Larry Bauer (00:14:52):

Good morning. I would like to welcome everyone tuning in today to this Externally-Led Patient-Focused Drug Development Meeting for people living with the rare disease Gorlin Syndrome. My name is Larry Bauer, and I'll be the moderator for today's meeting. So, to start the meeting off, I'd like to introduce my co-moderator Julie Breneiser. Good morning, Julie.

Julie Breneiser (00:15:15):

Good morning, Larry. Thank you very much. Welcome to the Externally-Led Patient-Focused Drug Development Meeting on Gorlin Syndrome. I'm Julie Breneiser, Executive Director of the Gorlin Syndrome Alliance. Our mission is to thoughtfully support, comprehensively educate, and aggressively seek the best treatments and a cure for those affected by Gorlin syndrome. As a retired physician assistant and head of this organization, I'm in contact with people affected by this syndrome every day and personally know several hundred individuals and families affected by Gorlin syndrome in the United States and worldwide. In addition to knowing how Gorlin syndrome affects them, I live with it. I have Gorlin syndrome as do my 29 and 28 year old children. My diagnosis came at the age of 12, the same number of years after my first manifestation, hydrocephalus was identified. I've had more than 20 syndrome-related surgeries and well over 1,000 basal cell carcinomas removed.

Julie Breneiser (00:16:26):

My 29-year-old daughter has had dozens of basal cell carcinomas surgically removed thus far as well as 15 surgeries related to her other Gorlin syndrome manifestations. So prior to the age of 30, she's had over 40 invasive surgeries because of this disease. And she was also born with just one kidney. My 28-year-old son has had about a dozen basal cell carcinomas removed today and 10 syndrome-related surgeries. He was diagnosed with pre-glaucoma, a Gorlin syndrome manifestation at the age of 13. As he will hear and see today, many are much more severely affected, and some have lost their lives. Without surgical procedures, this is a life-threatening disease. Gorlin syndrome can manifest in any organ system of our bodies. Let me say that again, Gorlin syndrome can manifest in any organ system and there are no FDA-approved treatments for any of our manifestations.

Julie Breneiser (00:17:36):

We urgently and desperately need better treatments for all of our manifestations. We hope that what you learned from our community today will help broaden the understanding of the realities of living with Gorlin syndrome. One of the major misconceptions is that the average Gorlin syndrome patient has just a few basal cells. Well, you'll hear today that while the basal cells are the most burdensome manifestation for most, we deal with so much more, and it's not just a basal cell or even just a few basal cells. Members in our community count their basal cell carcinomas in a hundreds and thousands. While at the same time, managing their other manifestations impacting other organ systems.

Julie Breneiser (00:18:26):

The large number of BCC experienced by people of all ages were reported in a recent Global Gorlin Syndrome Community Survey. There were 261 responders and the report is available on our website gorlinsyndrome.org. We urge you to review this report. While listening and learning today, I ask that you put yourselves in our places. Wear the boots of affected individuals, adults, kids, parents, caregivers, fiances, and spouses, grandparents. You'll learn that those boots are heavy with pain, scars, worry, fear, and most of all cancer. We live with a stifling lack of confidence and security in what the future holds. We hope that this meeting will encourage future research and successful new product development for

people living with Gorlin syndrome, who urgently need more options. Thank you to the U.S. Food and Drug Administration for giving us permission to hold this meeting and for attending. We're incredibly grateful for this opportunity to share our experiences with you.

Julie Breneiser (00:19:40):

Thank you also to our generous supporters who financially sponsored this meeting. These include Palvella Therapeutics, Sun Pharma, Mayne Pharma, Pella Farm, and LEO Pharma, as well as Feldan Therapeutics and Genentech. We're really pleased to have in attendance representatives from advocacy and professional organizations, drug companies, federal agencies, and universities from across the world. And to the people with Gorlin syndrome and your loved ones participating, this meeting is for you. We invite you to call or write in during the program and asked that you participate in the remote polling as well. We want to hear as many perspectives as possible. Understand that we'll do our best to get all of your comments and calls. Please, only use your first name and no other identifying information should be shared.

Julie Breneiser (00:20:38):

Let's get started. To begin today's meeting, I'd like to introduce Dr. Sally Lewis. Dr. Lewis works at the FDA in the Division of Dermatology and Dental Products within the Center for Drug Evaluation and Research. Dr. Lewis will provide some opening comments from the FDA perspective. Dr. Lewis, thanks for joining us.

Felisa (Sally) Lewis (00:21:03):

Thank you. Thank you. Good morning, and welcome to this Patient-Focused Drug Development Meeting for Gorlin syndrome also known as basal cell nevus syndrome and nevoid basal cell carcinoma syndrome. I'm Dr. Sally Lewis, a Medical Dermatologist and Clinical Reviewer in the Division of Dermatology and Dentistry in the Office of New Drugs at the FDA. Our division reviews drugs for the treatment and prevention of dermatologic and dental conditions, including basal cell carcinoma, which of course is a primary manifestation of Gorlin syndrome. We are one of many divisions that may focus on different manifestations of Gorlin syndrome. We are looking forward to hearing from you, the patients, and your loved ones, and care partners about your perspectives and experience with Gorlin syndrome, and what you consider important about potential treatments for conditions associated with Gorlin.

Felisa (Sally) Lewis (00:22:10):

I'm going to spend a few minutes explaining the role of the FDA and of drug companies and the development of new drugs so that people here today understand where the FDA fits into the process. It is well-known that the drug development process involves a series of many interactions between the two primary actors, pharmaceutical companies, and the FDA. The FDA protects and promotes public health by regulating drug development and research done by pharmaceutical companies and other researchers. The pharmaceutical companies conduct studies of new drugs for medical conditions, such as basal cell carcinoma. When they're finished conducting our studies, they submit marketing applications to the FDA to ask for permission to sell those drugs in the United States. It is our job to review the drug study plans, and then to review their marketing applications, to make sure that the possible benefits of a drug outweigh its possible risks.

Felisa (Sally) Lewis (00:23:16):

If we think that the company has done a good job and demonstrated through the conduct of their clinical trials that the drug does with the drug company claims that it does, which we probably efficacy or benefit and has accurately described the possible side effects, which we call the safety or the risks. And that the balance between the benefits and risks is favorable, then we will allow them to sell or market the drug in the United States. It is important to understand that the FDA is bound by legal statues to provide advice and recommendations to drug companies when they request such when a drug is being developed and to evaluate the overall benefit risk profile of potential drugs for the proposed conditions and patient population. When the company applies to market the drug.

Felisa (Sally) Lewis (00:24:15):

We also monitor the status of the drug once it's on the market. The FDA can not initiate action or direct drug companies to develop drugs for specific medical conditions. So where do patients fit into this process? Patients like you are the reason that drugs are developed. So, it is important that our evaluation of the benefit and the risk take into account, the perspective of the patient who will be taking the drugs. We want to hear from you today to help us understand how patients view benefits and risks of possible new treatments or the conditions that arise in Gorlin syndrome. We want to understand what the patient, as a whole considers clinically meaningful. A clinically meaningful outcome would be one that improves a patient's experience in terms of survival, feeling, and function.

Felisa (Sally) Lewis (00:25:15):

We consider very carefully the kinds of things that could be measured or should be measured, I should say, and looked at when evaluating a new drug and hearing your perspectives on this is very important. Lastly, these Patient-Focused Drug Development sessions are important because you help put a face to a name, so to speak. We appreciate hearing your experiences because you are living reminder of why we do what we do to ultimately help patients. So again, we're looking forward to hearing and listening to you and your loved ones about how Gorlin syndrome impacts your daily lives and what you value in a potential new treatment. Thank you.

Julie Breneiser (00:26:06):

Thank you very much, Dr. Lewis. And now I'd like to introduce Dr. Joyce Teng, who will be presenting a clinical overview on Gorlin syndrome to help create a foundation for the rest of today's meeting. Dr. Teng is a Dermatologist at Stanford University and a Professor of Dermatology there. Welcome, Dr. Teng.

Joyce Teng (00:26:30):

Hi, my name is Joyce Teng. I'm a Professor of Dermatology and Pediatrics at Stanford University. I like to thank the organizer and FDA for giving me this opportunity to give this a presentation on clinical manifestations, disease burden, as well as unmet medical needs, and the management to have a Gorlin syndrome. Here are my disclosures. Gorlin syndrome is a monogenetic disorder, was a tremendous lifelong disease burden. Each of the red dots on various of anatomical locations as shown in these photos to signify a basal cell carcinoma. And you can see that this is to give you a little glimpse of the unrelenting cycles that patient going through in regard to new cancer development, at least surgeries, healing and recovery, as well as the pain scar disfigurement that they suffered throughout their lifetime. The psychosocial burden on work, family and marriage are quite significant. Some of these skin cancer do metastasize and increase their risk of mortality as well.

Joyce Teng (00:27:45):

So therefore there's a significant need for a safe and effective treatment for Gorlin syndrome. Just to give you a little more background on Gorlin syndrome, it's also known as basal cell nevus syndrome or nevoid basal cell carcinoma syndrome. It was initially described by Dr. Gorlin and Goltz in 1964. It's estimated that about one in every 30,000 to 50,000 people in the U.S. may have Gorlin syndrome. And therefore it totals about 6,000 to 10,000 at least affected the population in the U.S.. One in every 200 patients that diagnosed, it was a basal cell carcinoma has this syndrome. However, in pediatric population, this percentage is much higher. As a pediatric dermatologist, if I see a child who's diagnosed with basal cell carcinoma, oftentimes I send them immediately for additional evaluation and genetic testing. So about 40% of Gorlin syndrome patients that carry de novo mutations. By large, it is a hereditary disorder inherited in an autosomal dominant fashion. More than 90% of patients who carry a mutation in PTCH1 gene on chromosome nine, a small percentage of patients have mutations within the PTCH2 and SUFU gene as listed here as well.

Joyce Teng (00:29:24):

World syndrome is a really a multi-system genetic disorder. And the patients that have the many characteristic, the clinical manifestations said that can be classified into a major diagnostic criteria, as well as a minor to assess to clinician in making their diagnosis, and before genetic testing became more prevalent and accessible. So, if a patient has two major or one minor diagnostic criteria, for instance, as listed gene clinical diagnosis can be made, or one major and three minor criteria as listed here. And you can see from this list, aside from cutaneous manifestations of like a palmar pits and many basal cell carcinomas and patients also can have many skeletal disorders as well as CNS and cardiac manifestations. And for instance, the medulloblastoma and that occurred sometimes in the Gorlin children, as I show you some clinical photos as well.

Joyce Teng (00:30:43):

So, here are a couple of patients with either palmar pits or the pits on the plantar surface, frontal bossing, and microcephaly another common manifestation. And here's a less than two year old with a shunt, intracranial shunt that you can see on this picture as well. And this is from a post surgical excision of medulloblastoma. And here are a couple of fib radiological imaging demonstrating the skeletal anomalies, such as by fit ribs and [inaudible 00:31:29] and calcification in the brain. So here's a jam up publication on several investigators including myself as Stanford published in 2017, highlighted the patients was a different risk of factors, as well as the significant disease burden in the U.S. population. And this is really quite a comparable to what has been...

PART 1 OF 10 ENDS [00:32:04]

Joyce Teng (00:32:03):

... quite a comparable to what has been found in Asia, as well as our European colleagues. The Gorlin syndrome population in general has approximately a total of 30% to risk of it having extra courteous in your plasmas and a significant percentage of patients was other complications such [inaudible 00:32:30] as well.

Joyce Teng (00:32:33):

So the data are quite comparable in different [inaudible 00:32:38] groups. And some of these tumors really manifest to at birth, since the birth, like a cardiac fibroma for instance. Very early on, as soon after birth.

Joyce Teng (00:32:50):

Medulloblastoma is another pediatric and CNS tumor, and that occurs in this population. And then as patient ages, there's a quite a tremendous increase of basal cell carcinoma and the other burdens and too including, especially in the female population, ovarian fibroma and it can be quite debilitating and the onset is usually closer to two decades earlier compared to the general population.

Joyce Teng (00:33:25):

So here's a list of current recommendations. As you can see that patients who require a lot of a surveillance and diagnostic imaging throughout their lifetime, aside from regular [inaudible 00:33:42] exam, they may need echocardiogram, a brain MRI, and other diagnostic modalities to follow up with a variety of different sub-specialties. So that's a really quite significant burden on their work and family lives. And this is a very young child that you can see already starts to develop many cutaneous, a small tumor. And this is a tumor that's very close to to the eye in a very young child. Obviously quite a large surgery and defat could result from the excision and that lead to significant disfigurement.

Joyce Teng (00:34:36):

And this is also from our previous publication in 2017 that showing you the number of lifetime basal cell carcinoma by age. As you can see that the basal cell carcinoma starts very early on in children. And then by the time they're in their fourth and the fifth decade, the number has really increased quite expedientially.

Joyce Teng (00:35:06):

And here's some more detail regarding the data that we have collected from a US population. In the average, and there are over 300 basal cell carcinoma per subject from our registry. And in the average patients have to go through over 200 of surgery over their lifetime.

