cane to walk, and has chronic fatigue.

James Valentine, JD, MHS ([02:00:15](#)):

Wow. I want to thank everyone who's been writing in with comments. You can continue to do so using that comment form under the livestream player on the webpage that you're at today. And we'll continue to read those comments out throughout the program. Know that if we can't get to every comment, and so if we don't get to yours that way, we'll still have that and we'll include that in the voice of the patient summary report.

([02:00:40](#)):

I do want to broaden the discussion a little bit. This certainly has already come up as we've been talking about symptoms and health effects, but we want to also understand how this condition really impacts daily life. And so to get us thinking about this topic, I'm going to invite you to participate in another polling question. So go ahead and open that tab on your web browser, go to your phone web browser, go to [pollev.com/plgg](http://pollev.com/plgg).

([02:01:09](#)):

So here, we want to know what specific daily life activities that are important to you or your loved one are you or they not able to do or struggle with as a result of pLGG. And we'll ask that you pick up to the top three of those daily life activities that are impacted. The options are A, attending school, B, the ability to walk C, biking or playing sports, D, self-care, E sleeping, F, working or having a career, G, attending social events with family or friends or H, some other aspect of daily life that's important to you or your loved one that is either impossible or difficult as a result of pLGG that you would rate as a top three impacted activity.

([02:01:59](#)):

So before I'd like to do, as you're making these selections and ranking these, you're probably have certain aspects of pLGG that are coming to mind that are impacting these activities and why you view these as some of the most important ones that are impacted. So hopefully as you're making this, you'll be thinking about what you might say if you were to call in or write in, and we'd encourage you to do so as we move out of this polling question. So interesting as we're seeing the results still come in, the number one selection is other, something we haven't listed or probably a number of things that we haven't listed. So we really want to hear what those are. So if you're making that selection, please consider calling or writing in. After that, at least as it stands, it looks like biking and playing sports is one of those top most impacted areas followed by sleeping, attending school, and attending social events with family or friends.

([02:02:56](#)):

But we're seeing every single one of these things rank listed in some number of our audiences' top three important activities that are either impossible or difficult to do as a result of pLGG. So we want to explore this topic a little bit more. And so to do so, I'm going to come back to our Zoom panel to get us started on this topic. Jennifer, maybe we can start with you on this. As you're thinking about the impacts of pLGG and what that means in terms of impacts on daily life, what stands out to you as a top impact?

Jennifer S. ([02:03:32](#)):

Well, I'm Jennifer in the DC area. My son Sam is eight. We found his tumor when he was about 20 months in the hypothalamic optic nerve area. He's doing really well now, he's overcome a lot of things, but just day to day right now, we still have to get him on a bike. So mostly he's pretty risk averse, but we've worked on finding... He plays basketball, but it's not in a real competitive, and then he's really gotten into golf because that's no, you're not out there risking physical contact. But it has taken us a

while to get here and he is on selumetinib now, which its side effects or extreme stomach pain, although that has gotten a lot better also.

James Valentine, JD, MHS ([02:04:23](#)):

Okay. So talking about some of the physical activities that he can do, you mentioned that he's risk-adverse. He's perhaps concerned about what maybe his ability to do certain activities or the consequences of those. Can you maybe just describe a little bit of what makes him risk-adverse? Is it certain physical limitations or symptoms or is it something else?

Jennifer S. ([02:04:57](#)):

Well, I think it's just from, they attempted a biopsy and it bled. The tumor bled. When he recovered, as Matt says, recovering, he had to relearn how to walk. His balance was off. So that has stuck with him a bit through time, even as he has gotten better, he's gone through years of physical therapy, occupational therapy, so it starts to affect their confidence a bit. He has a pretty rough sister who he tries to stay away from. I think they're just a little wary knowing their balance is a bit off. They may be not as able like climbing jungle gyms at playgrounds they don't want to do, or my son doesn't want to do that because he's fearful. But he has gotten a lot better.

James Valentine, JD, MHS ([02:05:42](#)):

Yeah. And were there any examples of times like maybe early on where he was doing something and he pushed the limit of what he could do or anything that could help us visualize that a little better?

Jennifer S. ([02:05:58](#)):

As he was recovering and learning how to?

James Valentine, JD, MHS ([02:06:01](#)):

Yeah.

Jennifer S. ([02:06:02](#)):

Maybe just fell easier? He also lost sight in an eye and then peripheral sight in the other eye. So he would bump into stuff sometimes, I maybe didn't notice at the time or mostly just falling or bumping into stuff, but I think he was so risk averse, he mostly would sit and watch, so he didn't even put himself in those predicaments or he would also with swimming, not want to go underwater at all.

James Valentine, JD, MHS ([02:06:27](#)):

Okay. And then in terms of he's gotten a lot better, he's able to do these things. You said he maybe modifies the way he plays basketball a little bit. In terms of is it balance, you mentioned that as one thing. Are there still things that stick with him today that give him a sense of his limits?

Jennifer S. ([02:06:59](#)):

It might be balance. I think it might be just reaction time. I think he fears being in a situation where he doesn't have full control of the physical environment, so he fears being pushed or kids run fast past you. He can't run as fast. So I think he's scared of getting run over a bit or not get out of the way in time. But we have just worked on gradually pushing him and getting him into situations where he might have to be uncomfortable.

James Valentine, JD, MHS ([02:07:28](#)):

Right, I see. Well, thank you so much, Jennifer, for being willing to share some of that. Christine, I'd like to bring you into this topic as well as we're trying to understand some of the impacts in daily life. Are there any things that are either really difficult or maybe even impossible that are important to you all?

Christine L. ([02:07:51](#)):

Thank you. I'm speaking to you from Northern California. My son was diagnosed around his third birthday. What brought him to medical attention was initially, deceased of his right side and he was younger. We presumed that he was a lefty, which initially was pretty exciting because we thought what an advantage that would be for sports. Now of course I know that it's not normal for kids to have a preferred sidedness at that early of an age of... I think like many of the parents here, we've learned a lot in retrospect, especially when we put a lot of weight on the opinions of the providers that had been fine for us when everything was fine.

([02:08:45](#)):

Peter came to attention because he wasn't able to hold things in his right hand. He was dropping his school bag a lot, dropping his jacket a lot, and then ultimately when we were doing potty training, he wasn't able to push down and pull up his pants. He was only using his left hand. So like many of the parents here, it took a long time to get someone to take us seriously. We spoke to the pediatrician many times, went to an ENT because he had some drooling, which of course during COVID, was a big problem wearing a mask. And so constantly, the mask would fill with saliva and he had to wear the mask. Further exacerbating that was his speech was delayed. So not being able to see his mouth, not being able to see others talk.

([02:09:40](#)):

So ultimately, even after seeing a neurologist who was dismissive, I just brought him to the ER and he had an immediate MRI and immediate surgery. But despite seeing the best of the best, everyone was a bit dismissive. However, I count my blessings in listening to the stories of the other parents that are here. My son is doing fairly well. This is all relative though for a disease where success is determined as not dying, which is horrible. My son still has right side weakness. He is in OT and he's doing well enough that the state has decided he doesn't qualify for PT. So we spend a lot of money on things like karate that force him to use both sides of his body that doesn't feel like work to him, and he's still at an age where he can participate.

([02:10:43](#)):

I fear, as others have brought up, those lingering side effects are going to impact. He's not going to be able to ride a bike independently or play sports in the way that perhaps he might want to. The main problem that we're having though is still residual with his communication. So along with the right side weakness that impacts his face and his tongue. So he can be quite difficult to understand and he still has drooling, and so we're working on that a lot. We're spending a lot of money and investing in speech therapy and occupational therapy to help him. He gets frustrated when he's not understood, and I can appreciate that.

([02:11:31](#)):

So I'm really hopeful that with the attention that we're giving here, we'll make some improvements. He'd been on a targeted inhibitor for two years. It had since been discontinued because it wasn't showing any improvement. And so at this point, we're watch and wait, and I think if there is growth, we're going to be in this situation where we have to think about surgical intervention, which is very scary, particularly given the unintended consequences-

Christine L. ([02:12:02](#)):

And particularly given the unintended consequences of an intervention like that. So thank you for allowing me to participate and share some perspective on my son.

PART 4 OF 10 ENDS [02:12:04]

James Valentine, JD, MHS ([02:12:11](#)):

No, thank you for sharing that perspective. And we haven't heard about this single-side weakness and certainly not so directly. I want to just explore and understand that a little bit more. I think you gave very vivid examples of, especially early on, how that impacted him. Today, he's able... As you said, with PT and OT and now able to do... And also doing karate is something that he can participate in. Is there an example of something that maybe he's tried to do but just still can't quite do it or do it as fully given the remaining right-side weakness that he has?

Christine L. ([02:12:58](#)):

So I think something that's important to point out is this spectrum of disability. So we're very fortunate in that he's mobile. But he's able to compensate in a way not to fully demonstrate his limitations. So when he carries things, when he uses things, he uses his elbow to hold things. And so he's not creating problems that would require an intervention, but he's also not using the muscles and limbs in the way a normal kid would. So he doesn't warrant intervention in a way that would help further.

([02:13:40](#)):

So he was diagnosed so young, our narrative isn't that he was playing baseball and he was a superstar and now he can't do that anymore. We don't know what his potential would've been. He's not naturally a lefty, right? So he's a lefty because the right side of his body doesn't work. So even with the good side of his body, he still can't hold a pencil correctly. He still has a limitation on the contralateral side. So it's presenting in ways that are subtle and he's able to compensate for that. And of course, as a downstream effect, it becomes more difficult to advocate for services when providers evaluate him and say, "Well, actually he's doing okay." But the question of course is, "Compared to what?"

James Valentine, JD, MHS ([02:14:30](#)):

Right. And you also mentioned that... Related to... You brought it up in the context of the speech impairment, that he gets frustrated when people don't understand him. How, beyond that or in addition to that, is he handling all of this? How does he feel about it and how does that impact his perspective on things and activities that maybe he's interested in or willing to do?

Christine L. ([02:15:09](#)):

I think it comes across as giving up or kind of throwing his hands up and walking away from it. If his sisters are there, his sisters will translate for him because we're used to what he sounds like. I think what can come across... He might say, for example, in karate, "I'm tired, I need a break." But really he's challenged and he can't do what the other kids are doing. And he doesn't want to say, "I can't do it, or I need help." So he'll take a water break. And so he's found ways to compensate for it that are convenient and acceptable for the caregivers involved and doesn't necessarily highlight the need for additional intervention, which as a parent makes it difficult to acquire those resources.

James Valentine, JD, MHS ([02:16:04](#)):

Absolutely. Well, thank you, Christine, so much for sharing all of this. I do see that we have a phone caller Caitlin from St. Louis Missouri, who's a caregiver that wants to share some of the impacts that PLGG has had on her daughter. So Caitlin, I'd like to bring you into this conversation and welcome you to the program. Are you with us?

Joan ([02:16:27](#)):

Yes, I am. Can you hear me?

James Valentine, JD, MHS ([02:16:29](#)):

We can. Welcome.

Joan ([02:16:31](#)):

Thank you. So my daughter was diagnosed with a ganglioglioma diffused into her brainstem deemed inoperable February of 2021. Our major symptoms were vomiting, a lot of vomiting followed by GI. They noticed some nystagmus and tremor ordered the MRI and kind of the rest is a whirlwind. We were rushed to the emergency room. They wanted to... She had hydrocephalus do a biopsy, but they did not think that this was a... As they still do not believe that this is a respectable tumor. But dizziness has been fairly debilitating for her. She gets very upset because she doesn't like being dizzy. It impedes her in school. She can't do horseback riding anymore. She gets triggered by loud noises, by the heat, sudden movements, and she's now 10 and at an age where she's understanding that she has to live with these symptoms. And it's heartbreaking for me as a mother that I can't do anything about it.

([02:17:52](#)):

So she did start Dabrofenib about a year ago, and we did see significant shrinkage, which lessened the vomiting and some of the dizziness. But she still does experience those vertigo episodes as I believe I kind of heard Shelley talk about, which is the first person I have really heard that is experiencing something so similar as my daughter, Adelaide. It was like I was listening to myself explain it. So it's been really hard to deal with the dizziness because there's just not a lot of pediatric vertigo out there and the doctors are perplexed. So she takes benzodiazepam for her dizziness. My ten-year-old's on a pretty heavy drug, but that is the only thing that works to make it better. That's what we're doing.

James Valentine, JD, MHS ([02:18:51](#)):

Caitlin, you said that some things were triggering for her, sudden movement. I think you said heat or temperature changes, maybe even bright lights, things like that. When you say triggering that, is that for the vertigo? Does that trigger a worsening of the vertigo? Can you just explain that a little bit?

Joan ([02:19:14](#)):

Yeah, it does. It's very strange. A good example would be we were at a baseball game and the crowd and the baseball game is at a pretty steady kind of sound. Sometimes the crowd gets a little bit louder, sometimes it doesn't, but maybe they hit a home run and the fireworks go off that'll do it. That loud noise will trigger her into a real big dizzy spell. They tend to have been lasting less than they were before we began treatment. I heard Shelley say that sometimes they're so bad that they're down for the day, in bed all day. I've definitely saw that more prior to treatment, but I mean, we still have those days. We still have those days when school calls, "She can't do it. She's tried and it's too much today." They've given her all her medication and we just have no other choice but to go home and rest.

([02:20:19](#)):

They also think at school that when she's concentrating... Because she does also have strabismus, the misalignment of her eyes. Which is making her struggle to track the board to the paper, keep her spot when reading a book. So these things we think might also be triggering the dizziness just because she's working so hard to concentrate. And she's overcompensating, which is making the brain work harder, which is triggering this part of the brain that is impeded by the tumor causing the dizziness. We had a big meeting with her doctors yesterday actually, and she does this head movement when she gets the dizziness and now they're calling... They think it's a tic. So it's just kind of been one thing after another. I feel like we're chasing the... Just chasing treatment, chasing control of these symptoms, and it's just like a never-ending kind of cycle.

James Valentine, JD, MHS ([02:21:23](#)):

And very, I think, interesting to hear about the focus and how that can be in itself triggering. Whether it's just the baseline dizziness or something that's one of these more severe episodes or attacks, how often is the school day interrupted or otherwise impacted for her?

Joan ([02:21:58](#)):

Yeah, prior to treatment it was... Well, she's at a new school now. I was actually working at her school prior to treatment, and she was probably down in my office at least once a week for a good amount of time. Then when she switched schools, it was still probably once a week we were getting calls. But since I wasn't there, I think she was resting and able to sometimes make it back. I'd say now, we're probably getting calls every other month where we do have to go grab her, but they're really good. She is also deaf in her left ear because of the tumor, and so she goes to a very specialized school. There's only three kids in her class. There's more adults than kids, so they're very in tune to her. They can kind of see it happening. They can encourage her to maybe rest or take some medicine, but I do fear when she goes mainstream, what that will look like.

James Valentine, JD, MHS ([02:22:52](#)):

Right. Wow. Well, Caitlin, thank you so much for calling in and sharing all of that. Even talking and kind of building on what Shelley had shared about vertigo. We've learned so much more about what that can look like and how that can impact daily life. So I really appreciate you calling in to share. I want to come back and check in with our Zoom panel here and maybe with a little wave of a hand if there's an activity or impact that we haven't covered yet. We knew that there was a lot of other mentioned in those polling questions. Is there something that either we've hit on but your child has had a somewhat different experience with it or maybe something we haven't touched on at all that you'd like to share? So just give me a little wave of a hand. Yeah. Joseph.

Joseph D. ([02:23:52](#)):

One thing that I think probably all of us have experienced, and it has been touched on some, is just medical anxiety for the child and PTSD from going back to the doctor. My son, we just tried to take him for a routine dental cleaning two, three weeks ago. And just the sensation of being laid back with people who appear to be medical personnel surrounding him is so traumatizing for him that he screamed and fought and begged basically for us to stop and even trying to hold him down and everything. We weren't able to get a teeth cleaning. And it's not only traumatizing for him, it's re-traumatizing for us because it reminds us of some of those initial hospitalizations. And so that is something that we know we're going to be dealing with for a long, long time. And we have to schedule a teeth cleaning six months in advance so he can be sedated just to have a standard dental procedure cleaning.



James Valentine, JD, MHS ([02:24:48](#)):

So I mean, I'm sure that is very difficult for him to have that anxiety associated with engaging with healthcare providers and healthcare system. I mean, does he describe it all in terms of what about going in is he worried about? Like pain or if there is something specific? What's driving that?

Joseph D. ([02:25:20](#)):

That's kind of the hardest thing is that you can't rationalize it with him. Just a fear that lives with him. And one thing we've noticed relatively recently is when we put him to bed at night, we'll hear him sometimes say, next to us, whisper to himself, "I'm safe here." And we don't know what exactly maybe he would be doing that anyway. But for us, it always harkens back to the amount of trauma he's experienced from all these medical procedures at just the age of four years old.

James Valentine, JD, MHS ([02:25:50](#)):

Yeah, absolutely. I guess since you're raising this topic... Well, I'll purpose this to the Zoom panel here as well, if anyone wants to add on the topic just in general of the mental health impact on your children. Yeah, Janet.

Janet H. ([02:26:09](#)):

Yeah. Just to kind of piggyback on what Joseph said, just regarding trauma, I don't know if it's more painful for us as parents or for our kids to see their peers experience milestones and rites a passage and know that they're not going to do that. And I did touch on... Before Kelsey's first really aggressive resection, she was four and she hadn't even been in kindergarten, and she could already tie her shoes. And after that surgery, she said to me, "Mommy, I used to be smart, but now I'm like not." And I know that all of these kids, whether it's wanting to play a sport or just have friends, that's a trauma in and of itself. And it's a trauma to the whole family because we grieve for our kids.

James Valentine, JD, MHS ([02:27:14](#)):

Yeah. I can't imagine how difficult to have that kind of loss and recognize that you have that loss, or as you also described it, seeing your peers hit certain milestones. Are there examples of that that you could share, Janet, that you've seen those types of milestones or rites of passage that maybe stand out in your mind?

Janet H. ([02:27:44](#)):

Well, there's the obvious that happens to kids that have behavioral or social issues, just not getting invited to birthday parties. For our daughter because she has chronic fatigue, she really honestly could care less about playing sports. And she's had the fatigue since she was very small, so that's not really an issue. But she's at an age where a good amount of her peers are married, having children. And I went to a conference years ago, and the amount of our kids that get married and lead typical lives is definitely in a minority. And also sadly, being bullied. It happens and you rely on school to fix that, but they don't. They often blame your child because your child has behavioral issues.

James Valentine, JD, MHS ([02:28:57](#)):

Well, Janet, thank you for letting me probe on that and share some of that. I think it's so important to understand not just the physical and the symptom kind of impacts, but the social and mental health ones as well. So with the time that we have remaining this morning, I want to shift gears a little bit

recognizing that as we've just heard, there's so much that people living with PLGG, your loved ones are experiencing going through, having to deal with and cope with on a daily basis. But we also know that you're thinking about your children's futures living with PLGG. For those of you living with PLGG in the audience, you might have things that you're concerned about thinking about for your futures. And so we want to explore that a little bit right now with a final polling question. So go ahead and go to that web browser.

[\(02:30:02\)](#):

Go to either a new tab on your computer or on your phone, go to [www.pollev.com/pLGG](http://www.pollev.com/pLGG). And here we want to focus on this question of what worries you the most about your loved one's condition in the future? And we want you to select up to the top three greatest worries that you have. The options are A, the worsening ability to walk. B, a worsening of seizures. C, impacts on social life. D, a worry that symptoms will actually get worse. E, the inability to live alone. F, falling. G, dying prematurely. H, the ability to start your own or their own family or I, some other worry that you have for yourself, living with PLGG or your loved one, living with PLGG that represents one of those top greatest worries you have for the future. We'll give everyone here a few moments to get their responses in.

[\(02:31:10\)](#):

As it stands, it's looking like our audience is reporting that the greatest worry that they collectively have is that symptoms will get worse from where they are today. We've heard a lot about the different symptoms that people are living with, and so I'd be interested as we move into the discussion to hear about what symptoms or worsening of symptoms are most concerning to you and what a worsening of symptoms might actually mean then for you or your loved one.

[\(02:31:43\)](#):

We see after that the worry about dying prematurely followed then by impacts on social life and the inability to live alone. However, a trend across all the polling questions we see is that there's a wide range of different impacts, and in this case, worries with every one of these options being in some number of people's top three, including again, a number of other things that weren't listed in the response options. So if you'd like to call in and share some of your greatest worries for your loved one or yourself living with PLGG, I encourage you to do so now. You can dial in at +1 703-844-3231, and that phone number is +1 703- 844-3231. But to get us started on this topic, I'd like to go to our Zoom panel again here. Maybe Shelley, we can start with you on this topic of the various different worries or concerns or even fears for the future. Is there something on that that you'd like to share?

Shelley K. [\(02:32:58\)](#):

Thank you. Yeah, I mean, I agree with a lot of the top ones that were showing up in the polls because you don't know based on the treatment options... Like Max has gotten vincristine and carboplatin, and he's done with that treatment. But we don't know if his tumor is going to continue to grow or what we're looking at in the future. So there's that constant it doesn't feel finished or in remission or it is just kind of there. And then we're wondering, "Yes, will his symptoms get worse?" And also kind of touching on that mental health piece, again. These kids are in their developmental time of their lives, they're identifying who they are as people and understanding who they are and how they relate to people. And it's such a sort of unusual thing because from the outside, when you first see Max, he looks like he's sort of... There's not anything really noticeable exactly. You'll start to notice his scar on the back of his neck or just the way he holds his body.

[\(02:34:03\)](#):

But it's not like... There's nothing that you can point to really clearly and be like, "Oh, he must have this." And there's nobody else that he has ever met that is in the same boat as he is. And I think that it really impacts who he becomes in the future because he's had to try to figure that out. He feels very kind of different and alone and isolated. And I know that other people have other conditions that make them feel alone and isolated, but there are often kind of support groups or different people that you can meet in your community that have this, and he hasn't met somebody that... I mean, so that mental health side of it impacting him socially, impacting his ability to start a family, his ability to do a lot of things that he wants to be able to do. Like we've talked about, those are some of my biggest fears and worries for him.

James Valentine, JD, MHS ([02:34:56](#)):

Yeah. And do you worry that... Is it just more of the nature of what is happening in life at older ages or is there that kind of where he's at today will just continue to impact him in the future as he kind of gets older and his living life? Or are any of those concerns or worries related to any specific worsening or further complications with the PLGG?

Shelley K. ([02:35:29](#)):

Yeah. Well, I mean, he definitely... I didn't even touch on the drooling and he has speech issues connected to where his tumor is as well. So sometimes he'll be talking and the drool will literally... There'll be a big blob that will just fall out while he's talking. And right now kids, they're starting to get into the bullying. So I can see that becoming a bigger issue as he moves forward. So if he has more involvement, people are having more trouble understanding him. If he has more treatment, if he has more side effects, his educational progress that he's making has been... He's missed so many hours of school from all his treatment. So even just that socially as a problem.

([02:36:15](#)):

But the more he has to do these kinds of things to try to address the symptoms and the treatments and the side effects and all of that, it's taking him out of so many things that he needs to be able to do to become what he wants to become in his life. So I guess specifically worrying about the vertigo, if it becomes problematic enough, will he be able to drive? Will he be able to have a job? Will he be able to be in a relationship? Will somebody want to take on a relationship with somebody who has a brain tumor? I mean, that might cause somebody to pause. So yeah, I have a lot of concerns, and it's that constant unknown, I guess, is not knowing where the tumor is going to go, what's going to happen in the future with that. It's hard.

James Valentine, JD, MHS ([02:37:10](#)):

I saw a whole lot of head-nodding when you said it's the constant unknown. So Christine, I'd like to have you chime in on this topic too of some of those things that maybe represent greatest worries for the future.

Christine L. ([02:37:25](#)):

A lot of what Shelley says resonates with me. My son right now is in transitional kindergarten, and it's a very nice environment. But as kids get older, differences become a bit more apparent. And what I've realized working with our school district is that they know what to do for peanut allergy, for diabetes, and maybe for epilepsy, anything beyond that it is very difficult to manage. It's very difficult to message and to have a consistent approach with. I struggle with how much information to share about my son. I don't want to share too much information. And so when he gets older, he's upset with me, but I also want to make sure that there's compassion and children understand there's a reason why he might be

doing some things differently. I struggle with making the wrong choice as a parent. With all my kids, we just want the best for them.

[\(02:38:36\)](#):

And in a situation like this, it's even more challenging. Mistakes are even higher because we have to make choices not only about things like this at school, with interventions at school and social things, but should we be more aggressive with surgery? Should we wait it out and hope for a better treatment to come so we can avoid that? This is all on me. I am the accountable person. It's not the doctor. It's not the surgeon. It's me because I'm the one who's pushing him through this medical system. I feel that weight. I feel that burden. I feel that responsibility. And I'm thankful to be able to speak with people like you who can uniquely share that perspective and understand. But it's making sure that we as a family make the choices that are going to set my son up for the most success. And that's really, really challenging.

James Valentine, JD, MHS [\(02:39:38\)](#):

I can't even begin to imagine how challenging. But I do want to follow up on one thing that you said just to better understand it. And you started off mostly describing this in the context of schooling, the lack of knowledge around this relative to other conditions like diabetes or epilepsy. And then even sharing maybe more broadly outside of a school setting to be able to create an environment that's more welcoming for him. But I guess one question is maybe more particular to school, is some of that education related to worries about what would happen if certain health events occurred or related to his safety, or is it more making it more accommodating to allow him to thrive or some combination of those things?

Christine L. [\(02:40:39\)](#):

It's a combination of the two. So I suppose this is quite unique to us, but there's been a lot of turnover in our school district, and so my son has discontinued his medication. We don't know what that means for him. We don't know how that will present with him physically. We need to know that the caregiver in the classroom is aware of that and understands what a concerning symptom is and what to do. And when there's a pool of substitutes circulating through the classroom, that's a major concern because there was no protocol at the school for how to pass on that information. That was kind of a big deal that we had to institute. So one is certainly physical and safety related. The other one of course, is social and emotional because we don't want to label him as different and then him not being held to an expectation. We think he's clever, we think he's smart, we want him be challenged. But at the same time, there has to be some acknowledgement of differences and limitations, and we haven't quite found what that balance should be.

James Valentine, JD, MHS [\(02:41:53\)](#):

Wow. Yeah. Well, thank you. Thank you for explaining that and sharing. Jennifer, I'd like to have you comment on this topic as well. As you're thinking about the future living with PLGG. Are there a top concern or worry or fear that you have?

Jennifer S. [\(02:42:16\)](#):

I mostly worry about any more loss of vision that would really change our whole day to day, running out of treatment options. We don't have a piece of his tumor because it was such a bad spot in vascular, so I worry that we'll have to make decision between no good options. We're on a MEK inhibitor now, and hopefully that keeps it stable. But so just the tumor growing and to the expectations that you don't

underestimate his abilities. In school, they say he can take more time on tests, but unless he needs that time, you don't want to underestimate them and then feed into any lack of confidence that they have themselves. I worry about if I don't make him wear his glasses, that he'll fall on his good eye just kind of day to day and then the tumor hovering over all of that generally.

James Valentine, JD, MHS ([02:43:21](#)):

Yeah. Well, thank you for sharing that, Jennifer. I do see that we've gotten a lot of written comments that have come in on this topic of worries for the future. So Courtney, what are we seeing?

Courtney Davies ([02:43:32](#)):

Yes, you're right. Quite a few comments. Leslie from Bridgewater, New Jersey. "My biggest fear as my daughter gets older is that she won't be able to live independently. And I also worry about her long-term health." Under the categories earlier, Chris from Lincoln writes in that, "Though death from these tumors is uncommon. It does happen and it should not be ignored as rare. Our son, David, diagnosed with pediatric low grade glioma in his optic chiasm when he was in fourth grade, had various forms of chemo over the years, experiencing many of these symptoms mentioned from the panel. When he was 17, David started experiencing severe hydrocephalus, excuse me, due to a blocked third ventricle. He ultimately died of this condition. We lost a really good kid with a lot of potential, just like all of these kids."

([02:44:35](#)):

And I do want to read one last one here. CJ, he writes in, "One of the most difficult things for us is knowing when to intervene again. He has had slow progressive growth of assist associated with his tumor, but there is a difference of opinion about when to intervene. I think our experience with the tumors feel like we're always lowering the bar for what we can expect of our child's life."

James Valentine, JD, MHS ([02:45:03](#)):

Yeah.

Courtney Davies ([02:45:03](#)):

... for what we can expect of our child's life.

James Valentine, JD, MHS ([02:45:03](#)):

Yeah. Wow.

PART 5 OF 10 ENDS [02:45:04]

Courtney Davies ([02:45:04](#)):

Yeah.

James Valentine, JD, MHS ([02:45:05](#)):

Well, I just want to thank everyone who has contributed in this morning discussion. Now, as we're out of time for this first topic. All of you on our Zoom panel, those of you that called in, and everyone who's been writing in. We've talked about such a wide range of different impacts as a result of PLGG. I don't think that our clinical overview quite captured it. It's impossible to, and that's why we had this

discussion. I know I've learned a tremendous amount from all of you, and not just what those things are, but just how significant the impacts really are on your loved one's lives and futures.

[\(02:45:51\)](#):

So, thank you all for this fantastic morning discussion. At this point, we're going to take about a 30-minute break. We'll be returning at 1:00 PM Eastern time for our afternoon discussion, which is going to pick up where we've left off, but with more of a focus on your experiences with treatments and ending with your perspectives on what you'd like to see from future treatments. So, we hope you'll join us back here at 1:00 PM Eastern. But for now, we'll take a short break.