Joyce Teng (00:35:35):

There are many different treatments [inaudible 00:35:38] that are used for basal cell carcinoma, aside from this list of surgical procedures as highlighted here such as a freezing, photodynamic therapy, maybe someone have a surgical laser procedures that can be used as well. Electrodessication, excision, Mohs micrographic surgery.

Joyce Teng (00:36:01):

There are some medical treatments that are currently being used and by larger they are still used especially to topical therapy or off label such as the topical retinoid and itraconazole and several other things, and 5-FU that'd being used.

Joyce Teng (00:36:21):

Hedgehog inhibitor is not so new anymore, but relatively new therapy on the block. And it has to change that many patient's life. However, it does have a quite significant adverse events and the risks associated with the therapy.

Joyce Teng (00:36:44):

So our recent survey have indicated that approximately 40 plus patients that taking this medication have to pause their therapy and have a little therapeutic holiday from time to time due to the adverse events related to it. But you can still see it can be quite efficacious and especially [inaudible 00:37:09].

Joyce Teng (00:37:10):

And here's a patient is showing a couple of the different anatomical locations with numerous in basal cell carcinoma as the treatment progresses. And the number of the tumors has reduced, and you can see on the left-hand side. And this is what the baseline tumor look like. And here's the histology with the treatment. You can definitely see improvement or shrinkage of tumor, as well as both the size and the volume. However, upon discontinuation of the treatment sometimes... In my clinical experience, as the treatment were going on continues that some of the tumor will escape and become resistant once the discontinuation of the therapy and the tumor will start to recur as well.

Joyce Teng (00:38:11):

So there are still a lot of gaps in both our knowledge, as well as management. And I can't say enough about the lifetime disease burden on these individuals and to those are some of the most courageous patients that I have taken care of and watching them going through these process again and again. And it's really heartbreaking.

Joyce Teng (00:38:42):

And there are a lot of gaps in term of the intervention and treatment. We don't have nearly enough information on the safety, and the efficacy, and the choices in term of the therapy for these patients without causing pain and disfigurement to [inaudible 00:39:00]. And there are also gaps in our care delivery as well as patients access to care. And here just listed a few common questions and [amberia 00:39:17] that came up in our day to day care of these patients.

Joyce Teng (00:39:23):

In summary that there's a lot of research and additional improvement in the delivery of the care that are needed and additional investigative research and better defining the size of this population and providing access to early diagnostic tools, education, and to identify some of these care surveillance management gaps and stratify patients risks and engage patients in our care team are very important. In addition, optimize current to measurement outcomes and endpoints, how we measure the safety and the efficacy of these therapies are very important as well.

Joyce Teng (00:40:18):

So this will hopefully lead to better and safer, more effective therapeutic management options for our Gorlin patients. Thank you very much for listening to me. Now, I'm going to send you back to the studio.

Julie Breneiser (00:40:43):

Thank you, Dr. Teng, and thank you again to Dr. Lewis. Larry Bauer is the moderator for today. He's a senior regulatory drug expert with Hyman, Phelps and McNamara where he assists the medical product industry and Patient Advocacy Organizations. Prior to joining the firm in 2019, he was at the US Food and Drug Administration where he was a regulatory scientist. And one of the co-founders of CDER's Rare Disease Program.

Julie Breneiser (00:41:12):

Before coming to the FDA, he worked in clinical research at the NIH for 17 years and the Cleveland clinic for six. It's my pleasure to welcome Larry Bauer.

Larry Bauer (00:41:24):

Thank you for that kind introduction, Julie. I have to say, it's been my pleasure to work with Julie over the last several months to prepare this meeting and to be with you here in the studio today.

Larry Bauer (00:41:35):

Although all of you are virtual, Julie and I are here in Washington, DC in the DC Metro area at a studio live, which is not far from the US Food and Drug Administration headquarters.

Larry Bauer (00:41:48):

So now that we've been provided some fundamental knowledge from the FDA, as well as a clinical overview from a disease expert, we turn to the core of today's meeting, which is to hear from and learn from you individuals, living with Gorlin syndrome, as well as their direct caregivers. We want to hear about the experiences of people living with Gorlin syndrome.

Larry Bauer (00:42:12):

Externally led Patient-Focused Drug Development meetings are a more systematic way of gathering patient perspectives on their condition and on available treatments.

Larry Bauer (00:42:23):

As you heard from FDA's Dr. Lewis, your input will increase the understanding of Gorlin syndrome from the patient and caregiver perspective and will help inform drug development and review. This is truly a unique opportunity today for this rare disease, especially since there are over 7,000 known rare diseases.

Larry Bauer (00:42:47):

While FDA has held many of its own Patient-Focused Drug Development meetings, today marks the 53rd externally led Patient-Focused Drug Development. And due to the ongoing COVID-19 pandemic, the 19th fully virtual externally led Patient-Focused Drug Development of its kind and with thousands of known conditions, this is a unique opportunity for the Gorlin syndrome community.

Larry Bauer (00:43:15):

Today's meeting is going to be interactive. So let me tell you a little bit about what we'll be asking of you and how today's meeting will be organized.

Larry Bauer (00:43:23):

First, we'll be exploring the patient and caregiver experience with living with Gorlin syndrome and its impact on your daily life. And then in the afternoon, our second session, we'll bring everyone back together after lunch to explore the various approaches to treatment, including experiences in clinical trials.

Larry Bauer (00:43:44):

We will also be asking you about your preferences for future treatments as they are developed for Gorlin syndrome. So what will our discussions look like? Today we'll be using three methods. First, we'll be hearing from two panels of caregivers and people living with Gorlin syndrome.

Larry Bauer (00:44:03):

The panelists are there to set a good foundation and to help open up the discussion. These panelists were all preselected and they were chosen to try and reflect a range of experiences of people living with Gorlin syndrome.

Larry Bauer (00:44:19):

So the second way we'll do this is we'll broaden the input through the use of polling questions. These polling questions will be for patients and caregivers only, will use telephones or tablets to respond, and we'll provide instructions when it comes time for the polling questions about how to participate.

Larry Bauer (00:44:40):

You can actually go ahead and get on the system now as once you are on, you'll be able to stay on through the entire day. So if you take out your cellphone or open up a tab on your computer, put in your browser or in the Google search pollev.com/gorlin, and that can be all in small caps, all in large caps, P-O-L-L-E-V .com/gorlin.

Larry Bauer (00:45:08):

Again, feel free to go there now. And we'll be able to get to the polling them very soon. And these polling questions, they're an opportunity to hear from everybody tuning in today that has Gorlin syndrome and who are in attendance, and it gives you the opportunity to aid in the discussion.

Larry Bauer (00:45:27):

And finally, the third way will be to have a facilitated audience discussion with all patients and caregivers listening, the discussion will build on what we learned from the panels and from the polling. I'll ask questions as your moderator, and then invite you to call in on the telephone number that will be provided on the top of your screen. Once your call is answered, you'll be put into a queue or kind of a waiting room until we can join with you live. But please be patient when you call in, you'll still be able to listen to the meeting while you're waiting. So you won't miss anything.

Larry Bauer (00:46:05):

And also when you do call in, please state your first name and where you're calling from before you speak. And then in our afternoon session we'll bring everyone together to explore the various approaches to treatment, including experiences and trials.

Larry Bauer (00:46:23):

There's also an opportunity to provide written comments for 30 days after the meeting. And all of today's input and the written input from written comments and these comments from the next 30 days after the meeting will be summarized into a voice of the patient report, which will be provided to the Food and Drug Administration and available for sponsors, developing new treatments for Gorlin syndrome.

Larry Bauer (00:46:49):

So since this is an interactive meeting, I'd like to just set a few ground rules at the onset. We encourage individuals with Gorlin syndrome and their caregivers to contribute to the dialogue via polling, phone calling and written comments. But it is limited to people with Gorlin syndrome and their family members and other direct caregivers only.

Larry Bauer (00:47:13):

The FDA attendees, drug developers, clinicians, you're here to listen and learn today. And the views that we're expressing today, they're inherently personal and the discussion might get emotional. So please let's respect one another, it's paramount. And to that end, try to be focused and concise in your comments so that we can hear from as many different people as possible. So to move into this next phase of the meeting, we'd like to start with demographic polling.

Larry Bauer (00:47:44):

The first set of polling questions is to help us better understand who's there in the audience with us today. These questions, as I mentioned earlier, are only for people living with Gorlin syndrome or their family members or loved ones.

Larry Bauer (00:47:59):

If you're a caregiver please answer the questions on behalf of your loved one with Gorlin syndrome. So this time, if everybody could go to your cell phone or computer, open a browser or a search site like Google and enter pollev.com/gorlin, and you'll see the first polling question.

Larry Bauer (00:48:21):

Everybody will be able to see your answers once entered and the polling will automatically go to the next question when we move on. So if everyone's ready, let's go to the first polling question.

Larry Bauer (00:48:32):

So question number one, are you an individual living with Gorlin syndrome A, or a relative or care partner of someone living with Gorlin syndrome?

Larry Bauer (00:48:46):

So as you can see, as the bars are moving, this is in real time the answers are coming in as people enter their answers on their cell phones. And it's looking fairly closely, we have a fairly even split The time's almost a perfect split 50/50 between people with Gorlin syndrome, as well as their caregivers. We'll give it just another second here.

Larry Bauer (00:49:27):

Yeah, it's just vacillating very close to the 50/50 mark.

Larry Bauer (00:49:39):

Okay. I think we can move to question number two. So we'd like to know where do you currently reside. A, US Pacific time. 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. Canada, J. Mexico is K, and then other is L.

Larry Bauer (00:50:29):

And the answers are coming in. It's not too much of a surprise that many of the people are in Eastern time. Just about half of the audience. Looks like secondly is US Central time. And then we have just about 15% of folks participating from the West Coast. Welcome to everyone from Canada. There's a group of folks from Canada. We have some folks from Europe, from Hawaii and a couple other places too. Didn't list. Okay. Can we move to question number three?

Larry Bauer (00:51:22):

Are you, or your loved one with Gorlin syndrome, A female. B, male. C, nonbinary. D, prefer not to identify, or E other. I think as we heard earlier, Gorlin syndrome can affect both men and women, boys and girls. Let's see who's with us today in the audience.

Larry Bauer (00:51:56):

Once again, as the numbers are coming in, it looks like it's a fairly close split, maybe slightly weighted toward female

Larry Bauer (00:52:14):

Okay. I think let's give it one more second until the bars stop moving.

Larry Bauer (00:52:22):

Great. So we're about 54% female, 39% male and 4 to 7% other. And question number four. How old are you or your loved one? Birth through five years of age, A. Six to 10 years of age, B. 11 to 15 years of age, C. 16 to 20 years of age, D. 21 to 35 years of age, E. 36 to 50 years of age, F. And 51 years of age or older, G. Once again, as we heard from Dr. Teng, people can develop Gorlin syndrome, sometimes it's identified at birth. And so we see people across the lifespan

Larry Bauer (00:53:22):

So for today, the greatest percentage about a third are people over the age of 51. Then we've got about another 30% in the 21 to 50 year old. So younger adult age group. And then we have almost about another third that's in the pediatric age range, maybe zero to 16.

Larry Bauer (00:53:47):

And then question number five. At what age did you, or your loved one first have symptoms of Gorlin syndrome? So this is just a little bit different. Once again, these are the same age ranges A is birth through five, B six through 10, C 11 to 15, D 16 to 20, E 21 to 35, F 36 to 50 and G 51 or older.

Larry Bauer (00:54:18):

We're definitely seeing a shift here from our last polling question. This is showing that people are diagnosed or not even diagnosed, but have their first symptoms very early in life with the greatest number of being birth through five years of age.

Larry Bauer (00:54:37):

It was interesting when Dr. Teng mentioned that when she sees a pediatric patient with the basal cell carcinoma, she immediately sends them for a broader workup, including genetic testing, because it's so unusual outside of Gorlin syndrome to see kids with basal cell carcinoma.

Larry Bauer (00:55:06):

So, yeah, we have about little over half had their first symptom at birth through five, 26% six through 10, 13% at 11 to 15 years of age, and only 8% older than 15. So almost everybody had a symptom before the age of 35 in our polling. Well, thank you. So that ends our first polling question. So this takes us to our first topic. This is our discussion topic for the morning, which will be what are the, and the impacts of Gorlin syndrome. And to start us off today we have a group of panelists that worked very hard to prepare statements for you today. And we will listen to them next. They will give us an introduction to the symptoms and impacts of Gorlin syndrome. So I'd like to welcome Kevin, Bob, John, Brandon, and Leslie.

Kevin (00:56:15):

Hello. My name is Kevin Golang. My wife, Kristen, and our twin 13 year old sons live in Fort Worth, Texas. Kristen has felt the effects of Gorlin syndrome since early childhood, having numerous benign tumors excess from her jaw throughout our teens and into early adulthood, and is accustomed to having had innumerable basal cells removed from her body.