[\(02:46:19\)](#):

Good afternoon and welcome back to the externally-led patient-focused drug development meeting on pediatric low grade glioma. I'm James Valentine, your meeting moderator, and I'm here in the studio with Courtney Davies from the Pediatric Brain Tumor Foundation, my cohost. And we're looking forward to continuing the discussion we had this morning where we learned so much about PLGG. But this afternoon, as we build on that with a focus on current and future treatments. But to help us get into this afternoon's session, it's my pleasure to turn it over to Courtney, who will introduce our afternoon speaker. Courtney.

Courtney Davies [\(03:14:19\)](#):

Yeah. Thank you, James. Well welcome everyone who is joining us for this second half of today's externally-led patient-focused drug development meeting on pediatric low-grade glioma. After this morning's session on symptoms and daily impact, our afternoon together will focus on current and future treatments. To get us started, I'd like to welcome Dr. Robert Lober, who is a neurosurgeon and director of the Living Biobank at Dayton's Children Hospital. Dr. Lober is a member of the Scientific Committee for the Children's Brain Tumor Network Collaborative, dedicated to the study and treatment of childhood brain tumors. Dr. Lober will provide a treatment overview of PLGG to serve as a scientific foundation for this afternoon's discussion. Dr. Lober, over to you.

Rob Lober, MD, PhD, FAANS [\(03:15:11\)](#):

Well, thank you for having me here today to talk about pediatric low-grade glioma, and thank you all for joining us today. Our goal is going to be to better equip families to share their experiences and perspectives, so that you can really be a part of the process of developing treatment strategies with the right outcomes. The discussion of these currently available treatments might be somewhat of a review, perhaps it's relevant to current decision making, perhaps it's in the past, but I hope it's helpful for me to discuss my understanding of the current state of things.

[\(03:15:49\)](#):

I want to share that I have no financial or professional conflicts of interest in regard to this, and I'm not discussing off-label treatments. My perspective is that of a pediatric neurosurgeon, and I don't have all the answers that you would get from your multidisciplinary care team. Remember, it takes a large team with a range of experiences to give you the best advice.

[\(03:16:10\)](#):

So, regardless of where you're at in your journey, whether it's diagnosis, recovery from surgery, consideration of treatment options, remission, or even perhaps bereavement, your perspective is extremely important. The low-grade glioma community has come to understand that quality of life should be a guidepost for conversations about future strategy. The cure is not enough. We need to focus

on functional outcomes. We're talking about maximizing quality of life or serving cognitive abilities, vision, fertility, psychosocial wellbeing. So, we can't stress enough how much your experiences matter.

[\(03:16:46\)](#):

So, I hope I can provide some tools or language that help you articulate them. Please scan my QR code, that leads to my email. I'll do my best to answer your questions or connect you with support. If you just have comments, I would share those with our organizers, Pediatric Brain Tumor Foundation, also Children's Brain Tumor Foundation, of which I'm a member.

[\(03:17:09\)](#):

So, if I could start with a patient who presented almost two decades ago and is now doing completely fine, his tumor is a good example of the conundrum that we face when it comes to this disease. We're looking at an MRI of the brain that shows the patient's nose on the left, back of the brain on the right. This is a boy who was scanned after a minor injury. We saw this abnormality in the back of the brain in an area called the cerebellum. He had no symptoms. Family didn't want anything done, so we just watched him. And a few years later, we began to see the lesion change. Development of new spots of contrast enhancement. Still had no symptoms, but the family didn't want anything done.

[\(03:17:47\)](#):

And a couple of years later, began to have headaches and symptoms, really couldn't be ignored and doing nothing was no longer a possibility. Notice this important concept that the family was calling the shots, and our role was to inform them of the options and then provide those options once the choice was made, so-

Rob Lober, MD, PhD, FAANS [\(03:18:03\)](#):

... To inform them of the options and then provide those options once the choice was made. So what are those options? In his case, the tumor had grown significantly, was taking off, compressing critical structures around it, placing him at risk for loss of function. So the standard of care in this setting is to remove the mass through surgery. It relieves the obstruction, potentially cures the disease and allows you to obtain a diagnosis by examination of the tissue and the molecular features. So once the tumor's gone, we went back to watching him and there was never an indication for further treatment.

[\(03:18:32\)](#):

But the next question, and part of why we're here today is what do you do if it grows back, especially in a way that surgery couldn't reach it? So this is when we really need to understand the other therapy options. With everything that's available, radiation can be effective. It's less and less an appropriate strategy because of the side effects. Chemotherapy, often compounds like carboplatin and vincristine or a similar regimen would be advocated for use prior to that, especially in the younger patients. But now we're at this new stage of technology in which we have a better understanding of the underlying features of the tumor. And based on this, we're creating strategies to address the molecular problem.

[\(03:19:14\)](#):

And in the last decade or so, I've been able to watch the knowledge around the biology of low-grade gliomas really increased exponentially. We have a much better understanding the mutations involved, there's this concept called senescence in which the tumors can actually die of old age before the patient. There's molecular profiling from our biopsy specimen going much farther than just looking at the tissue under a microscope like we did when I first started. And then there's attempts to generate preclinical models.

[\(03:19:44\)](#):

The MAP kinase pathway, you'll hear about, it's the machinery that's gone bad in low-grade gliomas. It looks a little bit like alphabet soup here, but what it's describing is a series of cellular reactions between molecules that causes a tumor cell to divide into more tumor cells starting at the top, RTK, short for receptor tyrosine kinase, that's on the outer surface of cells. It stimulates this chain of proteins, and you don't need to remember the names, but you might want to remember Raf, you'll often hear of tumors having what's called a BRAF mutation. And you might also want to remember MEK because when we start talking about drugs that block this pathway, you'll hear the term MEK inhibitor, which means it's blocking cell division at this stage, even if it's downstream of that overactive Raf mutation.

[\(03:20:32\):](#)

So now that we're in this era of MAP kinase, what do we do differently? And the short answer is we often don't do anything differently despite what we've learned and that's because some tumors can just be observed, that's especially the case for the incidental optic pathway gliomas associated with NF1, it can be the case at least temporarily for tumors like I showed you that are completely asymptomatic, very slow growth. And when we have no concerning features like that, I've followed them for months, sometimes years in some cases.

[\(03:21:04\):](#)

But when something absolutely must be done, most low-grade gliomas are resectable. And if not, the first line standard of care is the same chemotherapy we've been using since the paper came out in 1997, which is carboplatin and vincristine or a similar regimen. If a family decides to have the tumor resected, I can't get it all out, we're dealing with some kind of residual amount, we can watch that for years sometimes without seeing any growth. So we don't necessarily go straight to a treatment. We know that these mutations generate a high growth rate can lead to early senescence in the tumor tissue, meaning that the tumor actually dies of old age by the time the child is in their late teens or graduating high school, so that can happen.

[\(03:21:48\):](#)

So the question is, when do we turn to strategies that target this MAP kinase pathway? And that's essentially right now when we failed these other regimens that we've been doing. I just want to go over this kind of quickly. We use drugs attacking the MAP kinase pathway almost always in the context of a clinical trial with a few exceptions that are out there now. And so email me through the QR code, I'll get these slides to you or you can always see the most up-to-date list on [clinicaltrials.gov](http://clinicaltrials.gov), you can check that out. There are reasons though why we do this in the setting of clinical trials.

[\(03:22:22\):](#)

There was a phase two study in which Sorafenib listed here worked to disrupt the pathway in the laboratory, but when we used it in patients, it seemed to cause most of the tumors to accelerate growth. And so what that means is you can get very far down this pipeline through cell lines, mouse models, phase one studies to evaluate safety, and then you hit a wall. And so you find that a rationally designed therapy doesn't always yield a rational response because there's always something that we don't know.

[\(03:22:48\):](#)

Another caveat to consider is that we don't know the long-term effects of using these drugs in children. And that's something you have to discuss if you're trying to make a decision about treatment options or if you're on the other side of the coin trying to design the targeted therapy. In adults, BRAF inhibitor use is associated with emergence of skin tumors, leukemia, colorectal cancer. And so the question is, do we have a long enough experience to truly make an informed decision about this? That doesn't mean don't use it, it just means be aware.



[\(03:23:21\)](#):

And lastly, when trying to see what is best for your child, you have to remember that many of these agents require daily dosing. You have to fast before and after, which can be challenging for your young kids. Also, it's not clear what's the ideal duration of therapy? What happens when you take the drug off? Can you treat again with the same drug later if the tumor progresses after therapy? All of these are things that we want the answer to.

[\(03:23:45\)](#):

And this is moving fast so I can get these slides to you, but these are the drugs in the so-called pipeline right now. And you can see on the left I have the phase listed, including there's multiple phases going on including phase three that are comparing targeted therapies to conventional chemotherapy head-to-head. These are going to be very important trials. There's also trials here that are trying to improve response rates through combination therapies and these are likely going to be very beneficial. Take a look at the Children's Brain Tumor Network website, cbtn.org, if you want to learn more about preclinical models and challenges to developing new treatments. There are more than 20 projects right now involving low grade glioma and this can give you a real sense of what's going on at the basic science level.

[\(03:24:38\)](#):

So we could spend hours on this topic alone, but this is a summary slide of challenges that we encounter when developing new treatments. Preclinical, the question is how do we create a model using cell culture in a dish or mice and make it behave like a tumor when it's growing in a child? Design, we have to take into account that these tumors are very rare, they're heterogeneous, they're not always comparable, and that makes a difference. Trial management, we don't always have perfect ways to monitor the disease or responses to our therapies. And then outcomes, and this is where we really need you. We're dedicated to finding the right treatments for this disease, especially with quality of life as that guidepost for future studies. But the only way we can be successful is you sharing your honest perspective.

[\(03:25:26\)](#):

So I hope this information assists you in doing that. Thank you so much for what you're doing and please do reach out to me through the QR code or by contacting program organizers, I usually get back to you in a couple of days. I'm happy to help you in any way I can. I'm looking forward to hearing the discussions today and for now, I'll send it back to the studio.

PART 6 OF 10 ENDS [03:18:04]

James Valentine, JD, MHS [\(03:25:56\)](#):

Thank you so much, Dr. Lober, for helping set the stage for this afternoon by giving that treatment landscape and also setting the stage for the value of the patient and caregiver voice in driving future clinical trials for pLGG. So at this point we're going to move into our second session for the day where we're going to be asking all of you, our people living with pLGG and their family members, parents and other caregivers to be sharing. And as you'll see on the screen, these are some of the topics that we hope to get your experiences and perspectives on.

[\(03:26:35\)](#):

So we're going to ask you to share with us your experiences with different treatment approaches. And when we talk about treatment approaches, yes we do of course mean medications including direct and targeted treatments as well as general tumor treatments, as well as medical procedures and surgeries.

But we are not limiting it to just those types of treatments, we also mean the types of things that you might be doing to trying to help with certain symptoms like the symptoms that we heard so much about today, whether that's things like physical and occupational therapy, speech therapy, more holistic approaches or even lifestyle modifications. Anything you or your loved one are doing to try to make living life with pLGG a little bit easier counts in this broad discussion of treatments.

[\(03:27:27\)](#):

And so as you think about that wide range of things, we want to know, what are you currently doing to manage your or your loved one's pLGG symptoms? We want to hear your assessment of those things. How well do those treatments treat the most significant symptoms and health effects of pLGG? And whether or not those treatments are helping? We want to know what are some of the most significant downsides to your or your loved one's current treatments and how do those downsides affect daily life? So downsides could be things like side effects, the burden of keeping up with the treatment regimen, the way a treatment is administered, really anything that you see as a trade-off or a consequence of a treatment approach.

[\(03:28:10\)](#):

Once we've explored these currently available treatments, we're going to shift gears at the end of the discussion and I'm going to ask you, short of a complete cure for pLGG, what specific things would you be looking for in an ideal future treatment? Or another way to think about this is what factors would be important to you in deciding whether to participate in a new research trial, or if a new product were to become available, what would be the key things that would inform your decision of whether or not to try this new treatment?

[\(03:28:41\)](#):

So to help us get started in exploring these various topics, we have another panel of your peers who will be sharing some of their perspectives. We have Maria, Paola, Cathy, Chetasi and Evan who are going to be sharing some of their experiences. And so Maria, why don't you get us started?

Maria T. [\(03:29:02\)](#):

Hi, my name is Maria and I am mom to my fourteen-year-old son Gavin. We were unaware that Gavin had a tumor until he experienced his first big seizure in April of 2020, after which he was rushed to the hospital and we received the devastating diagnosis of brain tumor. Looking back, Gavin suffered from what we thought was just motion sickness, but he did not have symptoms beyond that. He was an honor student who was thriving, playing with his friends, playing soccer.

[\(03:29:28\)](#):

Shortly after Gavin was diagnosed, he had surgery to remove some tumor because removing more would put him at risk for impact on his functioning. Then he went on to a year of traditional chemo, which caused him to be nauseated, have vomiting and spend days in bed. He was taken off chemo, but the tumor grew, as expected, in this tumor type, FGFR1 DNET. He was placed on a targeted inhibitor for over a year. Despite significant side effects of extreme fatigue, gastrointestinal issues, and deep striations in his back that will never go away, the tumor kept growing. At the same time, Gavin suffered from seizures on an ongoing basis, which also made him tired and caused him to miss many days of school.

[\(03:30:14\)](#):

He recently underwent three brain surgeries at an attempt to reduce the seizures and debulk the tumor. Complete removal of the tumor is not a possibility for Gavin as it has infiltrated different parts of his

brain and is wrapped around a primary artery and linked blood vessels that if disrupted would lead to a stroke at the very least. Before surgery, Gavin suffered from seizures, extreme fatigue, gastrointestinal issues from the chemo and/or the tumor. He would be in bed for days or miss a significant amount of school due to seizure activity that left him extremely tired. Gavin gets scans every three months to detect tumor growth. Since he just went through surgery, he's not on chemo yet, but is likely he will have to go on something again. Anything given to him is not indicated for his mutation type, so it's a shot in the dark.

[\(03:31:08\)](#):

Gavin is also on Keppra, a seizure medicine, and his dosage has increased and he's now up to six pills a day to keep the seizures at bay. Additionally, he now takes a pill to slow down his urine flow as it was affected by surgery. Recently, he's most affected by loss of short-term memory and lack of sense of direction. It has affected his schoolwork. A once honor student in advanced classes is now receiving 40s on exams. He's also insecure about going places by himself for fear of not being able to get back. Gavin gets scans every three months and now we take trips to Memphis for his health management, so he misses time from school and friends as we travel from New York. Gavin was in the hospital for 24 days with his most recent surgeries. So besides the effects of surgery, he missed the whole first quarter of his high school year.