Kevin (00:56:36):

In her early thirties, a young dermatologist listened to her medical history and for the first time gave a name to her suffering. The timing of this revelation was important because she and I were wanting to start a family, but there was a one in two chance of passing it onto our children. Not wanting to run the risk of doing so we researched the possibility of in vitro fertilization accompanied by a pre-implantation genetic disorder testing, but this was expensive. Fortunately, a family member answered our prayers and loaned us the money to pay for these procedures so that we could try to have children who were unburdened by Gorlin syndrome.

Kevin (00:57:13):

However, the best laid plans of mice and men sometimes do go awry. Kristen went into the delivery in May of 2008 and gave birth to William who weighed three pounds, six ounces, and Patrick at two pounds, 12 ounces. Almost immediately she recognized the telltale signs of Gorlin syndrome in William. Macrocephaly, frontal bossing, and wide set eyes.

Kevin (00:57:37):

William remained in the pediatric Intensive Care Unit for 15 weeks. He was experiencing significant intracranial pressure caused by hydrocephalus, which resulted in incessant crying and continual projectile vomiting after virtually every meal.

Kevin (00:57:53):

We watched in horror as this frontal bossing became significantly more pronounced over the weeks and months. He was diagnosed with sagittal craniosynostosis, which means the bones, the toppest skull refusing to gather prematurely causing his forehead to become quite bulbous.

Kevin (00:58:09):

William was also diagnosed with hydrocephalus and this increased fluid in his brain only magnified the intracranial pressure that he was experiencing. At six months when he was old enough to withstand anesthesia, he underwent a cranial stripectomy in which doctors removed a 17 centimeter strip of bone,

which is roughly the size of a dollar bill from the top of his skull. They also implanted a ventricular peritoneal shunt to help alleviate the buildup of fluid on his brain.

Kevin (00:58:41):

During this time, Kristen underwent surgical intervention to remove both ovaries as a result of fibromas that were discovered during delivery, as well as a benign mass in our lower left abdomen. Both of these are related to Garland syndrome.

Kevin (00:58:57):

William is the happiest child you could ever imagine. His infectious laughter fills a room. But he has a disturbingly deep anxiety about pain, which is a terrible thing for a kid who has to continually go to the doctor with Gorlin syndrome. We try to explain things to them in terms that are age appropriate and for the most part, he understands it.

Kevin (00:59:17):

The annual MRIs to monitor for medulloblastoma became more tolerable over time. But the discovery of his first jaw tumor at age nine was psychologically impactful. His oral surgeon performed a marsupialization to remove the cyst, but the hardware from his procedure impacted him in a way that we had not imagined possible. It made him hesitant to smile for pictures. No nine-year-old should ever be made to feel self-conscious about smiling.

Kevin (00:59:46):

There've been other challenges along the way, resulting from his diagnosis. William can't roll his shoulders due to elevated scapulas from Gorlin syndrome, which makes throwing a challenge. The pain of always being picked last or worse, being left out entirely has turned him off of sports altogether, which is especially difficult because he has a twin brother who is more typical in that regard.

Kevin (01:00:08):

Comparing yourself to others is common. Although he doesn't necessarily verbalize it, not being able to do the same things as his twin is hard for him. During his tenure physical, William's pediatrician was concerned about the shape of his spine. So when appointment was made at Dialysis, Scottish [inaudible 01:00:25] Children's Hospital. His S shaped scoliosis was relatively minor at the time and didn't require treatment. But three years later, it's become more pronounced.

Kevin (01:00:35):

We have an upcoming appointment and are hopeful for the best. But the future is what concerns me and my wife the most. And that's because of our understanding of this cursive condition. He can't comprehend it yet, nor should he concern himself with it at this age. But his mother and I share the same prayer is that every parent of a child with Gorlin's. We pray that he will take his health care seriously, and that he will always have medical providers who understand the multitude and manifestations of the syndrome. But most of all, we pray for the scientists and the pharmaceutical companies who work tirelessly in search of treatments. Thank you.

Bob (01:01:17):

Hi, my name is Bob tuck. I'm from Southwest Florida. For me, life has been and continues to be a bumpy race, a race against my disease. My birth and toddler years were complicated by a very large head, as well as being slow to talk, a speech impediment requiring speech therapy as a child and challenges to this day.

Bob (01:01:41):

Bullying began at an elementary school and was relentless due to my head size. My brain required to go to the speech bus in the parking lot each morning only added to the ridicule. I would seen began having what were called sun cancers burned off my face by my dermatologist.

Bob (01:01:58):

Dental challenges began early as well, losing teeth to what would later be learned to jaw cysts from Gordon syndrome. Through middle and high school the harassment from my very large head would continue. Finding a football helmet to fit was a challenge with it rarely matching my teammates.

Bob (01:02:17):

The scarring from the continued removal of some cancers became a challenge in my teen years, both physically and mentally. My first jaw cyst had grown undetected for years was scheduled to be a routine tooth extraction, evolving into an all day surgery and loss of several teeth. I was 15 years old at the time. Having had many years of syndrome related issues this procedure being the beginning of a Gorlin's diagnosis and the life of reconstructive surgery.

Bob (01:02:50):

What had been previously treated as sun cancers would soon become known as basal cell carcinomas, far more invasive and required repeated removal [inaudible 01:03:00] 10 to 15 at a time, five to six times per year.

Bob (01:03:06):

For me, the Gorlin manifestations escalated with puberty. So my high school years were plagued with many oral surgeries due to OKCs, sinus reconstructions and several hundred BCCs. My friends and football teammates would visit me on weekdays post-op at home or in the hospital, knowing they could count on me to play Friday night.

Bob (01:03:31):

Beginning my sophomore year, my girlfriend, my family and I would make visits to the University of South Florida genetics learning more of my and her future, the risks of having children and my lifelong dream of being a dad.

Bob (01:03:47):

In early adulthood the burden in my life as a result of repeated surgeries and recovery reached an all time high. I began to realize the effects of repeated anesthesia realization that this condition would strive to dictate what I would do-

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

Bob (01:04:03):

... realization that this condition would strive to dictate what I would do and become for the rest of my life hit me hard. I started coaching Pop owner youth football, realizing that I, likely more than anyone else, would be able to demonstrate to young men that life leaves no room for quitting. I showed up at games and practices both bandaged and bloody. My girlfriend and high school sweetheart, previously planning life together, grew troubled over our struggle with childbearing. I found myself growing in a pattern of binge drinking, being quick to embrace a fistfight with the biggest and toughest I could find. Looking back on it, for means of establishing my worthiness, something that Gorlin constantly strives to strip us off. In hopes of fulfilling my dream of becoming an airborne infantryman, as well as having hopes of getting my life on course, I had begin meeting with an Army recruiter. I was forced to hide the truth while trying to prove to myself and others that this disease would not own my life. I would eventually be given a choice to go to prison for a while or join the Army. The latter obviously being my decision. Finally, doing what I had always dreamed of, this also meant that my medical needs would be ignored. It ruined my life would finally take back seat. Following my returning from the Army, the disease burden with reach an all-time high. With several surgeries per year, some very calculated and complicated, both BCCs and OKCs. I will start my own business, there are always been a financial burden brought on to my family by Gorlin Syndrome. The intensity of my disease burden has been relentless. Likely, more so today than ever before. I am 57 years old, two years older than I ever expected to live.

Bob (01:05:58):

I have planned my life around 55 being it. That moment in which all my nuts must be gathered. I can hear the disease invading me when I am idle. The only time I cannot hear it is when I'm creating enough noise to silence it. Therefore, I must work, I must run. You see, living with Gorlin is tough to explain, and even harder for others to understand. We are vulnerable, we are targeted. I compare our lives best to that of the mother hair, whose home is surrounded by wolves. A moment of rest costing her or her bodies their lives. The threat remains constant, peace something others are allowed to enjoy. For us, the battle raids. Thank you for listening!

John (01:06:55):

Hi, I'm John. And while I live here in London, I was diagnosed with Gorlin Syndrome in the U.S. in my early teens. Here's a bit of my story. Thanks for listening. It has affected many of my body systems. I have an enlarged head and especially the forehead and exceptionally thick hair, cut every three to four weeks. I've had Hydrocephalus, Meningeal Calcifications and have frequent migraines. I was born with a congenital cataract and then blinded my right eye. Also, having blepharitis in both eyes. I have painful arthritis in my neck, hands, knees and shoulders. My chest had a mediastinal mass, and I have Dextroscoliosis in my back. Other bony issues include bifid ribs, a missing rib. My legs are turned outward at the hips, which puts me in new shoes every three to four months. I have pairs of web toes on each foot. I have never known or seen a month of my life without at least one or more hospital or doctor's appointments.

John (01:07:56):

My me monocular world has no experience of depth. I have no idea how near or far things are. At six foot, five inches tall with an athletic build yet no right visual field, heaven to help those who are standing or sitting to my right when I need to suddenly outstretch my right arm. People waiting to my right to speak with me, simply assume that I'm rudely ignoring them until that happens. So, with no depth reception, ball sports have been out of bounds for me, for most of my life. So, all that has been left for

me are hiking, running, cycling, etcetera. And now even those are limited. Sports are such an integral part of so many people's lives. Yet as I can't play ball sports, it's difficult to watch them. It's like watching foreign television and a constant reminder of something I simply can't do.

John (01:08:45):

And likely will never be able to. I would give anything to simply catch a ball. These coupled with a lifetime of jaw cysts have made everyday tasks and pleasures challenging. The cysts have damaged the nerves to the lower half of my face. I even can't feel myself shaving. And without my right feel vision, I struggle to see half the face I'm supposed to shave. Without depth reception, I can't tell where the razor is in relation to my face. And without feeling I can't feel it when I've cut myself shaving. And I wouldn't know unless I've spotted the mess on my clothes or more likely someone else has spotted it for me when I get to work. It affects my lips and mouth as well. I would give anything to simply feel the pleasure of a kiss. A mediastinal mass what's put me in front of a doctor telling me I only had weeks, perhaps months at best to live.

John (01:09:37):

And while I survived, it damaged my abdominal one diaphragmatic muscular to the point where I, to lose my breath, it would be difficult to catch this. I found this out the hard way on a high altitude hike last year. I remember it the hard way every time I try to run. They say everywhere is walking distance if you have the time. I don't have the breath. So, I have to take the time. Running isn't an option. A sudden infection in my ankle recently had them telling me, I may have only had hours to live. Financial advisors often warn me of a need for me, maybe not to worry about saving too much for a retirement that I most likely will not live to see. Of course, the ironic thing about that retirement plan would be a medical miracle that would prolong my life.

John (01:10:23):

I just take many retirements along the way. My weakened respiratory system, cranial problems and high blood pressure collectively bring painful, pounding, headaches, nausea and dizziness at random times without warning. I must lie down immediately when that happens so that I can still be in control of when, where, how, and if I wake up. Otherwise, I wake up having vomited all over a room. I don't recall walking into with injuries from a fall I didn't feel. And no idea of how long I've been there or I risk not waking up at all. It's worse than a hangover and without the party. But what life does to you depends upon what life finds in you. I choose not to be defined by the failings of my ability, but to be refined through the furnace of my adversity. My disease may disable my body, but it will never disable my character.

Brandon (01:11:22):

I'm Brandon from Whitby, Ontario, Canada. I'm a 27 year old Gorlin warrior, a two-time cancer. I was diagnosed with Gorlin Syndrome when I was six years old and have many symptoms that have challenged my health over the years. Three symptoms that have had the most significant impact of my life are brain tumor, learning challenges and Pelvic Osteosarcoma. When I was four years old, I was diagnosed with a malignant brain tumor called Medulloblastoma. The tumor made me very sick. The surgery to remove the tumor left a big scar. And the radiation treatments left me with many challenging and permanent side effects.

Brandon (01:12:14):

One of those was an acquired brain injury, which means that my brain works slower and I find it hard to pay attention and to focus. The noise and confusion at school was often overwhelming. I still have trouble with time management and organization remembering things, and often need to be reminded to look after myself. It takes me longer to learn something new, which also affects my employability. When I was 19, I was diagnosed with Osteosarcoma. The tumor, the Malignant Peripheral Nerve Sheath tumor was a long term side effect caused by the spinal radiation treatments I received for the brain tumor 15 years prior. In other words, it came from me having a manifestation of Gorlin Syndrome. This massive tumor was embedded in my pelvic bone and was cutting off the nerves to my leg. I lost the ability to walk. It was inoperable even with amputation.

Brandon (01:13:23):

After a post-treatment surgical Hemipelvectomy, I now walk with a significant limp and require a one inch lift added to my right shoe, to help correct to shoulder leg length and to help with my balance and stability. The loss of muscle and reduced strength makes it uncomfortable to stand or sit for long periods of time, making mobility a challenge and finding a job very difficult.

Brandon (01:13:57):

Last year, I was diagnosed with another brain tumor called Meningeoma. Doctors say it is either a radiation induced Meningeoma from the radiation for the first brain tumor when I was four, or it could be from having Gorlin syndrome because it also happens to Gorlin Syndrome patients that have not had brain irradiation. Either way, it's there. There are other symptoms of Gorlin Syndrome that have seriously affected my life as well. The hundreds of Basal Cell Carcinoma that I have had, and the many that I do still have, have been a difficult and ongoing challenge. My skin looked great during chemotherapy for the Osteosarcoma, but the basal cell Llsions quickly started reappearing when I finished chemo. People react differently to you when you have a piece of your scalp healing from a skin graft after most surgery. It's not a pretty sight and most people don't know how to handle it, what to say, or even make eye contact with you. Makes it very hard to be in social situations, attend events or relationships.

Brandon (01:15:16):

Since the age of eight, I have had five jaw tumors removed. One of those tumors caused bone damage that prevented my teeth from meeting on one side of my mouth. I underwent a surgery for upper jaw expansion followed by three years of braces. Each oral surgery was painful and required a special diet for nutrition and healing. Time away from school. Family had time away from work for my mom.

Brandon (01:15:47):

Before the Pelvic Osteosarcoma, I was able to play soccer, basketball, and other sports with my brother and friends, go for long adventurous bike rides and was learning how to drive a car. Now, because of the damage to the nerves in my leg and the changes to my body from the Osteosarcoma surgery, I can't safely play any sports, propel myself on a bike or drive a car. As I age, the unpredictability of this disease, leaves me feeling anxious that some other serious diagnosis could further challenge my health mobility or that the skin cancers will increase in numbers. If my mother gets older, I am apprehensive about navigating the healthcare system on my own, even though she has been teaching me how to do so.

Brandon (01:16:44):

It's very frustrating. And sometimes disheartening that the seemingly endless list of ongoing issues with my health or actual side effects from treatments for the national brain tumor, part of Gorlin Syndrome. The unpredictability of this rare disease and the resulting side effects of treatments and surgeries have a serious impact on my employability, social life and my ability to be self-sufficient. Concerns that my family and I have for my future are ongoing. Thank you!

Leslie (01:17:24):

My name is Leslie and I'm the mother of Henry who is five years old. For Henry, life comes with many challenges because he has Gorlin Syndrome. Today. I will share how many manifestations of this syndrome have affected him in just these first five of years of his life. He has an incredible story. One is just beginning and as his parents, our mind is always on preparing for what's next. Henry has a twin sister, and when I was pregnant, his head size and large ventricles were of tremendous concern. We had a consult with a Pediatric Neurosurgeon, who told us that Henry had a Hydrocephalus, and we should prepare for him to have surgery, to have a shop place soon after his birth.

Leslie (01:18:03):

Fortunately, a few weeks later, we obtained a second opinion, that revealed that while he would need extra monitoring, chances of a hydrocephalus diagnosis were very slim. At 40 weeks exactly, Henry and his sister, Margaret were born without complications. We felt we had been blessed with two healthy babies. Henry was eight pounds, six ounces with a head that gave me rockstar status among the labor and delivery nurses. An ultrasound of his head shortly after his birth showed that his lateral ventricles both measured within normal range.

Leslie (01:18:39):

Several hours later, I noticed that Henry was nursing quite differently than his sister. A visit from my lactation consultant and then our regular pediatrician confirmed a surprise that couldn't have been detected on a prenatal ultrasound. Henry had a cleft in his soft palate. We soon began regular visits with his plastic surgeon and scheduled his surgery to have the cleft repaired when he turned 10 months old. In his first months of life, Henry had frequent ear infections. He had Tortecollis, which affected his movement on his right side. So, at four months old, we began weekly physical therapy sessions. As he grew, we continued with the PT as he was late meeting some other common milestones for head control, rolling over and later crawling and walking.

Leslie (01:19:28):

Henry turned 10 months old, and it was time for his cleft palate surgery. At this point, I remember thinking, this is it. This is the big one. Once this is over, things won't be so hard for Henry. It was a challenging and painful surgery. Afterwards, we had to keep his arms and restraints for two weeks so he couldn't put his hands in his mouth and disrupt the healing. We fed him with a special square bottle. Soon Henry was able to eat and drink normally and no longer had ear infections. Thanks to the combination of the cleft surgery and the ear tubes. Prior to his cleft palate surgery, I had noticed a lump on Henry's ribcage. His pediatrician thought it might be a lymph node, but it just did not go away. Our pediatrician referred us to the St. Jude's affiliate clinic at our local children's hospital. Little did I know, that would be the first of many hematology, oncology appointments that Henry would need in the first 10 plus years of his life.

Leslie (01:20:29):

After an ultrasound exam, an excisional biopsy was recommended. When the pathology came back, we had yet another unusual and seemingly random diagnosis for Henry. The lump was a Fetal rabdomyoma, a benign tumor that would require no further attention. But as Henry's mother, I never lost that nagging feeling in my gut. What's next? Why do all these things happen to Henry? Are all these different issues connected somehow? Dr. Heather Olson, a neurologist who specialized in genetic conditions recommended genetic testing. And first mentioned the possibility of Gorlin Syndrome. Henry was tested, and it was found that he had a PTCH1 deletion, consistent with Gorlin Syndrome. Getting the Gorlin Syndrome diagnosis was like the pieces of a puzzle finally fitting together. Henry's large head size, the asymmetrical lateral ventricles, the cleft soft palate, the gross motor delays, the Fetal Rabdomyoma, even the differences in his eyes, all minor criteria, but all linked to Gorlin Syndrome.

Leslie (01:21:36):

In many ways, it was a relief to have a diagnosis. We now had a clear path. We now knew what to expect, but it was also overwhelming. We decided to focus first on what seemed most pressing at the time. Careful attention to sun protection and avoiding other unnecessary radiation due to Henry's future likelihood of developing basal cell carcinomas and annual MRI screens for Medulloblastoma. The malignant brain tumor that develops an only 1-5% of Gorlin affected children typically around age two and [00:00:18:12]. Henry was 16 months old when he underwent anesthesia for the third time for an MRI, to evaluate a difference we had noticed in his eyes. This revealed a small grape-like mass in his Cerebellum, consistent with Medulloblastoma, especially giving his Gorlin Syndrome diagnosis. The next weeks would be exactly the nightmare you expect as a parent, who has just been told your child may have cancer. We made gut reaching decisions, while also getting the information needed to prepare for what was next. This time, next would be a trip to Boston, for a more focused MRI on the area with the tumor, along with his spine and a visit with a Neurosurgeon to discuss our options. We went home for a difficult, but very special Christmas with our family. On December 28th, Henry spent most of the day in surgery. His Craniotomy performed, with a aid of intraoperative MRI scans was successful. His surgeon, Dr. Gumna Rova, was able to completely remove the tumor, which he described as still just cells not even a completely formed typical tumor. Mercifully, we have caught the tumor so early. We had every reason to expect a best case outcome. But it wasn't over then since Medulloblastoma is such an aggressive tumor. Henry would need an intensive chemotherapy regimen. And we spent the next half of a year in treatment. Let's fast forward now. Today, Henry is five years old and he has been under anesthesia 20 times for MRIs and eight surgeries, all related to various manifestations of Gorlin Syndrome. Every time he goes outdoors, he must always wear a hat long sleeves and long pants, and he must wear sunscreen every day. And we reapply frequently. He receives weekly PT for lingering, gross motor issues and speech therapy for help with his articulation problems due to his palate function. He has a high frequency of hearing loss. We juggle a number of specialist appointments for him each year, including MRI, neuro-oncology, dermatology, cancer, genetics clinic, cranial facial clinic, ENT and audiology, ophthalmology, neuropsychology, neurology. In addition to his routine, pediatric and dental care.

Leslie (01:24:34):

While now he's three years and five months cancer free. We live with a knowledge that while chances of relapse at this point are statistically low. It is not impossible. Once your child has the brain cancer that only affects one to 5% of the estimated one and 31,000 people with Gorlin Syndrome. Statistics begin to lose their meaning because we know what it feels like to live in that tiny yet unlikely small percent. Now with Gorlin Syndrome combined with the latent effects of the aggressive chemotherapy he received, the

Medulloblastoma will likely be only Henry's first cancer, his first. Living with Gorlin Syndrome is needing to constantly prepare for what is next. Thank you!

Larry Bauer (01:25:25):

Thank you so much to Kevin, Bob, John, Brandon, and Leslie. We really appreciate your openness and being so candid in sharing your very personal stories. But they're very educational and helping us to take first steps in understanding what it's like to live with Gorlin Syndrome, from your perspective. So, now to continue with this topic of symptoms and the impacts of Gorlin Syndrome, let's go and do a couple more polling questions. So once again, if you could pull out your phone or your browser and go to PollEv dot com slash Gorlin. once again, that's PollEV.com/Gorlin. And we'll go to our first question.

Larry Bauer (01:26:13):

The first question is which of the following Gorlin Syndrome-related manifestations or signs do you, or your loved one have, or have had? And in this question, please select every symptom that might apply. A is basal cell carcinomas, B is Jawbone tumors, also known as OKCs or KCOTS, C is a brain tumor, such as Medulloblastoma, D is ovarian cyst, E Palmer pitting, F a large skull, G hydrocephalus or ventricular asymmetry, H improperly formed bones. I mood changes such as depression or anxiety and J is other. So, once again, please select all of these that apply to you or to your loved one.

Larry Bauer (01:27:04):

And we see the answers coming in in real time, And it's looking like basal cell carcinomas is getting the largest percentage closely followed by jaw bone tumors and large skull. Palmer pitting comes next. And then mood changes, such as depression or anxiety are also rating in the top five. But we do have people identifying each of these categories. Thankfully, the brain tumors are in the low range and hydrocephalus is also in the low range, but they're very present.

Larry Bauer (01:28:10):

Okay. So these haven't changed too much with the basal cells, jawbone tumors and the large skull I think being the top three. Now, let's move to question number two. which now we would like you to focus on the top three most troublesome Gorlin Syndrome-related manifestations or signs that you or your loved one have or have had. So, what's been out of all those, you identified in question one, what are the most troublesome? The orders, the same, a basal cell carcinomas, B Jawbone tumors, C the brain tumor, D ovarian cysts, E Palmer pitting, F large skull, G hydrocephalus, H improperly formed bones, I is mood changes, such as depression or anxiety, and J is other. Yeah, this one, I think, we will all learn something here. I don't it's necessarily intuitive about which ones are most troublesome to people, for people to live with. But it looks like coming out on top are basal cell carcinomas, followed by jawbone tumors. And third in third place is mood changes such as depression or anxiety. And on the lower end or the Palmer pitting and the hydrocephalus.

Larry Bauer (01:29:53):

Okay. So the top three are going to be the basal cell carcinoma, jaw tumors and mood changes. So thank you all very much for polling. Please keep this browser open. There will be more polling questions as we continue the meeting. Now, I would like to just review the discussion questions that we're going to use that are going to help frame the discussion that follows now. Just a reminder, we're going to ask you to call in when I start asking about these questions and that number is 7038443231. We ask you just to call in on your cell phone to (703) 844-3231. If you'd like to respond to one of the questions that that I post.

So in this session, we're going to talk about symptoms and impacts. We're going to talk of all the symptoms and health effects, which one to three, have the most significant impact on you or your loved one's life.

Larry Bauer (01:30:48):

Secondly, how does Gorlin Syndrome affect you or your loved one on best and on worst days? Three, how have you, or your loved one's symptoms changed over time? How has the ability to cope with the symptoms changed over time? And four, are there specific activities that are important to you or your loved one that you or they cannot do at all, or as fully as you, or they would like because of Gorlin Syndrome? And five, what do you fear the most as you or your loved one gets older? What worries you the most about you or your loved one's condition?

Larry Bauer (01:31:21):

So thank you! This is, like I said, those questions will guide us. Now, we are joined in the audience by a group of zoom panelists. Good morning, everyone! It's good to see. Good to see you all. Thank you so much for volunteering to kind of help us kick off the discussion. So, as you saw in the last polling question we asked, what were the top one to three symptoms that affect you with Gorlin Syndrome? So I'd like to call on Alice. Alice, can you share with us the top one to three symptoms for you?

Alice (01:31:58):

Sure Larry and thanks for asking. I'm Alice. I live in Shrewsbury, Massachusetts. I have Gorlin Syndrome and was diagnosed in 23. I would say my top three are similar to some of your survey responses. Number one would be basal cell carcinomas, but I would want to point out that for us with Gorlin Syndrome, in my case, I've had four to 500 in the 35 years since my diagnosis.

Alice (01:32:27):

So, we estimated two weeks time for treatment or surgery or topical solution. I figure that's roughly 40% of my life since my diagnosis I've spent in some kind of recovery or treatment or with bandages on my face or something and affected not only by disfigurement and scarring, but also just by disruption for 40% of my time. Second, I would say, would be my birth defects. In my case, that's a cleft lip and palate, bilateral. And for me, that continues to be a problem because with keratosis, like sinuses and jaws and it's always a risk with a soft palate like we are in one of the videos earlier, compromising that foundation, which would then be catastrophic for my mouth and my structure, my face.