[\(03:32:04\)](#):

I'm afraid with lack of a cure and a growing tumor, more surgical intervention will be required or radiation that will result in further brain damage. I have watched this disease slowly steal away my son's life bit by bit over the course of time. I'm not sure if he will go to college, be married, have children, what he'll be able to offer to another human being if he's not healthy. I'm frustrated that Gavin has been affected by this disease, I'm frustrated that many doctors and companies do not treat it as seriously because this is not considered malignant tumor. But it does not matter because in the end, the damage is the same, it just happens over a longer amount of time, loss of function and potentially death.

[\(03:32:53\)](#):

There are others who have lost their mobility eyesight. So with as much as Gavin has lost, we are always grateful that it could be worse. It is a gift of perspective, but a curse because no one should have to live this way. There is no medicine for Gavin's mutation type of FGFR1 as it is even a more rare mutation type for this already rare disease. And I'm not sure if a cure will be found, and research is expensive. Who will take this on? I would never wish this on anyone, but I often say it would take a celebrity's child being afflicted by this for the right level of investment to happen. I would give up all my money to have a cure. We need a targeted inhibitor that focuses on the FGR mutation. Many have benefited from clinical trials that target the BRAF mutation, but there is nothing that has been truly proven to help with the FGFR1 mutation.

[\(03:33:55\)](#):

My hope for Gavin is that he'll be able to live a life where he's not constantly managing a brain tumor. It has been one thing after the next for the last four years. I would love to see him be as healthy as possible, enjoy his friends, find a partner, have a career, all the things that we wish for our children and all the things that he was on track to achieve before 2020. Thank you.

Paola A. [\(03:34:21\)](#):

Hi, my name is Paola and I live in Zurich, Switzerland. My daughter Monica was first diagnosed with low grade glioma in 2012. She was only nine months old and we found out later a diagnosis before the age of one year is not a good prognosis factor. She had a slightly protruding eye, but nothing else, which was

how we first noticed something wasn't right. She was a very happy child, funny, full of beans. Soon after diagnosis, Monica started 18 months of carboplatin and vincristine. The side effects were very harsh on her little body and she suffered from many fevers that required hospitalization. She also needed several blood transfusions. Monica's immune system was completely diminished and the Hickman Line took a great deal of maintenance care.

[\(03:35:10\)](#):

She couldn't talk yet and we found out she was completely blind in her left eye and that the main goal of the treatment was to preserve the right right eye as the tumor was exactly in the chiasm where the two optic nerves cross. She also wore glasses to protect the good eye from possible external threats. Also, a hearing test was performed as one of carboplatin's side effect is the possibility to disrupt the hearing. We were told that stability is the best we can hope for as a surgery is not possible. It's like trying to separate coffee and milk from a cappuccino, this metaphor used by the oncologist will stay with me forever.

[\(03:35:50\)](#):

After the diagnosis, we lost some contact with family and friends. Some people didn't know what to say to us and slowly disappeared from our lives. Eventually, Monica's central line was removed by surgery, but she contracted an infection and went into septic shock. New treatments required a port that was placed into her chest that already had many scars. After a year and a half, she started with vinblastine, but after three months, the tumor continued to grow, so we needed to change therapy. Avastin and irinotecan were offered to her with the possibility to stay on this plan for two years or longer. After a year, Avastin started to give some side effects on the kidneys. We had to skip some treatment and then to post completely for a few months. We eventually did the biopsy to confirm Monica's tumor type.

[\(03:36:40\)](#):

The biopsy tissue was initially test for the BRAF V600D mutation, which was negative and the tumor was growing, so there was not much time to think about rolling her into the experimental therapy with inhibitors. Monica was to start TPCV, a cocktail of four old heavy chemotherapy drugs that come with so many side effects from destroying the immune system to secondary cancers. TPCV gave some stability for over two years, but then she had to restart again and this time the MEK inhibitor trametinib was a possibility of the new found Raf inhibitor from day 101.

[\(03:37:20\)](#):

Due to her weight, she should have taken only one and a half tablets to get the right dose of trametinib, but the tablets couldn't be cut, so we had to ask the company to allow us to use a liquid formulation. This came again with syringes and gloves, bottles and many things to carry so the idea of an easy tablet vanished fast. It was again difficult to travel and to leave Monica alone even for a sleepover. Additionally, trametinib must be taken one hour after a meal and she cannot eat for another hour after taking it. After only one month, the side effects started to show, ingrown nails, mouth ulcers, fever, and the pneumonia which required hospitalization. The mouth ulcers made it difficult for her to eat and she started to lose weight and become more fragile. Additionally, she started to lose her hair, fever once a month and again after a few months, another pneumonia. More hospital appointments were needed to check what was going on. Something was wrong as other kids didn't react so badly to this medication.

[\(03:38:27\)](#):

The inhibitor that we were waiting for so long was not so easy on her, so the doctor decided to decrease the dose. Due to the lower dose, the side effects decreased after 18 months. As the mouth ulcer largely disappeared, Monica could eat properly and slowly gained weight and was able to switch to a tablet,

which makes everything easier. For example, when you travel by plane, we no longer need a letter from the hospital to set that the liquid we have it's our child's medication.

[\(03:38:57\)](#):

Of course, an ideal treatment will be a targeted approach that gives stability with more manageable side effects. Would immunotherapy become a possibility for Monica in the future? Two years with trametinib for Monica will finish in March 2024, and then there is a big question mark of how long will she have stability. Monica is now 12 years old and we're worried about what the future holds for our daughter.

Cynthia H. [\(03:39:25\)](#):

My name is Cathy and my daughter's name is Erin. My daughter, her life has been nothing short of a tragedy. I know that that sounds awful to say about your own child, but it is the truth and the facts are the facts. In 2002, my daughter was a healthy and happy four-year-old child. She had her whole life in front of her until she was diagnosed with what some would refer to as a benign brain tumor. Benign, that is a grossly inaccurate word to describe a tumor growing inside the brain of a child.

[\(03:40:11\)](#):

For about a year before her diagnosis, I started to notice small changes in my daughter that I chalked up to normal toddler behaviors. Maybe she was just over tired, maybe she was coming down with a cold, maybe she was feeling a little bit jealous of her new baby sister, she just needed more attention. I don't know. At the time, what I didn't realize was that these symptoms that she was having were the symptoms of hydrocephalus. This is caused by a growing tumor in her cerebellum that was cutting off the spinal fluid from circulating and increasing the size of her ventricles, causing pressure in her brain. An MRI was ordered for her at her four-year-old appointment, but it was denied by the insurance company. We were sent to a neurologist, had to see a specialist before that MRI would be approved, and when we finally got in to see the neurologist and then finally got the MRI approved, it had been three months since the MRI had been ordered, three more months of growth of a tumor in her brain. By the time we got to the hospital for the MRI, we were told that there was an emergency and she would require surgery within 24 to 48 hours to save her life. That was the easy part of our story, so consider that for a second.

[\(03:41:51\)](#):

We were given no time to think, no time to research, no time to plan. We were not lucky enough to live in a city that had a pediatric brain tumor center of excellence. We were unlucky and we were rushed into allowing inexperienced surgeons to open our daughter's brain and practice on her. My daughter entered the surgical suite a happy neurotypical four-year-old and came out a completely different person. This was not the child I handed to them, this was no longer my child. Benign, benign tumor, I would say not.

[\(03:42:33\)](#):

After my daughter's disastrous surgery to remove the tumor from her brain, she underwent a year of high-dose chemotherapy to try to address the metastasized lesions that were spread to the lining of her brain and down her spine. She was unresponsive for months, for months not four months, more like 12 months. She suffered with a condition known as Posterior Fossa Syndrome caused by the surgery. She was mute, unable to swallow her own secretions, unable to voluntarily move her limbs. She was incontinent. She was unable to hold her own head up, she was unable to move her eyes, her fingers, or any other part of her body. She was fed by a tube for over eight months. Over time and with so much therapy that it would make your head spin, she started to regain some of the skills she lost.

[\(03:43:25\)](#):

My daughter is 25 years old now, she survived her cancer. She's still unable to walk unassisted. She has processing issues. She has ataxia. She has an irregular cerebellar speech pattern. She has issues with executive function. She has many traits of a person with autism. She has been on chemotherapy from the time she was diagnosed at four years old until her last treatment after she was 15 years old. She lost her hair several times throughout her adolescence. She suffered with debilitating daily seizures from the time she was nine years old until she had surgery at 23 years old to resolve them. That surgery was her second surgery for seizures as the first one that she had the day following her 16th birthday was unsuccessful, and not the way most girls get to celebrate their 16th birthday.

[\(03:44:27\)](#):

She will never drive. She will never be able to have a family of her own. She'll never live independently. She's not accepted by her peers and she cannot keep up with them. She went from a child that was ahead of the curve at four years old to a person that will never live a normal or independent life due to this benign low-grade tumor.

[\(03:44:49\)](#):

When my daughter required follow-up therapy after her surgery at four years old, we were given four different opinions by four different hospitals and had to choose ourselves which one to trust. The hospital where she received her surgery recommended that she receive full brain and spine radiation at four years old. I don't know if you guys know what radiation does to your brain, but it's not good at four years old. Boston Children's Hospital recommended chemotherapy with the gold standard drugs at the time of carboplatin and vincristine. The Brain Tumor Center at Duke recommended high-dose chemotherapy with cyclophosphamide. St. Jude recommended radiation followed by chemotherapy. What do you choose? This is the position we as parents are put in while we can barely wrap our heads around the idea that our child has brain cancer, nevermind having to choose how it should be treated.

[\(03:45:47\)](#):

These tumors are anything but benign to the family and the child that was not lucky enough to be treated by the best doctors, the best surgeons, the best hospitals available. These children with these tumors can and often do live a long lifespan, but at what price? The side effects of the treatments they receive, particularly surgery and radiation, impact their quality of life to a degree that is unfathomable. I'm happy that my daughter, or I guess I should say the daughter I have now, is alive, but I'm sad every day for the child that was taken from me and the life that was taken from her. Thank you.

Chetasi T. [\(03:46:35\)](#):

Good afternoon, I'm Chetasi, mom to our little three-year-old daughter Ashwi. We are currently in Memphis receiving care for her diagnosis of low-grade optic nerve glioma, specifically pilocytic astrocytoma located on the optic chiasm which spread throughout the spine. Ashwi was diagnosed in June 2021 when she was approximately nine months old. Before then, she started developing failure to thrive and she was falling off the growth curve and developed a syndrome called diencephalic syndrome. Further testing determined that the tumor was not resectable and treatment would include combination of chemotherapy, carboplatin, vincristine, and temozolomide not on clinical trial. Since she was nine months old, she was not eligible for any clinical trials at the time. We were told the chemotherapy regimen of carboplatin, vincristine and temozolomide would be planned for a total of 18 months or 18 cycles and she had a central line placed for chemotherapy administration.

[\(03:47:36\)](#):

This was still during the peak of COVID, only one parent was allowed with her while she received chemotherapy or for any visits in the hospital. We understood the reason why very well, but it was still very difficult when she was admitted to the hospital, especially during the first cycle. Simultaneously due to her failure to thrive, Ashwi had NG tube placement for nutrition which was later converted to a G tube after approximately six months or so, which she maintains today for nutrition as well. During her treatment course at nine months of age with a central line in place and NG tube in place, which was connected continuously to enteral feeding, she required 24-hour care from us. Due to the central line with her immunosuppressed state from the chemotherapy, Ashwi was at high risk for infections which we recognized. We were flushing her central line every day and cleaned her ports as trained, as directed.

[\(03:48:36\)](#):

Despite the precautions taken, she developed sepsis on two separate occasions requiring prolonged inpatient admission and extended home IV antibiotic course. Ultimately due to recurrent sepsis, her central line was replaced with a port on the left side. Ashwi's treatment scheduled required frequent visits to the hospital including for lab draws for cytopenias, physician visit at least once a week. Additionally, most weeks also require two to three visits a week due to need for specialty consultations, physical therapy, occupational therapy, speech therapy, or for actual treatment administration and this is not including the unplanned visits for replacement of NG tube if she pulled it out, evaluation of toxicities, management of toxicities, etc. Some treatments are intravenous with infusion requiring prolonged stay at the infusion center so our days averaged anywhere from six to 10 hours.

[\(03:49:36\)](#):

In addition to sepsis, Ashwi experienced other symptoms that included nausea, vomiting, diarrhea, tooth abscess requiring tooth extraction, rash, fatigue, etc. Although these symptoms or procedures seem minor, the decisions took a significant toll on us at each step. The nausea and vomiting were constant despite titrating the anti-nausea medications and at times this prevented us from administering her enteral feeds for few days around chemotherapy administration. She woke up with projectile vomiting unfortunately on many occasions.

[\(03:50:12\)](#):

Ultimately, she completed chemotherapy in February of 2023 with her disease status being stable disease as best response, and she has been receiving surveillance imaging every three months since then. This month in February 2024, it will be one year being off of therapy. Overall, the treatment has led to improvement in the diencephalic syndrome where she's now 50th percentile for weight compared to failure to thrive when we started this journey. Her oral intake has improved significantly from nothing to half a sandwich for a meal and we believe it'll improve continuously over time. Due to her NG tube dependency, unfortunately, we have not been able to place her in a regular daycare, however, we are grateful that she has been accepted in the public school systems special needs program where she's developing her social skills. She has experienced the...

Chetasi T. [\(03:51:03\)](#):

... where she's developing her social skills. She has experienced speech delay. However, she's receiving speech therapy and progressing fairly well at this time. What we are unable to determine still is the full impact of this tumor that she has on her vision due to difficulty of being able to perform this comprehensive testing, vision testing, given her age.

[\(03:51:22\)](#):

There are no approved drugs or regimens for these tumors unless there is a targeted mutation identified. The chemotherapy regimens are archaic and are often chosen due to lack of optionality.

[\(03:51:36\)](#):

We wish there were regimens that could provide overall lower burden on Ashwi as well as us as her caregivers. We wish there were new treatments that led to improved efficacy that led to potentially more shrinkage or disappearance of these tumors. We wish Ashwi had treatments with fewer toxicity so that she would be able to maintain a typical day at school.

[\(03:52:03\)](#):

Our hope for Ashwi's future is that she lives a very happy life, full of care, compassion, and is surrounded by love at all times. Thank you for listening.

PART 7 OF 10 ENDS [03:51:04]

Evan H. [\(03:52:17\)](#):

Hi, my name is Evan and I'm here to share the story of my son Nathan's journey with pediatric low-grade glioma. It started when Nathan was four years old and he broke his arm falling off the monkey bars. Nathan had always been a healthy boy, active and joyful. He walked at eight months and spread joy wherever he went. But after his arm healed, we noticed that he still had weakness in his right side. This did not seem like a typical outcome from a broken arm, so we took him back to the doctor.

[\(03:52:47\)](#):

The doctor ordered an MRI to evaluate what was going on. This MRI revealed Nathan had a brain tumor. The ER doctor told us it looked deep, dark, and looked aggressive, words no parent should hear. Soon after Nathan underwent surgery to biopsy the tumor and remove as much as possible. Because of the location of the tumor, the surgeon had concerns about removing more, and in fact told us, "I can remove it all, but your son won't wake up." The biopsy determined that Nathan had a low-grade glioma with the most prevalent BRAF mutation. Because the rest of the tumor was still there and inoperable, he needed to start standard chemotherapy.