Alice (01:33:22):

And lastly, I would say skeletal abnormalities. I have fused vertebrae from the syndrome and now arthritis and bifid ribs. And as I'm getting older, as we all are with arthritis and such, that's chronic pain and migraines daily from that.

Larry Bauer (01:33:41):

Wow. Thank you, Alice. And you mentioned with a, a cleft lip and pallet. Do you also have jaw cysts?

Alice (01:33:49):

I have had some near my wisdom teeth in the back, but mostly I have them in my sinuses.

Larry Bauer (01:33:55):

In your sinuses. Okay, thank you. And John, can you please share with us a little bit about your top three symptoms.

John (01:34:05):

Sure. Thank you! And I do want to thank the FDA and, and the Alliance staff for this opportunity. I'm John from Pennsylvania. I was the first one in my family through mutation to have this syndrome. We didn't even know I had it til I was 24. Although my first jaw tumor was in my lower left jaw when I was four years old. And I hear a lot of this through oral history because I'm the youngest in the family. I have two older sisters untouched by this syndrome and two parents untouched by the syndrome. And apparently one day I came out at breakfast and my dad said, "what's that in your mouth?" And I "I don't know" cause it was this huge bulge in my left lower jaw. And they ran around in Eugene, Oregon in Springfield, our hometown, trying to find someone to tell them what this was.

John (01:35:02):

I mean, the, the discussions range from tumor to cancer. And as a parent now, I can only imagine what they were going through. Fortunately for them, they referred to an oral surgeon in Portland, Oregon, and he became my best friend for most of my young and teenage years. And I had several jaw cysts as a young child. And then went for a period without them and then started having them in my upper jaw. And when I was in my twenties and thirties and the last one I had was a few years ago in 2016. So I've had them all life long, the average normal human adult mouth has 32 teeth. I have only 18 left. Fortunately, they're towards the back. So, I do have some in the front. Most people can't see this from the outside. General anesthesia has become a common occurrence for me.

PART 3 OF 10 ENDS [01:36:04]

John (01:36:03):

[inaudible 01:36:00] has become a common occurrence for me. So, that's probably the number one. Number two is the basal cell cancers. I had my first one diagnosed when I was 24 by a barber who took off my beard and saw this big lump here and said his wife had something like that and it was cancer. I should go see student health. This was fortunately in the university system where I was referred to dermatology. They didn't ask any questions. They just removed it. A little while later, I had another pain in my upper jaw. I hadn't had any jaw cysts or tumors removed for probably seven years, but ENT was looking at me and asked me about my history. And I told them, and somebody there actually made the connection. And that's the first time I heard of this syndrome. And as other people have said before me, I probably have them in the hundreds.

John (01:36:53):

I've been lasered on the shins. I've been frozen with nitrogen. I've been cut. I've been curettage, electrodesiccation, all types of approaches. Mohs in my scalp, I've lost, not only I said, well, it's beyond teeth. I've lost hair, skin tissue. It's now in my ears. And I did [inaudible 01:37:15] to avoid surgery because the problem with surgery and [inaudible 01:37:19] is once, even after you fix one spot, like everybody else has said here before, it comes back. And I think the dermatologist in the beginning was very perfect words. This is an unrelenting situation. I have lived with this from age four, my son has lived with it from probably from birth. He had a cleft palate, so he's living with it now. He had tumors when

he was in high school removed from his upper jaw that were golf ball size and he had to be in the ICU for recovery.

John (01:37:56):

So those are the two major. You've heard plenty of descriptions of them before, but it's just, there's no ending. This is a juggernaut that quietly churns away in your body. It's unstoppable. And you never know when it's going to make an appearance.

Larry Bauer (01:38:13):

Okay.

John (01:38:14):

Whether by tumors, cancer or all the other manifestations that are out there.

Larry Bauer (01:38:21):

Okay.

John (01:38:22):

The other thing I have that I found out was scoliosis and that wasn't much of a problem until as you get older. And I think like Alice said, arthritis kicks in, I now have nerve pain pitching from my lower back, down into my thighs on both sides of my legs. I have been walking dogs since I was in grade school. And now it's a painful activity.

John (01:38:53):

And like other people I've talked about before, it limits your interaction with others. I've had people in my office at work talk about when I come in with bandages or big red scars from the [inaudible 01:39:09] being fried with electric needle. "Oh, were you in a bar fight? Did you have an argument with your wife?" That sort of thing. So it's unrelenting, exposes you to infection. I recently had one removed on my forearm and ended up in the ER overnight, because for the first time it became infection infected in the bloodstream underneath the wound. So it wasn't anything I did. It was just something broke below the scar, below the stitches and was forming an infection all the way up to my shoulder. And I had to have IV. And-

Larry Bauer (01:39:55):

Thank you.

John (01:39:55):

-be in the ER overnight. So this has several manifestations. Mine are primarily the scoliosis, the skin cancer and the jaw cysts. And it has left its mark in my life. And my family. My mother had to spend time driving me up and down the Oregon I-5 highway.

Larry Bauer (01:40:20):

Right.

John (01:40:20):

Every six months.

Larry Bauer (01:40:21):

Okay.

John (01:40:22):

To a...

Larry Bauer (01:40:23):

Well, thank you John. Very much. I was wondering one of the things John talked about, the repeated jaw cysts. I was wondering from the zoom panelists we haven't heard from. Has anyone else have jaw cysts in your top three? Either Jenny, Ronnie or Beth? Can you raise your hand?

Beth (01:40:41):

I. Yeah.

Larry Bauer (01:40:42):

Okay. I saw Roni's hand go up first. Okay. All three of you. One of the thing, a jaw cyst is an unusual symptom that I think most people have never even heard of. I'm curious. Roni, can you tell us about jaw cysts and do you get symptoms before they, or as they progress or are they only discovered on radiologic exams? How does one, someone with Gorlin Syndrome know you have a new jaw cyst.

Roni (01:41:13):

So thank you, Larry. My name is Roni and I'm from New York and my son who's 30 years old has Gorlin Syyndrome. He was diagnosed at nine years old and similar to John. He came in one morning with a swollen side of his face and we thought it was teeth coming in. Didn't think much of it. And that started our journey. And he was diagnosed at that time. And I would say since then, it's more than 20 years, he has had tens of jaw cysts. We monitor him every six months. He goes for panorex's. He goes for MRIs to avoid the radiation treatment. He's had extensive dental work to bring down his teeth with chains because there's delayed development. And it's the stress of constant, repeated surgery. And we were under the misimpression that this would lessen and go away, really, as he became older, which has not been the case, at least in our case.

Larry Bauer (01:42:31):

So he continues to develop new jaw cysts even at 30?

Roni (01:42:34):

Yeah. He had surgery this year.

Larry Bauer (01:42:36):

Okay.

Roni (01:42:37):

For a jaw cyst.

Larry Bauer (01:42:39):

Okay. Thank you. And Jenni, I'd like to talk to you for a minute. It looks like you've recently had some procedures done. Thank you for joining us even. I mean, it looks like maybe that was done recently. Could you tell us about maybe what symptoms that you've had recently that have needed to be treated?

Jenni (01:43:02):

I have basal cell carcinomas. Hello. My name is Jenni, I'm from Northern Wisconsin. Last name [inaudible 01:43:09]. I want to do a comment that what I have gone through or go through, some of you, most of you, I hope don't have to experience. This is more so for our community, the GSA community with children. Yesterday, I went in for a Mohs procedure. Back in June, they removed 17 possible basal cells. My removal is biopsy depending on location. If it's around the eyes, ears, nose, mouth, it's a biopsy. If it's in scar tissue area, where there was a previous basal cell, it's a biopsy. Otherwise, it's EDC. A procedure EDC, which is they basically cut it. And then you go through a scrape and burn process of that area to hopefully remove all the basal cells. That was back in June.

Jenni (01:44:10):

I had the 17 areas for my dermatologist tested. We found out of those 17, I needed Mohs procedures on 1, 2, 3, 4, 5, 6, 7, 8 areas needed further treatment with Mohs. Mohs procedure is a, can turn out to be, which it did for me. Yesterday, actually, I was down seeing my Mohs surgeon. It's a very long day. They take one layer at a time of the area, put it under a microscope to look for cancer cells. Hopefully they come back after that first time and say, "It's clean. The area is clean. There are no more cancer cells." Or in reference to my scalp, and in front of my ear. The front of the ear, they had to go three different times, meaning they had to take samples three times under a microscope. There's about a 45 minute to an hour minute, wait while you're waiting for the results. Then you go back into the room, procedure room, and he tells you if we have to do another round, which means another cut, another microscope, another wait.

Larry Bauer (01:45:34):

Oh boy.

Jenni (01:45:35):

This was three times. The scalp ended up being... They had to go into the scalp six times, which equals nine and a half hours in the clinic.

Larry Bauer (01:45:46):

Well, thank you, Jenny, for sharing that experience and for joining us so soon after your surgery, that was very courageous. I see we have a caller, Sandy from Virginia, that's on the line. We'll get to you Sandy in just a second. One of the things I wanted to ask Beth, was Beth, how have you seen any of these top symptoms change over time? Do they get better? Do they progress? Can you think about that for a second and share with us?

Beth (01:46:14):

Sure. Name is Beth and I'm from Wheaton, Illinois, and I have two children. I have a 16 year old son and a 13 year old son Cole, who is affected. He was born with the skull abnormality. So we went through a typical surgery that you saw earlier to remove the skull and reshape it. He's got three plates in his skull where it didn't close. He was formally diagnosed when he was eight with a biopsy from what we thought was a skin tag. And it was a basal cell carcinoma. He's since had 139, he had removed in one surgery over two hours and he's sedated. He's 13 now, he's had probably over 200 basal cell carcinomas cut or scraped from his body. I would say for us and for him, he is a lover of all sports, similar to Kevin's son. He can't play sports because he can't see very well.

Beth (01:47:13):

He has no depth perception. He's got low muscle tone. So that's been really hard and challenging for him and also for me as his parent to see that. I would say the biggest challenge in his life currently is the sun. He's 13, he wants to go outside, he wants to play with his friends. He has to wear a bucket hat, he has to wear sun protective clothing. It's hard to tell your child, your son, when they want to go outside and play that they should probably stay inside because the UV rays are high that day. It's heartbreaking as a mom to wake up every morning and know that your son has cancer.

Beth (01:47:55):

It will never go away. There will always be more cancer. And every time he goes outside and has any sun exposure, it produces more skin cancer. So I would say for Cole, the basal cell carcinoma, the unending, unrelenting occurrence of that is painful for me as his mother and our family, but also extremely hard for a 13 year old to understand the life he has to look forward to. When he was earlier, after he was diagnosed, he started with some anxiety about all of these procedures.

Beth (01:48:33):

He proceeded to pull out all the hair on top of his head from the anxiety of just knowing what was coming next. He'd wake up at night not wanting to die. And these are words from a 10, 11, 12 year old. So we spent several years with a psychologist which helped him tremendously, but just the emotional weight of this disease on me his mother is extreme. I can't imagine a 10 year old, an 11 year old having to comprehend what the rest of his life is going to look like. So it's been a difficult process for us as a family. Luckily we have a lot of support and we have this incredible community that is with us along the way, but it's definitely a challenge.

Larry Bauer (01:49:22):

Thank you so much, Beth. That just sounds incredible. And the young ages that these kids have to go through is just unbelievable. So let's go to our first phone caller, Sandy calling from Virginia. Are you able to hear me? Are you with us?

Sandy (01:49:37):

Hi there, Larry. This is Sandy.

Larry Bauer (01:49:41):

Hi, Sandy. Yeah, we can hear you loud and clear. What would you like to say?

Sandy (01:49:50):

The last caller that was on just resonates so loudly with me. I'm Amelia's grandmother and she was diagnosed when she was born with Gorlin Syndrome. Thank goodness she had some really good doctors there in Colorado and they were able to diagnose it. And she had calcification on her brain, as well as, her head was larger. Her eyes were sunk in and just several different things that were going on there. And I remember getting the first call from my son saying, "Hey, mom, has anything like this ever happened in our family?" And I said, "No, not that I know of." You know? But ever since then, it's like, she's seven years old now. And I mean, she just goes through, I feel so bad. I just want to cry every single time that she wants to go outside.

Sandy (01:50:51):

I have to put her in these clothes and put on sunscreen and tell her she can't go outside sometimes or go in the pool with her sister or her cousins. And that's really hard to tell a seven year old, that they just can't do that. I mean, that's all I want to do is go outside and play. So just the being taken out of school and looking different and going through all the painful surgeries and just everything she has to go through. Just my heart goes out to every single one of you guys. And if I can do anything to help any one of you or with this Alliance, I would love to do that. So-

Larry Bauer (01:51:33):

Thanks.

Sandy (01:51:35):

It's really. Yeah, you're welcome. Perfect.

Larry Bauer (01:51:38):

Yeah. Thanks Sandy. Actually, by calling in, you are helping and thank you for sharing your granddaughter's story. We also have on the line, Patricia from Canada, calling from Canada. Patricia, are you with us?

Patricia (01:51:50):

Can you hear me?

Larry Bauer (01:51:55):

We can Patricia, go ahead.

Patricia (01:51:59):

Hi. Patricia from, with the Ontario, Canada. I wanted to speak to the aspect of caregivers and family members that are involved with caring for a patient with Gorlin Syndrome. Would that be all right?

Larry Bauer (01:52:12):

Yes. Go ahead.

Patricia (01:52:14):

Okay. So there is a definite heavy disease burden on the patient, but there's also a heavy disease burden on the caregivers and the family members of those helping care for the patient. And there is a lot of mental health issues that can develop from the caregiver side and the patient side. And I believe that's

an issue that leads to manifestations and future stresses on the body and the health and the recovery of not just the patient, but the entire family. And from our experience, that is an issue that needs to be addressed as well as to finding better solutions. Seeing what our loved ones go through with this disease is extremely stressful. And it's really hard because the future is so unknown and you don't know what they're going to be facing next. And when these things might happen. If they're going to have the support they need at the time. All kinds of things go through your head. I'm sure many parents on here and other caregivers can appreciate my comments. And that's basically what I wanted to say. I mean, it's so important that we also recognize the burden on the caregivers on this journey, because that is the best support system that the patients have sometimes. And sometimes it gets to be a little much. So if any of the other caregivers out there need any support, find a way to contact me through the organization. I'd be happy to help.

Larry Bauer (01:53:47):

Thank you so much, Patricia. Yeah. Thank you for sharing that perspective on the effects of the family. Very important aspect to this disease. Julie, I was wondering, do we have any written comments coming in?

Julie Breneiser (01:53:57):

We have a number of great comments, Larry. Thanks so much. The first is actually from a woman that I spoke to on Monday. Maybe it was Wednesday. Anyway, Connie from Lawrenceville, Georgia, her story speaks to the delay in diagnosis. She wrote, "My 32 year old daughter was diagnosed with a medulloblastoma when she was 15 months old. She had two years of chemo followed by radiation to whole brain and spine at the age of three. She's had multiple meningeomas in her brain, ovarian fibromas as well as multiple basal cell carcinomas. Just last week, a very astute physician assistant," go PAs, "suggested she had Gorlin Syndrome and that diagnosis has been made." So she had all the classic puzzle of pieces and finally, at the age of 32, they made a diagnosis. So that's a really impactful comment in my mind. Another comment here came in from Boston. Dolores writes, "When you're missing the gene that inhibits tumor growth, there always seems to be something growing.

Julie Breneiser (01:55:11):

The weeks or months between symptoms being diagnosed should be a relief. Instead, the reprise is just the waiting room for more cutting, draining, or burning. It's a constant cycle, a riptide of anxiety, fear and resentment." I have multiple other great comments here. Maria from Pittsburgh writes this regarding her affected son, "The daughter explained that the LeFort procedure that he wanted to do included breaking my son's jaw beneath his nose, and basically cracking his head open, like an egg, in order to get the best access to clear the cysts." And from Colorado, a comment from Ave, "I'm in my twenties. Over the next four weeks, I will have Mohs three times on at least 11 BCCs. When I was 11 years old, I had what we called a surgical summer with an operation to remove a calcified ovarian fibroma that was the size of a grapefruit. A month later, two jaw cysts had to be removed, followed by surgery to remove multiple basal cell carcinomas. That's for an 11 year old."

Larry Bauer (01:56:24):

Wow. Thank you, Julie. Yeah, that was one symptom we haven't heard before about ovarian tumors and, but a great fruit sized ovarian tumor's significant. Well, thank you everyone. I'd like to just shift gears slightly here. So I'd like to start this next little section with another polling question. So if everybody could, once again, take out your cell phone or your laptop and go to PollEV.com/Gorlin. And

this question is, what specific activities of daily life are most important to you that you struggle with or are not able to do because of Gorlin Syndrome? And please select the top three. So "A" is, impacts on your travel or vacationing. "B" is, spending time outdoors. "C" is, participating in social engagements or events. "D" is, participation in sports or recreational activities. "E" is, attending school or having a job. "F" is, all of the above. Or "G" is, other. So what are the top three things that you see on this list that, how does Gorlin Syndrome impact your life and your activities? You know, daily activities of daily living?

Larry Bauer (01:57:50):

And as we see the answers coming in, there's clearly a leader in "spending time outdoors". As we just heard, when we heard our caller talk about her seven year old granddaughter and having the anxiety about every time she goes outdoors and having to put on sunscreen and hats. Secondly, is "participation in sports and recreational activities." These are once again outdoor activities. But we have people answering each of these and selecting each of these items. Vacationing, social engagements, attending school, and there's at least 10% of you that say that you have all of these symptoms, all these impacts on your life.

Larry Bauer (01:58:44):

Okay. So could we go back to our zoom panel? Maybe to talk about this a little bit more? So I was wondering, would any of you like to talk about the impacts on your lives and the impact on your activities in your life due to Gorlin Syndrome? Please raise your hand if one of you would like to speak. Beth. Go ahead.

Beth (01:59:08):

Yeah. We have two sons, so it's a struggle to do things, family things, family vacations, go to sporting events with one son who's healthy and the other son who has Gorlins. It's a balance and anything outside is a struggle. Water sports, they love water sports, being in the water. Every time we're outside, it's harmful for Cole and it's just hard as a parent to balance their life and their growing up and their childhood being taken from them with, knowing that every time they're exposed, you're going to have surgeries down the road. So, it's hard as a parent and I appreciate the woman who called in and talked about the caregivers and the effects on the caregivers.

Beth (02:00:04):

It's very... It's exhausting as a parent to struggle with the balance of letting your child grow up and have a normal childhood, but also knowing that you need to take these steps to protect them from surgical procedures and cancer growths and all that comes along with that down the road. So, it's a balance. And when you have one son who's healthy and the other son who has these limitations, it's difficult to give them both what they need and taking care of Cole and making sure that he's not being negatively impacted by the activities that we're doing as a family.

Larry Bauer (02:00:42):

And Beth, you mentioned that your son, that he's had many basal cell carcinomas and they've had to be treated and he's had to suffer through those treatments. Does he make the connection? Is he able at that young age, able to realize that going outside is what's going to lead to him having to go to the hospital and have these procedures?

Beth (02:01:03):

Yeah, I think he does, but he still, every morning, part of our school routine is putting three different topical medications on his face, some to some topical chemo to get rid of the spots that are the lesions that are growing, we have to put on the sunscreen. And he absolutely, I think, understands. He's 13. He understands that not doing that is going to cause more surgeries, but at the same time, he's angry. He's angry that he has to get up and go through this process every morning, every night. And all of his friends, this is not part of their lives.

Beth (02:01:39):

So it's a... it's really hard as a parent to pick your battles with this disease and let them be... Have somewhat of a normal life. But also knowing that I have to keep this treatment. And I know Julie and I have talked about this. At some point, he's going to have to handle this on his own. And that's a constant worry for me that he's going to put sunscreen on and take the proper precautions and see his doctors. And as a parent, I worry about that tremendously when he's no longer living with me, how he's going to be able to handle this medical care because it's overwhelming.

Larry Bauer (02:02:22):

Yeah. Does anyone else like to weigh in on this, about the impacts that you've had on your life from Gorlin Syndrome on activities? Sure. Alice.

Alice (02:02:31):

I would say kind of from the opposite perspective of Beth as a parent who has the syndrome with a child who I feel blessed every day to know that does not have a syndrome. It's been a challenge for me. And just trying to keep things as normal for him and have him not be affected by kind of being sucked into the routines and the stress of being treated all the time. I know when, for me, I was always out doing, out in the sun, but trying to protect myself and keeping things as normal as possible so that he wouldn't have to worry about being different like I had when I was growing up.

Alice (02:03:12):

But as I've gotten older, it's harder with daily migraines, with treatments that end up leaving us this figure, like in having surgeries around my eyes. My eyes don't close completely so I have other eye issues and at the risk of a big reveal, this is a wig. And one of the treatments that I've done has eliminated my hair growth. So even though I've hidden it for 50 years, it's now not something that I can hide. And I feel embarrassed for him. The issues we have, it's fine when I'm out in public or when I'm working, it's not as obvious there's something different about me that I've been able to hide before.

Larry Bauer (02:03:50):

Thank you, Alice, for sharing that.

Alice (02:03:54):

Yeah.

Larry Bauer (02:03:55):

And for showing us what you've gone through. So are there, what are some of the emotional impacts as a mom with Gorlin trying to raise a child?

Alice (02:04:10):

I think that was some of the things I was touching on. I don't know if somebody else wants to chime in, are there other moms with children? Go ahead, John.

Larry Bauer (02:04:17):

Go ahead, John. John, go ahead.

John (02:04:19):

Yeah. Well, our son, Kyle, beyond the effects of the syndrome on him, he is also high functioning autism and he only pays attention to things that he's truly interested in. And that's a limited range of subjects, and unfortunately does not include his health.

Larry Bauer (02:04:39):

Hmm.

John (02:04:39):

So he's now 31 and we've routine off and on gone with him when he's gone to visit the dermatologist to make sure he talks to him about all the issues he needs to talk to him about. Fortunately, he has got a good team here at the Hershey Medical Center of Penn State with Dr. Billingsly. And we've also developed a very good relationship with his dentist who's also mine. He finds this quite fascinating, 'cause this is his first time with this syndrome. So he's keeping track of doing biennial, every two year panorex's on our son to make sure Kyle keeps up with his jaw health.

John (02:05:22):

And Dr. Billingsly and her staff are tracking him or his skin health, but my wife and I aren't not going to be around the rest of his life. And that is a constant worry for us that he's... And who knows what doctors he'll have in the future and how mentoring they will be in helping him manage the situation. So that's a daily worry. I used to have a nice full beard, but [inaudible 02:05:55] left being unable to grow one. And my hair is much thinner, so I'm constantly reminded every day that I have to shave when I used to enjoy going days without having to worry about my face at all. And it used to cover some of the scars, but... So yeah, you wake up with us every morning. And like I mentioned before the back pain and leg pain, so it's a daily, daily issue-

Larry Bauer (02:06:19):

Daily issue.

John (02:06:21):

-for many of us.

Larry Bauer (02:06:21):

Okay, thanks, John. We have a caller, Ann from Maryland. But before we get to Ann, I wanted to go to Jenni. Jenni, how has having Gorlin Syndrome impacted your activities in life and the things you like to do?

Jenni (02:06:37):

Thank you, Larry. Again, I got to echo what my other panelist here has said. This just doesn't affect me. This affects anybody in my circle, in my family, in my friends, when we're planning events. They have to plan, is there shade? Are we going somewhere where there's shade? Can Jenny find shade? Do we have to plan our events during cooler times, in the evenings or early mornings? We recently went camping and it was a group of us, RVing and they took the boat for drive on the [inaudible 02:07:23] which is multiple lakes connected. We had two boats, we had to get a special boat with an awning for me. Luckily some of our friends let us borrow one. They proceeded to go to a sand bar where they got out with their lawn chairs and their balls and all their adult fun things. And my nieces and nephew had their toys that couldn't go, couldn't even get out of the boat. I had recently had biopsies done on my legs and my legs had open wounds. So I couldn't get out of the boat to go enjoy my family and friends in the water.

PART 4 OF 10 ENDS [02:08:04]

Jenni (02:08:01):

Family and friends in the water. It affects everything. Every day, we have to think of it. Making plans, we have to plan for it. If you're planning a vacation with multiple people, it affects everybody in that group.

Larry Bauer (02:08:21):

And Jenni, are you currently working or...

Jenni (02:08:26):

I am looking to collect disability. I was on a cream. I believe my treatment was a topical cream that caused my autoimmune system to go into overdrive. And as a result of that and family history, I now have autoimmune issues. I have connective tissue disease which affects my whole body.

Larry Bauer (02:08:55):

Wow. Okay. Well thank you for sharing. So let's go to our phone call, to Anne from Maryland. Anne, are you with us?

Anne (02:09:09):

I'm on now, right?

Larry Bauer (02:09:10):

You're on now. Anne, we can hear you. Yes.

Anne (02:09:14):

Excellent! I am calling because I have Gorlin's. I was not diagnosed until I was in my thirties. I'm now in my fifties. And one of the things I wanted to offer was the perspective of having problems, medical problems throughout your life and being a teenager. And so we've heard from parents, and we've heard from other caregivers, and we've heard from adults with the disease, but one of the things that just jumps right out... I have other things that happened to me, and I can see the patterns. So, for example, I had a head injury when I was 13 and died and was revived and grew through my teen years with a real sense of mortality. And then chronic disease crept in and Gorlin's, just being the syndrome it is, when one is young and faces something that is never going to end, that does affect everything about them, a real understanding of how precious life is, can be founded in that time, but it also has costs.

Anne (02:10:28):

And so people say... I've heard today things like, "And then there were years when I was drinking," for example. And it's that conviction that this burden is on you for the rest of your life that may make you choose self medication, or it may make you choose investing in some sort of worthy future, but nearly obsessive dedication to things. So that teenage years really is key, and managing people psychologically through that is so important. And I didn't hear anybody really discussing that yet.