[\(03:53:33\)](#):

As a scientist who works in drug development, I was devastated to learn of the limited treatment options available. Nathan faced the same chemotherapy treatments that had been used for decades. Was this really the best we could do? No new drugs had been approved for pediatric brain cancer? Really? Here he was, only four years old, not even in kindergarten yet, getting an IV port implanted so he could receive weekly chemotherapy infusions and then came the side effects. No child should experience this: extreme fatigue, constant nausea ruining his appetite, vomiting away whatever calories we could get him, rushing to the hospital at every sign of a fever, which could become life-threatening.

[\(03:54:20\)](#):

In the end, Nathan entered kindergarten at six years old, having completed several kinds of chemotherapy. He did physical therapy and occupational therapy to relearn how to use his right arm and relearn how to walk and how to compensate for his visual field loss. Eventually he learned how to walk again and became an active kid playing hockey, skiing, bicycling, baseball and through it all, Nathan never complained. He never missed a hockey practice, never let his tumor slow him down.

[\(03:54:53\)](#):

By first grade, he was the mayor of the elementary school, everyone's favorite kid, but we weren't done yet. His tumor was still there, and for 75% of kids like Nathan, they will need further treatments down



the road. The odds were not in our favor. When he was 10 years old, he started to show signs that his tumor was growing again. I remember watching Nathan play hockey one day and noticed he was having trouble holding a stick up. I knew something was wrong. I was the only one in the arena who knew, but I knew and it was painful to watch him never give up but struggle mightily on the ice that day. We knew what was coming.

[\(03:55:33\)](#):

We went to the doctor and an MRI confirmed the tumor was growing again. This time there were new treatment options available to us if we were willing to put Nathan on the clinical trial. Through the intervening years, through philanthropic funding, Nathan's doctors at the Dana-Farber Cancer Institute had conducted research into new drugs that might be good candidates for kids like him. Groundbreaking research funded by parents like me, and through the work of Pediatric Brain Tumor Foundation, we were able to discover a drug called TAK-580 that had shown promise in the lab but was untested in children. We reviewed the potential options available with this doctor, including clinical trials and research protocols. In the end, we chose to enter the clinical trial for TAK-580, which is now known as Tovorafenib or DAY101.

[\(03:56:36\)](#):

At the time, this new medication hadn't been tested on children with low-grade gliomas. There was pre-clinical data and there was also data about its use in treating adults with melanoma where it had not worked very well. But while little was known about how a child would respond to it and the potential side effects, this drug seemed to be our best option. Nathan was too young to weigh in on the decision, so my wife and I decided. We talked a lot about it and eventually we decided yes, that this clinical trial for TAK-580 was the right option for him. He ultimately became the first child in the world to enter the trial and to receive TAK-580.

[\(03:57:19\)](#):

Since Nathan was the first to receive the drug, his first dose had to be administered in the outpatient clinic and was carefully monitored. No one knew what side effects he might observe. He did develop some side effects, but far fewer than we had with IV chemotherapy. And overall it was a huge benefit that the drug was an oral medication, meaning we didn't have to go in for weekly infusions. Within two months, we could tell the drug was working. Nathan was improving in hockey, he could ski again. He had restored his normal function. He could throw a ball and ride his bike down the street. Follow-up scans showed significant responses. Tovorafenib shrank his tumor. That was the first time in his entire journey we had heard the words, "His tumor's shrinking."

[\(03:58:08\)](#):

That was 2018. Nathan was on the study for two years and had great results. It was a game changer, and I still have a hard time believing it's real. Nathan is now a freshman in high school and thriving. My hopes for his future have never been brighter. I hope that he lives a full life, as full as possible. I imagine us going to Bruins and Red Sox games for years to come. I imagine his future is bright, but he still has the tumor and he always will. We live with the constant threat of it, never knowing what the future brings, but we're hopeful that the next time he needs help, that the research will have kept up and will be there ready for us. Everything else is a cherry on top.

James Valentine, JD, MHS [\(03:59:01\)](#):

Thank you so much, Evan, for sharing Nathan's treatment journey and to all of our panelists here this afternoon who have shared the journeys that they've had in navigating early and ongoing treatment approaches. And to begin the discussion about what you would like to see from future treatments. Now

we have the opportunity to bring all of you in again as we did this morning, all of the people in the audience living with PLGG and their caregivers, to hear your experiences. So if you have a treatment experience that you would like to share, you can do so by calling in. That phone number is +1 703-844-3231. Again, you can call now at any point during this afternoon session at +1 703-844-3231.

[\(03:59:52\)](#):

But to get us thinking a little bit more about this topic, we're start off with some polling questions. And so this is for our patients and caregivers only. If you can go to that webpage, [www.PollEV.com/pLGG](http://www.PollEV.com/pLGG). Again, you can go to go there now, [PollEV.com/pLGG](http://PollEV.com/pLGG). Just keep this webpage open throughout the afternoon session as we go to new questions, they'll automatically appear there. You can click off the responses. There will be no need to hit submit. As soon as you click a response, it will count that response.

[\(04:00:33\)](#):

And so our first question here is what medications or medical treatments have you or your loved one either currently or previously used to treat symptoms associated with pLGG? You can select all that apply. The options are A., surgery, B., radiation therapy, C., chemotherapy, D., seizure meds, E., targeted therapies, F., pain medication, G., antidepressants or antianxiety medications, H., other medications or supplements that aren't listed here, or I., if you have not used or your loved one has not used medications or medical treatments.

[\(04:01:13\)](#):

And so here, just as a reminder, this is a question where our audience could select more than one option. So the percentages you're seeing on the right side are not a percentage of people who have selected any one option, but a percentage of total responses. So for these types of questions, you can just look at the yellow bars as a sort of relative ranking amongst our audience.

[\(04:01:38\)](#):

So we'll give everyone a few moments here to log what different medications or medical treatments have you or your loved one either used previously or currently to treat pLGG and its symptoms.

[\(04:01:52\)](#):

As it stands, it looks like remaining at the number one is surgery as the top most experienced medical treatment, followed by other medications or supplements, chemotherapy and targeted therapies. After that, we see a good amount of experience with seizure medications and pain medications and antidepressants and antianxiety medications after that. No one is reporting experience with radiation therapy and no one is reporting that they've not used medications or medical treatments for their or their loved one's pLGG.

[\(04:02:27\)](#):

So if we move to our next question. So as I mentioned when we were going through the discussion questions, we don't want to focus only on medications and medical treatments, but the broader range of therapy and management strategies. And so here we're asking about those types of things. So besides the medications and treatments that have been used currently or previously, what has your loved one used to help manage the symptoms of pLGG? And you can select all that apply. The options are A., physical or occupational therapy, B., speech language therapy, C., assistive devices, D., acupuncture, E., aqua therapy, F., CBD, G., counseling or psychotherapy, H., some other treatment, kind of broader treatment approach or management strategy to help manage the symptoms of pLGG that's not listed anywhere else or I., if you are not doing anything to help manage symptoms. So again, we'll give everyone a chance to log their responses here in this category of what we're kind of broadly calling our

treatment approaches. We're seeing that physical and occupational therapy is the most reported treatment approach, followed by speech language therapy and counseling and psychotherapy. After that, again, we're seeing a lot of other things in addition to CBD and assistive devices. The only category with no one reporting is that they're not doing anything to help manage symptoms. So that's, I think, a really standout thing is across both of these questions, no one is reporting that they're not using either medications or medical treatments or some of these broader strategies. Everyone is doing something to try to help manage living with pLGG, and we want to hear about those experiences.

[\(04:04:24\):](#)

One more question for now, at least. In this next polling question, we want to know how well does your current treatment regimen treat the most significant symptoms of pLGG? So you told us this morning about what are some of those things that are most impacting you and your loved ones. So here we want your assessment, thinking about all of the things that we showed on the last two polling questions, how well do they manage the symptoms of pLGG? The options are, A., not at all, B., very little, C., somewhat, D., to a great extent., or E., this is not applicable because they're not using anything.

[\(04:05:06\):](#)

So this is really the why question. So as you're picking these, this is a little subjective, what do you consider, for a little over 50% of you saying that your treatment regimen helps somewhat, what does that mean to you? How did you kind of assess that overall, how this is helping somewhat? What experiences or examples came to your mind as you were making that selection? Those are the things that we really want to hear as part of this discussion.

[\(04:05:39\):](#)

So it's holding strong. We're seeing around 60% of the audience saying somewhat. After that, we're seeing about 20% of the audience reporting that current treatments help very little, about 10% saying to a great extent, and 5% saying not at all. So we really want to hear about those range of experiences. These may be referring to different treatments that different people have experienced because we know there's a wide range of different things that are being tried. So we do want to hear about the wide range, and we are getting on this question about 5% of people saying that this is not applicable because they're not using anything.

[\(04:06:19\):](#)

So I want to thank everyone for participating in those polling questions. It's always valuable to kind of see broadly what our audience's experiences are and perspectives, but now we're going to dive into that discussion. And so if you'd like to share maybe a little bit of what you picked and why, you can call in. Again, that phone number is +1 703-844-3231. Again, +1 703-844-3231. You can also write in using the comment box under the player on the web page you're following along today, and we'll be reading out some of those comments throughout the program as well.

[\(04:06:54\):](#)

But to get us started in this discussion, I'd like to welcome our afternoon Zoom panel. Some of your peers will be sharing their experiences with us throughout this session. Maybe for the beginning of this conversation, we'd like to focus on some of the things that maybe of all of those different treatment options have been the most helpful in some way, even if it's a small way or a large way.

[\(04:07:17\):](#)

And so Caitlin R., maybe we can have you start us in this discussion. As you were looking at all of those options, where do you all have experience and is there something that stands out as most helpful?

Caitlin R. (04:07:32):

Sure. Thank you, James. My name's Caitlin and I'm from Boston, Massachusetts area. And my son has a pilocytic astrocytoma in his cerebellum. We have been through four separate treatments. We're currently holding because there's not another one available for him. So we're in the watchful waiting stage. But significantly throughout, what's been the most helpful is simply the ability to trial new things, be it the medications, additional services that have been provided via outside funding or internal fundraising.

(04:08:08):

We've been fortunate enough to be at MGH, which does their own marathons. And so the therapies that have been helpful include the medications, but also those aspects like art therapy or the engaged activities for kids all going through treatment at the same time that allow them to continue being social children and to not feel segregated from their peers because it is so easy. My son will run around and he's accepted the fact that he's Iron Man with his port because he was lucky enough... sounds funny, but lucky enough to not know life differently. He's had his port since he was 1-year-old. So for him, I'm very happy that he knows life no differently. But as he ages, we have seen that importance of going through treatment with other children and having the opportunity to be in those additive therapies with kids that are going through the same thing.

James Valentine, JD, MHS (04:09:00):

Yeah, no, that's really valuable to hear. And like I said, we want to cast that wide net. So in terms of talking about treatment, so very thankful that you brought up ways to normalize and make your child feel... be able to have that opportunity to have a normal social life. You mentioned one of the things that has been most helpful is being able to trial different things. And I guess one question for you is were there certain aspects of pLGG or certain symptoms of pLGG that you were... as you've trialed things over time that has been what you were kind of seeking help with or looking to somehow impact? Can you maybe just share a little bit about those treatment goals?

Caitlin R. (04:09:53):

Sure. So he's been on both MEK inhibitors and chemotherapy. The chemotherapy when he was extremely young, as pretty much everybody has shared, was the gold standard for decades of Carboplatin and Vincristine. That was your Zofran coming to the rescue for nausea and being able to titrate the medications. I'm very thankful that his providers have had levels of confidence in that, that you can balance to an extent the efficacy of the chemotherapy, but also trying to maintain the fact that the child needs to gain weight and if they're not eating, they cannot gain weight. When it came to our MEK inhibitors, two in the same class, one was phenomenal, Trametinib we had two years of tumor-free progression. Towards the end, it started to begin in being ineffective, and we moved on to selumetinib because the trial had closed for DAY101 or Tovorafenib. And so we're hoping that opens up. But as much as the selumetinib didn't work, we ran out of options.

(04:10:56):

We trialed a lot of interventions and the side effects that he exhibited were unlike any that had been reported separately, they were primarily behavioral. He had a lot of stomach issues. So we started going down the road, trying to figure out with other experts, is this the case of kids, which has been paralleled in autism? Kids that are autistic that undergo treatment frequently have very strong behavioral changes or responses to their physical discomfort. And when we cannot regulate the physical discomfort, it just sort of rears its ugly head in a different way. So whereas we weren't able to find a way to handle his GI symptoms, the behavioral aspects seriously damaged his relationships at school. And he's currently in

first grade, to the point where we made the decision to stop the medication, continue watchful waiting and monitoring, and after three months, the side effects dissipated. But at that point, we had no answer because we could not find something that really mitigated those physical aspects that he was receiving or that came forward as a result of the selumetinib.

James Valentine, JD, MHS ([04:12:06](#)):

Wow. Well, thank you for sharing that. One last thing to just follow up on. You talked about in a couple instances, the benefit risk weighing balancing like titration for example, where you saw benefit or felt like there was efficacy, how was that being measured? Was that stability of the tumor? Was that relief from some symptom?

Caitlin R. ([04:12:35](#)):

Sure. It was a very fine balance, right? Our providers went in the 25% range. So we went from a 100% dose to a 75% dose. And as long as our next scan demonstrated no further growth or no iodine uptake in certain types of scans that we had and his symptoms were under control, then we would maintain treatment at a 75% dose. And that seemed to be his magic number where we could still see efficacy against the low-grade glioma, but he was able to maintain a lifestyle with minimal symptom management.

James Valentine, JD, MHS ([04:13:11](#)):

Sure. Well, Caitlin, thank you so much for sharing all of that. Kate, I'd like to bring you into this topic, thinking about what maybe has been most helpful out of what you all have tried.

Kate B. ([04:13:26](#)):

Yes, hello. Thank you. My name is Kate. My daughter is Raelyn. She's five years old. She was diagnosed just before her fourth birthday, and her tumor is in her optic chiasm, so it has strongly affected her vision. We started treatment immediately due to her vision loss. So we didn't really have a lot of time to process everything from the finding of the tumor to doing a biopsy, placing a port, and then starting treatment. And she did the 15 months of the Carbo and Vincristine, such as many other people.

([04:14:18](#)):

She handled that treatment pretty well as far as symptoms go, compared to what some people have. So a little bit of neuropathy, which she did physical therapy for. That tended to help a lot, building her strength up and her balance, which was affected from the tumor also. It helped with... and now she is off of treatment since December of last year, she finished up. So her neuropathy is not really an issue anymore, and she was just discharged from PT, which is wonderful.