Anne (02:11:15):

And then, other, people have talked about how Gorlin's affect everything you do. Recently, I was diagnosed with breast cancer and the treatment for breast cancer always has to go through the filter of, "Well, will this have any effect on the aspects of Gorlin's that I manifest?" It is unrelenting, and that's all I wanted to say.

Larry Bauer (02:11:35):

And Pat, could you tell... or Anne could you tell us a little bit about that, being as young as you are and having to cope with your mortality, that is not typical at that age. How do you cope?

Anne (02:11:53):

Well, in my case, I can talk about myself. And I think that psychologically, looking back now, psychologically it was one pathway that was pretty well-trodden by others who had faced mortality. And my particular method was, having faced down death at 13, I every day said, "If I were dead tomorrow, which is a likely possibility because [inaudible 02:12:20] do I want to have done this?" You know, whatever the "this" was. Typically, this was clean your room, make your bed, do your homework. No, of course not. If I were dead tomorrow, I would like to have had fun. Well, that is a terrible way to get through to adulthood, you know? An it takes a lot of mental management to step back from that and demonstrate to yourself that you are going to make it longer.

Anne (02:12:45):

And then there were people I knew who had juvenile diabetes, for example. And they would say, "Well, if I make it to 20, that's going to be some sort of miracle. So I also am not doing my homework." But then there were others who had faced down death and they're like, "I'm going to make the day meaningful," and so it was all about self-sacrifice and giving to others, which is beautiful, but also a burden. So either of the extremes really do result in not healthy behaviors, but it's very difficult to manage that if you're not recognizing, that's what you're seeing.

Larry Bauer (02:13:19):

Wow. Thank you so much for sharing that story. And for once again, this is the second time now that we've heard about potential alcohol or drug abuse related to Gorlin Syndrome, as a method of coping. We have another caller on the line, Erika from Massachusetts. Erika, are you able to join us?

Erika (02:13:41):

Hi. Yes, hi. Can you hear me?

Larry Bauer (02:13:43):

We can hear you loud and clear. Go ahead, Erika.

Erika (02:13:47):

Thank you so much, Larry and Julie, for putting this together and for the FDA for giving us the opportunity to chat and speak about the range of issues with this. I live in Boston. I have a daughter who is 11 years old with the Syndrome who has had multiple manifestations, mostly jaw cysts. She's had about four surgeries since she was four, multiple basal cell carcinomas. And one thing I want to touch on, just building on the idea that these kids, as a caregiver, you basically have a medical time bomb in your hand. And one of the previous callers spoke about the mindset of how you have to approach this on a day to day basis. And it hit me about a year ago where I was talking with my daughter, or she was speaking to me, and I wasn't even looking at her. I was examining her. And I realized how many times [inaudible 02:14:40] everything she's saying, because I'm staring at her eyelids, or I'm staring at her jaw, or I'm wondering what's happening with her ears.

Erika (02:14:46):

And you become this clinician instead of a parent, and it really takes the joy out of it. Or doesn't take it out. You forget the joy of what it's supposed to be like for a parent because you have a medical time bomb in your hand. And one of the things I do to cope... everyone talked about the coping mechanisms, or some people did... you have to live. I think of it like the clouds in the sky and then the ocean. But then the ocean is total reality and the clouds are total denial. And you just got to float between the two of them like a bird. Because if you dip your foot too far into the reality of the ocean, you're going to drown. And if you go too high up, you're going to miss something. And it's just a constant state of panic, unless you can pare back.

Erika (02:15:32):

We also have two other children who do not have the Syndrome, and it's been very apparent the feelings of resentment that one of them has towards the attention that the other is getting for these procedures. And it's ongoing. It's not something where you have the conversation about, we found a tumor, or we found a cancer once, which is enough for any family or marriage to have, just once. But when you're having the, " Oh, we found the 11th tumor and you're going to miss your vacation because Sam has to have a procedure on Monday," it's a lot of resentment, and that's the whole psychological 360 of this disorder. That is, it is just a train wreck. I said to my husband one day, "If you knew you were going to get hit by a train every single day, would you even get out of bed?" That is what this is like.

Erika (02:16:26):

And I'm so grateful for this opportunity to realize that it's not these viable treatments that are viable for someone, if they have cancer once or twice, are viable options. But if a viable option is considered maintenance, then that's the issue is that this is not a maintainable viable option. If you keep cutting and cutting and burning, there's only so much skin and epithelial tissue. And I think the idea behind getting better treatments that are maintenance and getting to the core of it, instead of just putting a Band-Aid on something, it needs to go deeper than that, for viable options is a different definition for Gorlin's patients.

Larry Bauer (02:17:11):

Wow. Thank you, Erika, for those very vivid descriptions. The one about being a bird needing to stay between those two realms was incredible. It almost sounded like you have to fly with never touching ground, which just sounds exhausting. Julie, do we have any comments coming in on this topic?

Julie Breneiser (02:17:31):

We do have some comments, and I'm going to start out with my own. As a parent of young adults, I have done my best now to hand off the care to my kids. I've provided them with names and phone numbers of practitioners that they need to see where they live, and, to a degree, it's very hard to hand over the responsibility of care and without being a nagging, "Have you been, when's your next appointment?" type of parent. Anyway, that's a perspective from an older parent. So going now to the comments that I have, there's one from Roni, in California. These are on impacts of daily life and quality of life: "Gorlin Syndrome impacts my life and the life of my family every day, all day. Scheduling surgeries, recovering from surgeries, the anxiety of more surgeries, time off from work, deformities, pain and the pain of our loved ones who suffer as well. Staying out of the sun without suffering and losing life's precious gifts."

Julie Breneiser (02:18:41):

Really impactful stuff. Toby, from Maryland, writes, "My uncle and mother had so many surgeries, grafts, radiation burns, et cetera, that they seldom went out in their later years. People stare at oddities. This disorder results in severe disfigurement, especially to one's face, causes lots of downtime, and as one recovers as one recovers from various surgeries, blistering, scabbing, bleeding, erosion from the various creams."

Julie Breneiser (02:19:14):

And Trudy, from Pennsylvania, writes, "I'll have surgery every two months, because if I don't, this disease will become unmanageable really quick. I already have 11 to 14 skin cancers removed every two months. I use my vacation days solely for Gorlin Syndrome appointments, so I can maintain employment to finance this relentless disease."

Larry Bauer (02:19:42):

Thank you. Thanks so much. And I see we have a caller, Elizabeth from Utah? Elizabeth, are you on the phone?

Lizzy (02:19:56):

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

Larry Bauer (02:19:59):

Yeah, we can hear you clearly, Elizabeth. Go ahead.

Lizzy (02:20:03):

Perfect. Just listening in and hearing the comments of somebody that had an ovarian cyst. And you said that you hadn't really heard that; that struck a chord with me. At the age of 12, I looked six months pregnant. I had an ovarian cyst that was... well fibroma, that grew to be football size in a week. Essentially, it took out one of my ovaries. And growing up, as I started dating and seriously dating, my older brother and I both have it as well as my mom, my mom took the time to pull our spouses aside and say, "This is something you need to know about."

Lizzy (02:20:50):

And I am lucky and blessed to have three kids of my very own. Of the three, only one of them has the Syndrome. And we are dealing with him. He has had cleft lip, not the palate, luckily, and he's also has the ribcage issue where one of one side of his ribcage is now sticking out a lot, and the other side is going in. But I've dealt with the day to day life of impacting my life in the fact that I worked at my dermatologist's office, he's my uncle. I worked at his office, and while I was working there, I would even have surgeries, clock out, go have a surgery, come clock back in, and get back to work. It got to the point that when new 20-something year olds would come in with their very first skin cancer, that the MAs would say, "Oh, just go out and talk to Lizzy on your way out. She can sympathize with you better than any of us can."

Lizzy (02:22:04):

And to have them come out with tears in their eyes and say, "Wait, you've had this?" and I explain that I've had hundreds removed, and all of a sudden life wouldn't seem as hard for them.

Lizzy (02:22:21):

While some people talked about their coping techniques, I don't drink. Wasn't raised around that and have no intentions to. But for me, my coping technique is, and this is going to sound bad as a Gorlin Syndrome patient, is I have to take time off mentally for myself. I take that time off to refocus. I have a lot of anxiety even going in for surgeries that my dermatologist, even the MA staff that I worked with didn't even understand. It's the building up the courage to go in for that surgery after you've had the biopsies. Building up that courage takes a lot.

Lizzy (02:23:06):

There are frequent times that I'm walking in at the last minute for my Mohs surgery appointment because I'm giving myself a pep talk in the car, that I can do it, but it is hard. I mean, my mom works there now. Julie commented about being the parent. My mom works at that dermatology office now. And so she'll say, "Hey, it's that time to book your skin check. And I say, "Yep, you're right. I'll call you when I feel like it." It's hard. It's hard to be a parent, a mom, and take time for yourself, let alone working with the child aspect of it too.

Larry Bauer (02:23:46):

Elizabeth, can we go back? Earlier you said you had the ovarian cyst when you were, what age?

Lizzy (02:23:54):

12. At the age of 12, I looked six months pregnant. It was...

Larry Bauer (02:23:59):

That's such a vulnerable age for any child, a 12 year old young girl. What was it like for you? How did that impact your life? Looking like you were pregnant?

Lizzy (02:24:14):

I think the blessing for me was that it grew in a week. So I didn't look...yeah. They kind of wonder if it was sitting a little bit lower at first, but it really pronounced itself within a week's time. And they didn't know if it was a solid mass or just fluid. They couldn't see any of my internal organs until they went all the way to my sides. It just covered my whole abdomen. So I actually have a scar that goes from down

low, kind of, all the way up and around my belly button. They thought they would only have to go to my belly button, but it was a solid mass that took over my one ovary that they were able to get it all out in one piece. And it was football size.

Larry Bauer (02:25:10):

Wow. That's incredible. Well, thank you. Thanks for sharing that story and for sharing all the aspects of your story. We have a final polling question for this morning. So I'd like to go to polling question number four. Once again, on your phone or laptop it's pollev. com/gorlin. Please open that in a browser. And we will go to question four. So this question is, "What worries you the most about your, or your loved one's condition in the future?" And we ask that you select the top three from this list. So this is: "A: The stress of not knowing how Gorlin Syndrome will progress, B: Increased basal cell carcinomas, C: Worry about social impacts, D: Facial scarring, E: Passing it on to your children, F: The time commitment for treatments and recovery, G: Fear of dying H: All of those above, and I: Something other than what we have on our list here."

Larry Bauer (02:26:17):

So please choose the top three from this list, that these are your worries for the future, for either yourself or your loved one. And the answers are coming in, in live time. We'd heard some about people expressing the anxiety that they have, and that's where we're getting the largest number of votes, for the stress of not knowing how Gorlin Syndrome will progress. That was about a third of our responses. The next biggest worry looks like it's the increase in basal cell carcinomas. The next three after that, it looks like we have facial scarring, the time commitment for treatments and recovery, and then there's a significant number of answers that are all of the above. But there's some people have selected all of these things. Okay. So, thank you. I think the stress of not knowing how Gorlin Syndrome will progress has definitely come out on top. So now I'd like to go back to our Zoom panel. Roni, would you be willing to share with us, what are your worries and concerns?

Roni (02:28:01):

So I actually put all of the above. I thought it was a laundry list of all the things that kind of keep me up at night, when I go there. And I try really hard not to go there. I agree that that first point was the most persuasive and the most powerful for me, because I say it feels to me, I like the clouds and water. I always say it's like living on a volcano, that you absolutely have no idea what's coming next. And that, you know though, it's coming. But it's a disease of such variability and a lack of data, a lack of reliable information that could give you a chart forward to say, if you have X, you're likely to have Y. I would add also just this idea that's come out as a parent, the idea of transferring your child's care to them, is something that really worries me.

Roni (02:28:58):

Another thing that worries me that was touched upon very briefly, which is the limitations of treatment for other diseases, because you have Gorlin Syndrome. So it limits the diagnostic and treatment opportunities you have if you're diagnosed with something else. So, for example, when my child breaks a limb and they want to do an X-ray, I'm like, "Nah, I think I got this." I think, "You're going to put him in a cast no matter what." Well, that's a really big compromise for cancer treatment. If someone's diagnosed with cancer, you can't have a lot of the treatments that are considered very common. So I would say that's something that I worry about as well.

Roni (02:29:42):

The grind of it, the daily grind of it, it never leaves you. So you don't have that moment in life where you have that release where you could say, "I just don't need to worry about this for now." I think these are all things that really, kind of, when you go, there consume you, consume me, consume our family. And, as other people said, it doesn't affect only the person who has it, or even the caregiver. It's your entire family, and how you spend your time, and what you do with it.

Larry Bauer (02:30:23):

No, that's a great point, Roni. I never really thought about that, about how often some type of radiation or X-ray is used to diagnose so many medical problems. Did that situation with a broken leg actually happen? Or is that your thinking?