([04:15:09](#)):

We've been enjoying a new life of normalcy without having to go quite as often to the hospital and receive treatment. She was doing a speech therapy, which she started prior to diagnosis and the claim, it's not related. So she also was involved in that therapy, but treatment has not helped our main concern with the tumor, which is her vision loss. There is no treatment that is bringing that back.

James Valentine, JD, MHS ([04:15:53](#)):

I see. Well, thank you for sharing all of that, Kate. One area that I'd like to understand a little bit more... glad to hear that she was just completed or discharged from physical therapy in addition to coming off the treatment regimen. But in terms of that physical therapy, maybe could you describe where she was

in terms of physical function, what she was working on at the beginning of physical therapy to now what she's capable of today?

Kate B. ([04:16:28](#)):

Yeah. Yeah. Other than having some clumsiness and coordination issues from the vision loss caused by the tumor, she really didn't have many physical symptoms. If you saw her, you wouldn't even know she had a brain tumor. She has adapted so well, but due to the chemotherapy, it caused the peripheral neuropathy in her feet. So that was what the physical therapy was concentrating on and working on was trying to help the neuropathy in the feet and just with her treatment having to be dose reduced halfway through and then now finishing up treatment, the neuropathy has not progressed, and it's actually... we noticed it getting better after starting physical therapy. So they've been working on building strengths and everything as well. But we have been very lucky that the neuropathy was the biggest physical thing coming from treatment for us.

James Valentine, JD, MHS ([04:17:51](#)):

Sure, sure. And in terms of the neuropathy, were there things that you were able to notice or tell that were harder for her when she maybe was experiencing it more early on versus now with it having been managed and reduced?

Kate B. ([04:18:12](#)):

Yes. She would trip over her feet while she walked more often in the beginning, and then just the doctor doing her evaluations before each dose of chemotherapy in the office. Having her doing some of the walking exercises, she would notice herself that she wasn't able to lift her feet up as much. She didn't have any of the tingling or pain associated with that, thankfully. So it was more of an observation and the tripping over her own feet a little bit.

James Valentine, JD, MHS ([04:18:53](#)):

Well, thank you for helping me understand that and giving us some insights into the overall treatment journey that you've been through so far. I'm sure we'll be talking more about some of those aspects here shortly.

([04:19:05](#)):

But Danielle, I'd like to bring you into this first topic as we're thinking about the direct medical treatments as well as the broader range of things. Is there something that has made living life with pLGG just a little bit easier or maybe even helped treat the condition or its symptoms?

Danielle R. ([04:19:28](#)):

Sure. So I'm Danielle. I live in Orlando, Florida. My daughter, Emma was diagnosed at 17 months old with a pilocytic astrocytoma. Her tumor has the FGFR1 mutation. She kind of falls a little on the opposite side of the spectrum than we were just talking about in terms of she was diagnosed when her tumor had a spontaneous bleed. So she's been disabled from kind of the onset of her diagnosis. So that's been something from the onset we've had to deal with. Looking at those therapies, overcoming the disabilities that have come with the tumor from day one, along with finding those treatments available to help keep her tumor either stable or as we all hope, shrink it. So it's kind of been a balance of both sides of that piece.

([04:20:29](#)):

She just turned eight, so really in the last six plus years she's been on multiple treatments. We've really only had success or somewhat of success on one, which was carboplatin, which a lot of us have talked about, tends to be the initial one that people go to. She eventually developed an allergy to it, which is pretty common and unfortunate because it had worked for her. And so we've really struggled over time finding that kind of next home run for her.

[\(04:21:06\)](#):

And during that time, it's seeing tumor growth and the fluctuation in her disability and how it affects her from the tumor, because with tumor growth, whether it's vision or for my daughter, she's never been able to walk independently, she's nonverbal, how that affects her. So for us, those things have been hard. And with the mutation she has FGFR, which I think Dr. Fangusaro mentioned briefly, there's no specific inhibitor that's really available right now to target it. So we've tried MEK inhibitors and things like that. And she actually just this past month started a trial at St. Jude for a newer MEK inhibitor. So we're hopeful, and we always love seeing these newer things come available. That's why we love this meeting like this today. We want to see this research and finding these things because the morbidities that we've talked about associated with the low-grade gliomas and the fact that we've discussed that, it's kind of like this childhood disease that affects our kids for their life.

[\(04:22:40\)](#):

That's the part that's hard. And I think, who was it? Caitlin touched on the idea of running out of options. I think that's a fear all of us have. And that's something we've run into where it's like, "Gosh, we've tried six different chemos, none of them have worked." And you start to, after each one feel like, "Well, when are we going to run out of an option?" And so I think that, not to ramble, but I guess my point is the longer you're on the journey, there's so many ups and downs with the different treatments, and you might have a success, and then that treatment stops working and you have to find a new one. And it might be hard to find a new one that works again, which is why it's so important to find these newer, more effective treatments.

James Valentine, JD, MHS [\(04:23:34\)](#):

And Danielle, if I can just follow up quickly on one thing that you just said that related, I think, to a number of experiences that you shared, which is kind of that up and down. Can you maybe give us one example of where something was initially helping or effective? In what way was it effective, and then how did you notice or what was that loss of benefit? Obviously, there's probably many, but-

James Valentine, JD, MHS [\(04:24:03\)](#):

... benefit. So obviously, there's probably many, but is there an example you could share of that?

PART 8 OF 10 ENDS [04:24:04]

Danielle R. [\(04:24:07\)](#):

Yeah, I mean I think for a lot of us, I know my daughter gets scans every three months has kind of been what she does. And that's kind of a short time period to live your life by on the edge of your seat, wondering what's that next scan going to look like? And so we have had times where we'll start a new treatment and that first scan in it's like, hey, the tumor is looking stable or maybe a little better. And you have a lot of hope and you feel really positive. But by the time you hit that six month mark, there's growth.

James Valentine, JD, MHS ([04:24:38](#)):

I see.

Danielle R. ([04:24:39](#)):

And so it's kind of like your world's turned upside down again and you're kind of scrambling to figure out what is the next plan going to be? And that can be in any form of maybe you made it nine months, maybe that first three months scan didn't work. So it's kind of those kind of ups and downs make it really hard along the way.

James Valentine, JD, MHS ([04:25:01](#)):

Sure. Well thank you so much Danielle. I do see that we have a phone caller. We have Joan from Philadelphia who is a bereaved mom of her son with PLGG. And so she'd like to give some of her perspectives on their experience with treatments. So Joan, I'd like to welcome you to the program. Are you with us?

Joan ([04:25:25](#)):

I'm here.

James Valentine, JD, MHS ([04:25:26](#)):

Welcome.

Joan ([04:25:28](#)):

Thank you.

James Valentine, JD, MHS ([04:25:30](#)):

Yeah. So we'd love to hear if there's a treatment experience or treatment experiences that you'd like to speak to and any perspective that you have on that.

Joan ([04:25:41](#)):

Okay. I think the main thing or main reason I'm here is I have stayed in touch with the brain tumor community. My son died in 2006 and he was diagnosed in 1998. And the eye-opener for me is that the treatments that he went through and the treatments being offered today, not all but are essentially the same. And I just can't believe after all these years that there hasn't been anything really new that I've seen. And when he was diagnosed 1998, he had what they called a Pilomyxoid tumor and it was disseminated, it was in his brain and his spine. And when he started treatment, he was three and a half years old and they put him on vincristine and carboplatin. And at that time they told us that that drug had been around since the '50s, if my memory serves me.

([04:26:57](#)):

So all these years later it's still being used and I guess it's working. I'm hoping it's working. Kyle was on it for probably about 18 months, then he developed drop foot from it. So we were taken off of that.

James Valentine, JD, MHS ([04:27:18](#)):

I see.



Joan ([04:27:19](#)):

And then after that we went on to a drug called Temodar, or Temodar, I'm not sure of the correct pronunciation, which really didn't do anything for him. And then they did another resection, in hopes of getting the remaining tumor out. Because when they first did surgery, they didn't get it all. So they went back in and they got all of it out, believe it or not. And except the spine was still an issue, but the brain tumor itself was taken out. So then they put us on a brand new clinical trial at that time called [inaudible 04:28:02], which I haven't heard of since. And that did nothing for us.

([04:28:10](#)):

So then we went on PCPV, which I know is still being used. And at that point he was in kindergarten and it was really difficult. I remember all the different pills and the different times I had to go to school and give him the medications. And it really was harsh for him. So we ended up taking him off of that. And then he went on vinblastine, which I see is still being used. And at the time he went on vinblastine, it was relatively new for brain tumor kids.

([04:28:50](#)):

Dr. Bouffet from SickKids in Toronto is the one that had recommended that for us. Kyle was treated at CHOP, but I went through all over the place trying to get different opinions and help and Dr. Bouffet came through with vinblastine, which actually did help him for a while.

([04:29:14](#)):

But then what happened in the end, the spread to his spine caused spinal compression and we were faced with doing nothing and the chances of him becoming paralyzed or doing radiation, which we had put off since he was diagnosed, because he was so little.

([04:29:43](#)):

But in the end, we chose the radiation and sadly he became paralyzed anyway. And what happened it seems is that the morphed into a high grade tumor. So he passed away in 2006. But the main thing that my concern is... I'm sorry, they're doing construction here.

James Valentine, JD, MHS ([04:30:16](#)):

No worries.

Joan ([04:30:17](#)):

For the kids who are still fighting, I just worry, I'm just praying that more options will come up. So that's my concern. My hope is for the kids still fighting, that something does come up, that will really help these kids live a normal life.

James Valentine, JD, MHS ([04:30:40](#)):

Yes, and I think we all, that's why we're here today and why I'm so appreciative of you, Joan, sticking with the community and the organization and sharing your perspective as a mother of someone who has been through it all. And so I just want to thank you so, so much for sharing that perspective on treatments. And I think it is important to hear that experience that you had started, starting in the 1990s to what is still being used today. I see that a number of treatment success or things that may have helped, comments have been coming in. So want to make sure we hear some of those. So Courtney, what are we seeing there?

Courtney Davies ([04:31:30](#)):

Absolutely. A couple here under the treatment success, Derek from Naples, he writes in, "My son was a part of a clinical trial for two years that eventually led to him gaining access to his current treatment. This medication has proven to keep his tumor stable over the last couple of years and has been a great blessing to our family." Also, Heather from Scottsdale, she writes in, "My daughter is on oral inhibitors. Her treatment continues to keep her tumor stable, which is great, but there are many unknowns. She has some vision issues but is otherwise doing well." And James, I want to read one more. CJ writes in, "I would say the therapies do help to recover some of the hearing loss and the loss of balance and right side weakness that is a result of the surgery to save his life from the brain tumor. But we are certainly not back yet to the child that we said goodbye to on the day of his first surgery."

James Valentine, JD, MHS ([04:32:37](#)):

Wow. I want to thank everyone who's been calling in and writing in. Please keep the comments coming as we expand our discussion now. Of course, if you want to continue to share things that have been helpful, we want to hear those. But we do want to broaden the discussion a bit about current treatments and recognizing that there may be some things that have not been as helpful or whether or not something's been helpful. Maybe it's come with some important trade-off or downside. And so to get us thinking about this topic, we're going to go to a polling question. So go ahead and go to [www.PollEV.com/pLGG](http://www.PollEV.com/pLGG).

[\(04:33:19\)](#):

Our next polling question for you here is we want to know what are the biggest drawbacks of your current treatment approaches or the current treatment approaches available? And you can select up to three. The options here are A, it's not very effective at treating the target symptom. B, it only treats some, but not all of the symptoms. C, the high cost or copay or it's not covered by insurance. D, the limited availability or accessibility. E, the side effects. F, sorry, that's a typo there. F should be route of administration. H, other and I, not applicable as you're not using any treatments. So again, please select here the top three biggest drawbacks of your current approaches, those things that represent the top three of those biggest drawbacks.

[\(04:34:18\)](#):

And as you're picking these, again, we know there's such a wide range of different treatment approaches out there, which of those treatments maybe have these different drawbacks and how have those drawbacks impacted your or your loved one's lives?

[\(04:34:40\)](#):

As it stands, it looks like the top drawback that's being reported is that it's not very effective at treating the thing that it's supposed to treat, the target symptom or health effect. After that, we're seeing the next biggest drawbacks being reported as the high cost or copay or not covered by insurance. It's limited availability or accessibility as well as side effects. Right behind that is that it only treats some, but not all of the symptoms. We do have some people reporting route of administration or other things as biggest drawbacks and some saying that reporting that they're not using any treatments, so this is not applicable. So let's talk about this a little bit more and let's check in with our Zoom panel here to get us started.

[\(04:35:26\)](#):

So Caitlyn B., maybe you can get us thinking about this topic of maybe things that you've tried that haven't been as helpful, whether at treating the target symptom or only treating one but not all, or maybe one of those other downsides. What kind of rose to the top for you all?

Maria T. ([04:35:46](#)):

Yeah. Hi, my name is Caitlyn. I am from St. Louis Missouri. I actually called in earlier to the other Zoom panel. My daughter is Adelaide. She was diagnosed with a diffuse ganglioglioma on her brainstem, cerebellum, pons, medulla. She is currently on Dabrafenib, which is a targeted inhibitor. She has a BRAF V600E mutation. Of course, the treatment we really wanted was a gross total resection. That would've been ideal to... they said the first best case scenario is not having a tumor and the second best case scenario is a gross total resection. And those were neither of our options. Since she was a low grade, grade one, it came back, we did go ahead with a watch and wait protocol. We didn't feel that her symptoms were worth putting her through a traditional chemo at that time, which was, all that was really offered was traditional chemo or watch and wait or clinical trial. And I wasn't ready to go into any of those.

([04:37:10](#)):

So I guess in the beginning it was just the lack of options kind of in treatment. So we were managing symptoms. We're still managing symptoms and it's frustrating. The Dabrafenib did shrink her tumor. I'm greedy, I want to shrink it more. It's holding it stable as of now. I fear that 75% of kids that get off of this drug after two years show significant growth in tumor. So I'm scared what that would look like. I know we have other options out there, but I think the lack of options makes it in the beginning and other people have said there's just not enough. And I guess that's what's been really hard for us in making the decision as the parent, sometimes feeling like I have to be the doctor.

James Valentine, JD, MHS ([04:38:11](#)):

Yeah. That is certainly something that would be, I don't know, impossible to maybe navigate and do, but clearly you have to. There's no other option. You did mention that there was some shrinkage of the tumor, but that you still do have to manage symptoms. Was there any change in symptoms that were corresponded with the shrinkage of the tumor. And then along with that, has there been anything that, what symptoms and has there been anything that's been helping with those symptoms besides that treating the tumor directly?

Maria T. ([04:38:57](#)):

Right. Yeah, absolutely. So Dabrafenib, I was pretty happy with the shrinkage. We saw significant reduction in vomiting and nausea, which was excellent. She was vomiting three to five times a week and she hadn't gained any weight or grown in almost two years, which the doctors were like, "Oh, that's no big deal. And it's not because of the tumor." But as soon as she started the Dabrafenib and we saw reduction in size, we saw the reduction in nausea, we saw significant weight gain to the point of having us seeing a dietician. And I'm just happy she's eating and not vomiting up her calories. We did see a decrease in some of the dizziness and the length of severity of that dizziness, but I also think as parents and as Adelaide gets older, she can recognize kind of that feeling of when she's going to be getting dizzy and can medicate before it gets too bad. But those are kind of the things that we did see improve. But I just want the dizziness... the vertigo and the dizziness is what is just really affecting her everyday life and it's just really difficult to control.

James Valentine, JD, MHS ([04:40:08](#)):

Right. And even when it was reduced, I guess, can you somehow describe where it started and then where it came down, but also how it is today? I mean even with her being able to recognize it and kind of get ahead a little bit on some treatment for the vertigo, how much is it still affecting her?

Maria T. ([04:40:37](#)):

It's still like a weekly... it's a weekly thing. She has two medications. She takes a meclizine, that's kind of our first line of defense, which is pretty much like a Dramamine. And then if that doesn't work, we move on to pretty heavy duty lorazepam, which works almost every time, but we know that's addictive. She's young, so we try not to use that. She has a ton of other stuff, like she can't hear out of her left ear among other things. But really, if you sat her down and asked her what is the worst thing about having a brain tumor, she would tell you the MRIs every three months, she has to get an IV, as I'm sure all the other parents can relate to. But the dizziness and missing out on things in her childhood because of it. Having to be picked up from school. And it seems to be triggered sometimes by excitement. So now you are so excited for something and now you're missing out on it because you got excited, and now you're sick. So it's just kind of a mysterious beast we're trying to live with and figure out how to manage.

James Valentine, JD, MHS ([04:41:56](#)):

Yeah. Well Caitlyn, thank you so much for sharing that and diving into some of those topics with me. Nora, I'd like to bring you on this a kind of topic. We're exploring current treatments. Are there areas that treatments that kind of fell short of your treatment goal or maybe they helped but they had some important trade-off or burden associated with them? What comes to mind for you?

Nora M. ([04:42:25](#)):

Yeah. Hi, I am Nora. I'm from Plainfield, Illinois just outside of Chicago and my son Beckett, who is seven, just got diagnosed at April of last year. So we're getting ready to hit our one-year mark of diagnosis and he has a polycystic astrocytoma that is between his hypothalamus and optic nerve. So it's not operable. And it was right where his third and fourth ventricles meet so that he got hydrocephalus and that's how he's got diagnosed. We of course started with the carbo, vincristine combo and after the 10 weeks of the first round, they had the MRI and they considered that failure. Plus, he was getting neuropathy both in his feet and he had an eye droop and also had to start wearing glasses. He also was on Zofran almost 24/7 for nausea and was not gaining any weight. In fact, lost dramatic amounts of weight so much that he had to be on an appetite stimulant also.

([04:43:34](#)):

So that had a lot of side effects. He was, they considered two options, either oral or vinblastine, and they ultimately decided to go on vinblastine. So he's been on that for just over six months. We just hit our halfway of 52 weeks of weekly vinblastine. After his first three months MRI, it was stable, so no growth. He also does have nodes and lobular on both his brain and his spine. So that's something they watch. It's not just the tumor that is affecting him.

([04:44:10](#)):

And being on vinblastine has actually helped his neuropathy. He is in both physical therapy and occupational therapy to help with it. And also, aqua therapy, which I feel like has been the biggest help for strengthening everything back. He no longer has to wear glasses and his eye droop has completely gone away. So we've seen a little more of his personality come back and that we did just have the six-month MRI. Unfortunately, we don't know the results of that due to Lurie's system being down. So we have to wait for Lurie's system to come back up to compare it with past MRIs. But we are hopeful that we're still stable and that he's doing a lot better than he was.

James Valentine, JD, MHS ([04:44:58](#)):

Yeah, wow. So much there. And I guess maybe one place to start is seeing so many side effects, really burdensome things that popped up that each required then their own cascade of treatment approaches. How did your family think through the pros and the cons of going through treatment for the PLGG that was then causing so much in terms of these side effects that led to needing so much more treatment approaches? I'm glad to hear now that many of those things have been reduced or managed or maybe even eliminated. But as you were going through that journey, how did you think about those trade-offs and consider how to handle that?

Nora M. ([04:46:06](#)):

I think going through the carbo, vincristine, like I said, we only got to do one round before we realized it was failing and it wasn't working because of growth and spreading. So I think what we told ourselves with all those side effects is, "Hey, hopefully this is taking care of it and we are going to see shrinkage or stability," which his type of tumor is probably never going to have shrinkage. Although, as a parent, that's what you want to hope for. So we just kind of pushed through and helped him as much. Luckily, most of that treatment was through the summer, so he wasn't having to miss a lot of school, otherwise he would've been missing a ton of school because he was sick all the time. With this new chemo, like I said, we've seen a lot of reduction of symptoms. He still has to do physical and occupational therapy and aqua therapy, but we are finally seeing progress instead of regress.

James Valentine, JD, MHS ([04:47:06](#)):

Yeah. And just to maybe understand, when you talk about seeing progress, are there either things in your daily life with him that you notice or that you could describe that maybe he struggled to do or couldn't do that he's able to now do again or do for the first time? What do some of those things look like?

Nora M. ([04:47:31](#)):

Sure. So for instance, in October when he was just starting the vinblastine, he was playing soccer because he was a determined kid and said, "I'm still going to do all the stuff I want to do." And the coach really great with it too, but he couldn't run like the other kids. He couldn't run as fast and he had a weird gait when he ran. So now he can actually run, maybe not as fast as everyone else, but it looks like a run. And soccer coach actually just saw him a couple weeks ago doing baseball evals and was just blown away. We've seen the progress as the weeks have gone on and stuff, but it was really great to see somebody who hadn't seen him in a couple months and just be blown away at the progress he's made.

James Valentine, JD, MHS ([04:48:21](#)):

Wow, that's incredible to hear. And I love hearing that when you're the parent, you're obviously looking. But when others like coaches can see that and that helps make such a big difference. I do see that we have a number of written comments coming in also on this topic. So Courtney, want to check in with you on those?

Courtney Davies ([04:48:42](#)):

Absolutely. Thank you. So Lacey from Pittsburgh writes in, "The most significant downsides of selumetinib are the eating restriction times the damage it does to his skin and the diarrhea it causes, along with stomach aches. He also has to take it daily, so he has a daily reminder that he's a brain tumor and he has to treat it." Let's see. Lisa from Connecticut, she writes in, "My daughter's tumor is a chronic condition where treatment has caused many disabilities. One of the most significant impacts is that

every drug protocol has caused extreme fatigue, which has affected her ability to learn and understand." And let's see here. Keith from Manhattan, Illinois writes, "Our biggest concern is that we don't have many treatment options left and are desperate that more treatment options become available. Her tumors always start growing again after treatments or during. We need more options."

James Valentine, JD, MHS ([04:49:52](#)):

Wow. Well, thank you for everyone who's been writing in and for all of this discussion we've been having about current treatments. I do want to make sure that we spend some time looking towards the future and get your perspectives on what would be meaningful, short of a complete cure for PLGG, which we all want. But thinking about what maybe would come down the pipeline before that. What would represent important and meaningful benefits or what other aspects of new treatments would be important to you?

([04:50:29](#)):

So we have one final polling question for today. So one last time, go to [pollev.com/PLGG](http://pollev.com/PLGG). And here, we want to ask short of that complete cure, what top three specific things would you look for in an ideal treatment for PLGG? And again, you can select up to the top three. The options are A, stopping disease progression. B, improving daily functioning. C, increasing energy. D, treating emotional symptoms. E, treating seizures. F, preventing falls or G, some other specific thing that you would look for in an ideal treatment for PLGG that's not listed here as one of the response options. So we'll give you just a couple of minutes here to think about this. This maybe is the hardest question of the whole day of asking you to prioritize what it is that you'd like to see in terms of a new treatment that could come along here.

([04:51:40](#)):

So as it stands, it looks like there's kind of a couple that are right at the top. We see that stopping disease progression as well as improving daily functioning are being reported as top two of the top specific things that our audience is looking for from future treatments. After that, there's a little bit of a drop-off, but we see treating emotional symptoms, increasing energy and treating seizures being reported as a number of people's top three, as well as other things that weren't listed here. No one has reported preventing falls as one of their top three goals for a future treatment. So I'd like to come first to our Zoom panel and thinking through this question. Perhaps Kate, we can start with you on this one. Thinking of all of the ranges of things we could be looking for from a future therapy short of that cure, what was at the top of your list?

Kate B. ([04:52:35](#)):

To stop progression. My daughter just finished her first round of treatment and her tumor has remained stable through the whole time. No shrinkage and no growth. So we consider that a win. She will have her first three-month rescan in a couple weeks. We're also at Lurie, so hoping by then, their systems are back up and we can compare it to her previous scans as my anxiety is out of this world with knowing what has been happening in her body these couple of months off of treatment.

([04:53:19](#)):

But I don't know what next treatment will be for us if vision declines more or if tumor grows. I just pray that there is something out there that can be targeted towards her. Her mutation is very rare, so there is nothing currently. It's unknown in the database, so something that can break through that blood-brain barrier as that is critical to get to the tumors to stop them. Something that does not have to be given through her port as her biggest wish is to get her port removed. So just anxious to know what's next, but grateful that today we are not in need to look for another treatment.

James Valentine, JD, MHS ([04:54:20](#)):

Right. That's so helpful to hear, Kate. And I hear you loud and clear on stopping or the progression of the tumor of symptoms like the vision loss, and not insignificant having something that maybe doesn't need to use that port. So thank you for sharing that. Nora, coming around here. What would you say is a top treatment goal, something that would be important that you'd look for in a new future treatment?

Nora M. ([04:54:54](#)):

Yeah, obviously, stopping progression and also be able to provide shrinkage is top priority. Also, I did the emotional because Beckett's nodes are on his nervous system, so it does cause him to have a lot of emotions, especially when the nerves are bothering him. He is great about communicating that now and he recognizes that. Through all this therapy, he's learned that stuff. But obviously, something that could help with the nerves would be great.

James Valentine, JD, MHS ([04:55:29](#)):

Yeah. And what would maybe success or even if not complete success look like in terms of helping with those issues and managing emotions?

Nora M. ([04:55:44](#)):

I think just some type of drug or treatment that can shrink the nodes because the same with the tumor, we're never expecting the nodes to go away and shrink on current treatments.

James Valentine, JD, MHS ([04:55:56](#)):

Sure. Thank you so much for sharing. We're going to come around here because this is such an important topic. I want to make sure we hear from everyone. So Caitlyn B, maybe you can go next on, what would be an aspect of an ideal treatment that you'd like to see?

Maria T. ([04:56:13](#)):

Yeah, I feel pretty lucky on the Dabrofenib. I feel like it kind of almost is an ideal treatment. We've seen shrinkage. It's medication that she takes, very low side effects. We had some skin issues, some weight gain, and she can't eat for two hours. There's appetite restriction. So I guess I would like to see everyone have the opportunity to have a medication like this. Like I said, I'm kind of greedy because you get a little bit and I want more. I want the tumor to be gone. So I guess really, I know you said short of a complete care, but at this point I think that's what-

Maria T. ([04:57:02](#)):

... a complete cure, but at this point I think that's what we're really looking for. With the BRAF mutation, there's a lot of drugs out there for Adelaide and for that, I'm incredibly thankful. But I just think a drug that can and shrink these tumors significantly, low side effects. And like Kate said, I'm so thankful that we have never had to go through the typical chemo. She's never had to have a port. So I think if we can just continue on this targeted therapy route, where it's effective and it stays effective when they don't come off of it, it stays minimized, I mean, I think that's what we all want.

PART 9 OF 10 ENDS [04:57:04]

James Valentine, JD, MHS ([04:57:50](#)):

Yeah. Well thank you, Caitlin. Danielle, coming around here, what would be the top of your wishlist for a future treatment short of that complete cure?

Danielle R. ([04:58:05](#)):

I think twofold with what you were asking. One, treatment-wise for us is seeing an expansion on the targeted treatments for us would be a targeted FTFR inhibitor in the near future, because there's always the fear of we might not have 10 years, so hopefully just more public funding and research so that we can get that as soon as possible for not just our kids with that mutation, but just beyond these BRAF ones that we've seen be so successful. It's just something that I'm really looking for and I know so many others are. And then on the daily functioning side, something I've thought about is looking at those morbidities and side effects like the vision loss or for my daughter.

([04:58:56](#)):

Motor disabilities is maybe how we can look at improving the lives of the children and patients who are affected in those ways. So looking at is there a way we can fund, or I don't know, help with other aspects of curing blindness, other ways of improving motor disabilities where maybe shrinking the tumor isn't going to be the way to get there when it's affected a child their whole life, but are there other avenues to help these kids when these are the things they're going to have to live with? So I think those are the two things that I would really like to see.

James Valentine, JD, MHS ([04:59:41](#)):

And just a quick followup with you, Danielle, so you would be view it as success if you had a treatment that did one of those things but not the other. They don't have to be together in terms of halting any progression or shrinking the tumor separate from those, more of the symptom treatment or reversal. If something could do one thing and not the other, you'd be happy with that in either case. Certainly if they could do both, that would be the best. But I just wanted to clarify that.

Danielle R. ([05:00:17](#)):

Yeah, I think it depends on everyone's scenario. For us. Like I mentioned, my daughter's tumor had a bleed over six years ago, so we know that there's some extent of the disability her tumor caused, that even if we found a miracle drug that came out next year and shrunk her tumor 90%, it probably wouldn't resolve some of her issues. But of course we would be over the moon that it shrunk her tumor. So we would be happy on either side of the coin, but of course, in a more acute stage of someone finding a tumor and being able to stop growth and prevent advanced vision loss, that would be amazing for that situation.

James Valentine, JD, MHS ([05:00:59](#)):

Of course. Yes. So thank you for clarifying. It's very helpful. All right, so Caitlin R. will round out our panel here with your thoughts on this topic.

Caitlin R. ([05:01:11](#)):

Sure. I think a lot of it's been shared. So the point that I'd like to highlight is really we have our children facing lifelong battles here. I think at least I frequently heard you have options, now we don't, but there are options. And so how long can we get progression free? That's always the goal. And if we want to have treatments that can help us stabilize, we need to look to the future and think, is there a way that we can get these children to grow into adulthood having to deal with this chronic state. Much like a



diabetic, right? How can you deal with that and still be an active adult or an adult who can contribute to society and not be somebody that we are supporting for the rest of our life? Not because we would never do that. We are parents and of course we would, but what kind of life is that for our child to get to a point where they're not fully functional, or at least fulfilled in their life, even if that requires adaptations or emotional support.

[\(05:02:08\)](#):

How can our children grow up being confident that this is something they deal with, but actually being able to deal with it and not having the three-month anxiety and literally living life three months at a time? Anything that helps us get to that point is success.

James Valentine, JD, MHS [\(05:02:25\)](#):

Wow. Well said, Caitlin. And I just want to thank all of you our entire Zoom panel for your contributions. You've been so thoughtful and all of your insights, particularly on this last question have just been incredible. So I have a phone caller that I want to get to, but just wanted to thank you all while I had a chance before we go and bring in Mandy from Iowa, who's our caller here. So thank you again. So we do have Mandy from Iowa who's a parent of a person living with PLGG. And so I'd love to, Mandy, bring you in on this topic as we're focused here on what it is that short of a cure, would represent an important or meaningful improvement over current treatment approaches. I'd love to hear your thoughts on this topic.

Mandy [\(05:03:25\)](#):

I really think that families need options that give their children a higher quality of life on and off treatment, and reduce side effects long and short term. We have been battling a hypothalamic-pilocytic astrocytoma for the last seven years. Our daughter has been through three major brain resections, two chemo protocols, one MEK inhibitor and she just finished two years on Day101. She's been sick on drugs when she had Avastin and arenateken and we were sick every other week. We tried everything possible and nothing worked. And they finally said, "Okay, let's try an IV inpatient, see what this does." The kid never got sick and then insurance turned around the next time and said, "You're not sick enough to do it this way." And so we had to go back to being sick every time for the next three months. One of the problems I see is that we had to fight to get her on the Day101 drug.

[\(05:04:26\)](#):

We had seen growth again and insurance said, "We're not going to send you out of state to get treatment because the closest options..." We live in Iowa and the closest options were Ann Arbor, Michigan and St. Louis and I had written the drug company and I introduced my oncologist. I said, "Okay, here, what do we do?" And they wrote back, "Well, this is going to take seven, eight months." I said, "Well, if I can't get Gabby to the drug, why can't I get the drug to Gabby?" And we were able to get it on compassionate use and she became the first patient at her hospital to receive that drug. And I want families to know that, because other families said yes to drugs like Tremetinib, we had the opportunity to take that drug. And because we said yes to Day101 or drugs like it, other families don't have to go through this whole litany of, "Well, do I do surgery? Do I do chemo? Do I do radiation? Do I do this thing? I don't know."

[\(05:05:20\)](#):

We have to do better for these children because they need a future. Our daughter has severe memory issues from the surgeries that saved her life. That's collateral damage. My 17-year-old will always act like an 11-year-old because she doesn't have a fornix on the right side of her brain. And so she's the

sweetest, most wonderful child, but her cognitive function is always going to be impacted and we need to be able to reduce those impacts so that again, as others have said, these kids have a future that does contribute to not only their lives but the lives of the world around them.

James Valentine, JD, MHS ([05:05:54](#)):

Right. Wow, Mandy, that's really powerful and I just want to thank you for calling and sharing that and not only sharing some of the specifics based off of your daughter's experience and as you phrased it, the collateral damage, but also just the importance of participating in research and clinical trials is part of this ecosystem of moving us forward towards that. And I think we've heard that from some others today in terms of eagerness and importance of participating in trials. So thank you again so much Mandy, for calling in. As we're at the end of our time here, do know that we've had a number of people write in with comments on what they're looking for from future treatments. So I want to pause here for just a moment so we can hear some of those preferences for future treatments from those on the web. Courtney?

Courtney Davies ([05:06:56](#)):

Wonderful. Thank you. Let's see here. Lisa from Connecticut, she writes in, "We need treatments that will stop the tumor but have little side effects. PLGG is a chronic condition and current treatments still have too many side effects that increase over time." Joan from Pennsylvania writes, "My hope is that new drugs with better results and better quality of life can be found for these kids." And I'm going to read two more.

James Valentine, JD, MHS ([05:07:29](#)):

Yes.

Courtney Davies ([05:07:29](#)):

Alice from Massachusetts writes, "We need more targeted therapies," because if she fails her current treatment combination, there are not any other good or effective choices to keep her alive. And Amy from Oregon, she writes in, "We are hoping and praying that we can even get access to new targeted treatments. Right now, we and our team are holding out hope for Day101. My daughter is a beautiful 16-year-old and I don't want her to have to fear for her future and worry about her vision and memory loss.

James Valentine, JD, MHS ([05:08:04](#)):

Yeah. Well, again, thank you to everybody who has contributed their voices and shared their voices throughout the day. At this point, we're concluding the part of the day where we are in listening mode and hearing from all of you. Before we move to some summary and closing remarks, I just want to pause as your meeting moderator and personally thank each and every one of you, all of our panelists, our zoom panelists, phone callers. You all have been so brave. These topics have been very difficult. I know it's so hard to share about your children and what they're going through and their struggles. What struck me was how many voices we heard who shared so many different impacts and we could not have appreciated all of the different things that your children are going through if you all weren't so willing to raise your hand and share those experiences today.

([05:09:10](#)):

The treatment decisions and the significant trade-offs, and ultimately not just side effects, but disability that can come with those that you described, I can't imagine being in your shoes having to make those decisions, but I just want to thank you for being willing to talk through and share what was going through your minds and your family's discussions around those trade-offs so we could really understand how you consider those risks and what you're looking for from benefits. We aren't moving anywhere towards better therapies if we don't understand what's important to you all. And you were incredible at bringing that out today.

Courtney Davies ([05:10:00](#)):

Absolutely.

James Valentine, JD, MHS ([05:10:02](#)):

So now we will move to our summary remarks. It's an impossible task to summarize everything covered today, but we're in good hands with my friend and colleague, Larry Bauer. Just to introduce Larry, he's the perfect person to give some summary remarks here. He is a nurse by background, spent 17 years at the National Institutes of Health where he was in clinical research and then he went to the Food and Drug Administration where he co-founded the Rare Disease Program where he worked as a regulatory scientist for 10 years and he has been an incredible partner in helping plan this meeting. And so without further ado, I'll hand it over to you, Larry to summarize.

Larry Bauer, RN, MA ([05:10:48](#)):

Thank you so much, James. Yeah, I'll try to give a very high-level summary of what we heard today. We heard a lot of information. I apologize in advance if there's any detail that I missed that you thought was an important, but please know that these things will be summarized in the voice of the patient report to come. So our meeting today, it was opened by Courtney Davies, who's the president and CEO of the Pediatric Brain Tumor Foundation. This was followed by a presentation from Dr. Elizabeth Duke, who's a clinical reviewer in the division of oncology two at the FDA. Dr. Duke shared with us that these meetings can help the FDA review staff with identifying areas of unmet need and can help them to advise drug sponsors on their development programs.

([05:11:34](#)):

Next, we heard from Dr. Jason Fangusaro, who's the director of developmental Therapeutics at Children's Hospital of Atlanta and a PLGG expert. He gave us a clinical overview and shared that PLGGs are the most common pediatric central nervous system tumor. Acidic pilocytic astrocytomas are the most common group. These tumors are diverse and there are about 1000 to 1600 new cases per year in the United States. In neurofibromatosis type one patients, about 15 to 20% will develop a low grade glioma. Some of the symptoms can include headaches, nausea, vision problems, seizures, endocrine problems, balance issues, confusion, sleepiness, and behavioral changes. These tumors are diagnosed by imaging studies after presentation of some new symptom, and many patients survive into adulthood. So quality of life impacts are critical to consider when thinking about the approach.

([05:12:38](#)):

After the clinical overview, we heard from five families that were affected by pediatric low grade glioma. The first person we heard from was Sam, who's father to a six-year-old daughter, Maddie, who lives with PLGG. She first developed symptoms at age three with severe headaches and nausea. She developed hydrocephalus and needed a shunt. Maddie's had several surgeries and is incredibly empathic and mature for her age, maybe as a result of her experience. And her parents are always evaluating her new symptoms, worrying are these emergencies or not? Next, we heard from Cynthia, who's mom to two-

year-old Brayson, who has had seizures, vomiting, and staring episodes. He's had a debulking surgery that could only remove part of his tumor. He has seizures and developed asymmetrical gait and left-sided weaknesses. He's very young, but has signs of possible cognitive problems and developmental delay.

[\(05:13:40\)](#):

Then we heard from Khadija who's mom to her 12-year-old daughter, Anaya. At age three and a half, Anaya developed vomiting and excessive sleepiness. She developed posterior Fossa syndrome after her brain surgery, and Anaya needed a shunt and it currently is unable to walk on her own. She's dependent on help with bathing and transporting because of balance and coordination issues. She requires a one-on-one aid at school, which we heard some other kids do as well, and she hopes that she'll one day be able to walk again. Stephanie is mom to her son Declan, who has PLGG. Declan developed 15 seizures a day and has had many side effects from chemotherapy. He has left-sided weakness and speech issues. He also has behavioral issues, which are very challenging and has developed anxiety, PTSD and ADHD.

[\(05:14:33\)](#):

He yells and throw things at times and has aggression and a hard time making friends. His tumor is still lemon-sized in his brain with no cure in sight. And finally in the morning, we heard from Katie who's mom to her 22-year-old son, Alexander, who was diagnosed with PLGG in 2021 after biopsies of his spine and his brain. He had terrible migraines, vomiting, papilledema, seizures and loss of sight in the right eye. Alex has tried several therapies and at one point lost his short-term memory, which has since improved. Alex says he feels like a lab rat at times, but appreciates the treatments that he's received.

[\(05:15:13\)](#):

So overall, in the morning we heard that children develop seizures, balance issues, speech and vision problems, nausea and vomiting, and severe headaches. There is rarely a complete cure, so these kids have chronic issues with treatment and monitoring. And mental health issues often develop with the chronic impacts of this disease and the treatments.

[\(05:15:33\)](#):

Then in the afternoon we shifted gears to talking about treatments and we first heard from pediatric neurosurgeon Dr. Rob Lober, who's the director of the Living Biobank at Dayton Children's Hospital. He shared that quality of life is crucial when considering the approach to treatment. Some of the options include surgery, radiation therapy, chemotherapy, targeted therapy, or do nothing. And he said that sometimes the tumors die of old age. He talked about the MAP kinase pathway disruption leading to tumor cell proliferation, and he talked how targeted therapy can affect the MEK or BRAF pathways. Most PLGGs are resectable, but it may not be able to remove all of the tumor. We heard this again and again. And many of the targeted therapies are currently being studied in clinical trials. The long-term effects of these medical treatments are not always well understood and may lead to other tumors. Some of the challenges for trials include the small populations, heterogeneous tumors, long-term toxicities, and rebounding after the treatment.

[\(05:16:42\)](#):

We then heard from a panel of five families that talked about their treatment experience. First we heard from Maria, who's mom to 14-year-old Gavin. He was diagnosed four years ago after having a seizure. Gavin had partial tumor reduction surgery followed by chemotherapy, which led to nausea and vomiting. He had three more surgeries, but his tumor involves a critical artery so it can't be fully removed. He takes Keppra for seizures. He's missed significant amounts of school and they worry because no targeted therapy is available for him.

[\(05:17:17\)](#):

Next, we heard from Paola, who's mom to her daughter, Monica, who was diagnosed when she was nine months old and is now 12. She had early chemotherapy with many side effects and needed blood transfusions. She's on Trometinib but has side effects of ingrown nails, mouth ulcers, fever, and pneumonia. These side effects have led to her needing to go onto a lower dose and they worry about what her future will bring. We heard from Cathy who's mom to her 25-year-old daughter, Erin, who was diagnosed at age four. After brain surgery and chemotherapy, she said that Erin was just not the same child. She was unresponsive for months, mute and unable to swallow and was tube-fed for eight months. She's still unable to walk unassisted has processing issues, ataxia and traits of autism. She's had two surgeries for seizures. Kathy says these tumors are anything but benign.

[\(05:18:15\)](#):

Next we heard from Chetasi, who's the mom to her three-year-old daughter Ashvi. She was diagnosed at nine months of age after developing failure to thrive. Her tumor was unresectable, so she had chemo and an NG-II placement. She needed frequent checks for cytopenia and has had PT, speech therapy and OT. Her treatment has caused severe nausea and vomiting. They feel that the chemotherapy regimens that she's been put on are archaic and were selected due to lack of other options.

[\(05:18:48\)](#):

And finally, in the afternoon we heard from Evan who's dad to his son, Nathan. When he was four years old, he had an MRI that showed the tumor. He had partial tumor resection at that time, but the tumor was partially inoperable. He went on to chemo, which had many side effects with extreme fatigue, fevers and vomiting. He had new symptoms then at age 10 and tried an experimental treatment and was the first child to ever receive this treatment. He had a good response after two years of treatment with improvement in playing sports after the tumor shrank. He does, however, still have the tumor and they live in constant threat of it growing.

[\(05:19:26\)](#):

So overall in the afternoon, we heard that there continues to be a great unmet medical need for new treatments for PLGG. Some of the currently available treatments, surgery, chemo, radiation, those all have significant downsides and side effects. People are using many types of supportive therapy including PT, OT, speech therapy. But these do not help, unfortunately, in any way to help the underlying tumor. And people we heard when talking about research are generally open to trying new therapies or enrolling in new research protocols. So thank you so much. And now to close the meeting, let's go back to Courtney in the studio.

Courtney Davies [\(05:20:09\)](#):

Thank you for your thoughtful summary, Larry. This has been an incredible day and has helped us better understand PLGG, the impact on patients, survivors and their loved ones, and the need for therapeutics for the most common brain tumor diagnosed in children. Thank you to the FDA staff who tuned in today. And thank you to Will Lou Allyn, Ethan Gabor, Karen Jackler, and Lena Merzog from the FDA's patient-focused drug development staff who guided us through this process over the many months of planning. Thanks also to Larry Bauer and James Valentine from Hyman, Phelps & McNamara, whose assistance in planning and moderating today's meeting has been invaluable. Thank you to the Dudley Digital Works media team for the production planning and all the behind-scenes work that they have done today. A big thanks to the Pediatric Brain Tumor Foundation board members, staff and volunteers who have devoted many hours to the planning of today's meeting.

[\(05:21:12\)](#):

I need to give a special thanks to my PBTF team, including Ian Joyce, Amanda Hicken, Heather Held, Ryan DeBeaux, and Jeff Still. And finally, a huge thanks goes to you, the community of the PLGG patients, survivors, and families. Thank you for your honesty, for sharing your lived experiences of PLGG. 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 of the information from today, including polling data and comments into a voice of the patient report, which will be available on the Pediatric Brain Tumor Foundation's website. The form to submit comments for the report is open for another 30 days. So please, please consider submitting additional comments which will be added to the voice of the patient report. A recording of today's program will be available on demand immediately following this meeting.

[\(05:22:15\)](#):

We're planning to hold a forum also with any patients or caregivers that would like to discuss the impact of today, and this is going to be held on February 29th at 1:00 PM Eastern time. A Zoom link will be emailed to all patients and caregivers that registered for this meeting. Today's meeting will have a lasting impact on the future of PLGG research and drug development. So once again, to the entire community, thank you for making your voices heard today.

PART 10 OF 10 ENDS [05:24:06]