Roni (02:30:37):

Oh yeah. Like broken bones, right? In general. Your kid falls. Do you give them an X-ray? I'm like, "No," like, "I don't think so." Is your treatment, could it be any different if you confirm this or not? Let's [inaudible 02:30:54] that. And that also just doesn't even go to cancer treatment, right? So radiation therapy, that's not an option, really. So you have to weigh all these things, and sometimes you consent to those diagnostic or treatment tools because you know that it's necessary. But other times, you don't, whereas the average patient would. And then the question is, how did it compromise your treatment and your outcome?

Larry Bauer (02:31:25):

I could see that. I mean, a fracture, sometimes they're compound fractures, sometimes they're complicated and need surgery, but if you can't do an X-ray to determine that, I could see how that would make it very challenging.

Roni (02:31:36):

Or, Larry, you do it, but you feel horrible about it. Right? So, sometimes you do... often you say yes, right? So it's not an absolute that you say no. But you have to weigh it really carefully, and that's a burden.

Julie Breneiser (02:31:52):

And I think, I'll jump in with a point here. Obviously, if it's a life threatening situation, you have to go with what is advised. But you also live with that fear that you are fertilizing the garden of basal cells by having any form of ionizing radiation, whether it's an X-ray for a broken bone or a CAT scan, because maybe you've got diverticulitis, and radiation therapy is something that really should be avoided unless it's the last option available.

Larry Bauer (02:32:26):

Yeah. And Beth, I was wondering, you've got a young son. What are your worries for the future for him?

Beth (02:32:34):

Yeah. This is a sad thought that I have sometimes, but honestly, sometimes I wish that he had leukemia or a brain tumor or something that was treatable. And we could say, "Now you're in remission, and we can move on from this." There will never be a day that I will wake up when I will know my son is cancer-

free, and there will never be a day for him that he will wake up and say, " I am cancer free." And one of your callers touched on the mental aspect. And I think she was absolutely right. It's so under-focused. We hear "cancer," and we just put all our resources into trying to fix the cancer, but that emotional, for a young child to be worrying about waking up, when he is 10, 11, 12 years old, at night, to be worrying about dying is just so unnatural and so horrifying as a parent.

Beth (02:33:29):

And I tried to walk him through that once. And we talked about Jesus, or we talked about seeing his grandparents, and I realized in that moment when it just made it worse, that, as a parent, I'm not equipped to have those conversations with my 10 year old. I'm not emotionally equipped, and he's not emotionally equipped for my answers. So then we had to get a psychologist involved, and it's helpful. And I would encourage anybody who's listening today, if you haven't had that intervention with somebody who can deal with the emotional... I feel like the emotional toll of having Gorlin Syndrome is as much or more than all the physical symptoms that we see.

Beth (02:34:11):

And it so often goes undiagnosed. And it's horrifying as a mother, to watch your child have these unnatural thoughts because of this disease. So it's just, it's exhausting. It's daily. Alice and I were texting... every morning I have to wake up, and he has to wake up and intentionally have positive thoughts so that we don't let our heads go to, and our brains go to these places of dealing with this syndrome. So it's really, it's exhausting.

Larry Bauer (02:34:44):

Thank you, Beth. We have a caller on the line. I'm hoping that Barb from Florida is with us. Barb? You know, we're talking about worries for the future. Are you with us, Barb? Can you...

Anne (02:35:01):

Yes. Yes, I am. I can hear you.

Larry Bauer (02:35:03):

Thank you for... Barb's been in the queue for a while, and we thank you for sticking with us. Barb, would you go ahead and share? Like I said, we're talking about our worries for the future.

Barb (02:35:15):

My daughter has Gorlin's. Her name's Jennifer Werkmeister. And my worries for the future for Jennifer is they removed brain tumors when she was nine. And they found more when she was... in 9/9 of '99. My worries is, am I going to get that phone call one day? That, and Jennifer had her surgery yesterday on her Mohs. And the one on top of her head didn't come back with a clean margin. And what are they going to do now that she doesn't have a clean margin?

Larry Bauer (02:35:58):

That sounds incredibly stressful.

Barb (02:36:03):

For both me and Jennifer.

Larry Bauer (02:36:05):

Yeah. Well, we send our best wishes for Jennifer, for her recovery from that. So thank you very much for...

Barb (02:36:13):

Well you can tell her, she's on your panel.

Larry Bauer (02:36:17):

Oh! Jen. This is you, Jenni, okay. This is your mom. Thanks for calling in and making the connection, connecting all the dots for us. We really appreciate it. Julie, do we have any written comments on this topic?

Julie Breneiser (02:36:34):

We do, and I'm going to start them off with my own, kind of related to what's just been brought up. And it relates to my first comment. We are not cancer survivors. We are cancer livers, and I'm not talking about the organ, the liver. We live with cancer every day. Dan, from Austin, Texas, writes, "I am not a survivor. How can I be a survivor, when I know every six to eight months, I have to go endure five more skin cancers removed that were not there six months ago? I have done more than 40 years. And until there is a cure, will continue to every year I am still alive. I'm not sure many people understand the psychological pain to a disease like BCCNS. It's a toll. A 50 year old man, lying on a table, tearing, not from pain, but just knowing I'm in a fight I can never win. So many facets of this syndrome are brutal."

Julie Breneiser (02:37:38):

Excuse me. Sasha, from California, writes, "There is a constant fear in the back of my mind of what the future will hold with this syndrome and how much money I have in my bank account for possible medical expenses. Choosing not to have kids for fear that I will pass this on. The medication available for this syndrome right now, from what I've seen, are intense and makes me fear what else I will lose, if and when I take them. I've already lost out on being able to live my life without constant fear."

Julie Breneiser (02:38:13):

And Cindy from Creston, writes, "Fear of continuing to have cancer, 200 plus on me now, fear of getting other cancers due to us missing the tumor suppressor gene, emotional stress, not only worrying about myself, but my daughter and grandson. He already has a jaw tumor."

Julie Breneiser (02:38:40):

So those are some pretty poignant comments that we have.

Larry Bauer (02:38:43):

Those are incredible, Julie. I want to thank you all this morning. Our panelists, our Zoom panelists, for the people that have called in or written in. It's been an incredible morning. I feel like we are lifting a curtain to see behind the scenes on Gorlin Syndrome. This is not what we read in the medical books, but we are actually learning from all of you.

Larry Bauer (02:39:05):

If you were on the phone and we did not get to you yet, we're going to take a break for lunch. I ask that you please try to call back in the afternoon, and we will try to get to as many callers as possible. So thanks. We will take a 30 minute break for lunch now, and we will reconvene at one o'clock Eastern Standard Time. And we hope that all of you will come back and join us. And for this Zoom panel, we won't see you again. And I just want to say, thank you so much for being here with us today and sharing your stories. So see everyone back at one.

Beth (02:39:39):

Bye-bye.

PART 5 OF 10 ENDS [02:40:04]

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PART 6 OF 10 ENDS [03:12:00]

Larry Bauer (03:14:57):

Hello and welcome back to this Gorlin Syndrome Externally-Led Patient-Focused Drug Development Meeting. My name's Larry Bauer, I'm the moderator for this meeting and I'm here in the studio with Julie Breneiser, my co-moderator. And we had a wonderful discussion this morning about the symptoms and impact of Gorlin Syndrome. And this afternoon, we're going to move into a different topic. We're going to focus more on treatments, things that people have used to try to treat Gorlin Syndrome, how have they worked or not worked, as well as what are people's hopes for the future? What would you like to see in new treatments?

Larry Bauer (03:15:33):

So to start off this session, we're going to have five panelists that have prepared statements related to this topic of treatments. Their names are Rocki, Bud, John, Stacy, and Meredith. We thank you and we invite you to join us, panelists.

Roxanne "Rocki" (03:15:54):

Hi, my name is Rocki and I'm a widow. My late husband of 30 years, Jim, passed away in November of 2009 at the age of 53 due to metastatic basal cell carcinoma or skin cancer or Gorlin-Goltz Syndrome. This turned our world upside down. He had multiple skin cancers and several jaw cysts throughout his life. Even though he was proactive in his own care, the skin cancer went from his lymph nodes to his lungs, and he had an agonizing and breathless death. At one point, he even tried pinpointed radiation at Hershey followed by chemotherapy in Lancaster. He had tried several clinical trials, such Efudex and Aldara in New York and Erivedge in Baltimore. The one that did the most for him was Erivedge.

Roxanne "Rocki" (03:16:42):

Both our son and daughter, 38 and 37 years old respectively, have inherited this genetic disorder. They're now both taking Erivedge to manage their BCs, after what I call them, putting themselves in a danger zone. They both have had major surgeries related to BCC, NS, or Gorlin-Goltz Syndrome. They take Erivedge for three months, and then they take a break for three months. Almost all of the skin cancers have disappeared. Some do reappear while they are not taking Erivedge, but not as bad. There are some side effects such as leg cramps, loss of taste, and most notable is hair loss. For a woman, this is

very tough, but not so much for a man. But the good thing is they're not being cut. This Erivedge also helps shrink some very small jaw cyst.

Roxanne "Rocki" (03:17:33):

They have decided not to have children, so our name will not continue on. The emotional and physical, financial toll that this skin cancer takes is unmeasurable on patients, caregivers, and their families. Please keep researching for a cure.

Bud (03:17:52):

Hi, my Anthony Caruso and I'm 60-year-old Gorlin Syndrome patient. I'm married 39 years to my wife Paula, and we have two children and six grandchildren. I've been a real estate broker for 35 years. As a Gorlin patient, I've had a variety of issues to deal with. The keratocystic odontogenic tumors in the jaw, along with ongoing abdominal issues like IBS, polyps in my colon. Seizures are a feature that impact my daily life. I expressed many other features of the disorder such as palmar plantar pits, and calcification of the falx. I've endured pretty much every modality of removal for the BCCs, ED&C, burning and scraping, excisions, photodynamic therapy, interferon injections, Efudex cream which is the 5FU, and eventually leading to the gold standard of Mohs surgery.

Bud (03:18:47):

Early on with all good intention, I was treated with ultraviolet light treatments weekly to eradicate acne so the doctors could be certain what they were removing were actually basal cells. This led to a rapid excessive growth of the BCCs later in life for me. Since being diagnosed at the age of 10, I've had thousands of BCCs removed using the various modalities. Certainly, this have been my primary burden from the disorder. Once I got to a point where it's decided that most micrographic surgery would be the best option for my facial lesions, the resulting defects were leaving me increasingly mutilated at an alarming rate. A better method was needed if I was to preserve my appearance well enough to stay in business and have a social life, as well as regular marital and family relationships.

Bud (03:19:40):

With Mohs, the cutting continues until a clear margin is achieved. In my case, often the surgeon would run into another lesion by the time a clear margin could be accomplished. When I had the lesions that were so close to my tear ducts, the doctors cautioned me, "This next round, Mr. Caruso, it's a good possibility we'll have to remove one or possibly both of your eyes." Fortunately, that did not happen but continuing down this path, I'd soon be left so mutilated, I could become recluse. Undoubtedly, I wanted there to be a better way.

Bud (03:20:13):

With assistance from my medical team and a great deal of research, I set out on a path of exploring clinical trials. I've just entered my ninth clinical trial and on this quest, I've reached out to researchers across the country and literally around the world. I've traveled to Germany, Holland, and England meeting with some of the top researchers for the disorder who have developed new treatments or led the way with therapies for the disorder. I've always been surprised and grateful at how welcoming they've been in meeting with me and sharing their knowledge.

Bud (03:20:44):

In the end, at this point in time, I'm left looking more like a burn victim than anything. It's not unusual to get comments like, "You're so brave to go out in public looking like that. I know a little boy who was burned up in a fire and his family can't get him to go outside anymore. I wish that he could meet you." Or, "Hi sir, I'm a firefighter and I know what you go through," or "What happened to your face? Were you in some kind of accident?" Always with good intention from well-meaning people, but usually on a day when I'm thinking, "Dang, I look good," well at least until that point. What a turnaround.

Bud (03:21:18):

While taking the hedgehog inhibitors, which have been much better than the surgical options, the side effects have been very difficult to live with on a daily basis and perform the task necessary to run my business. Extreme fatigue, abdominal issues like nausea, cramping, and bowel problems, extreme cramping throughout the body but especially in the legs, hair loss, or the bigger problems associating with the therapy. I'm basically tolerant of these side effects, and I do feel extremely fortunate as compared to my predecessors to even have the option, yet it is still a horrible way to live day to day. Definitely makes it difficult to keep up with a job or run a business.

Bud (03:21:58):

This type of cancer looks you in the mirror every day. One can't help but feel as if it is taking you a piece at a time with only so many pieces in the whole. When will it spread to my lungs, my brain, or my bones? When will I develop other types of cancers associated with the disorder? When will it be the end? I'm hopeful that in the future, there will be a combination of therapies to complement the hedgehog inhibitors, allowing individuals to take a lower dose or longer breaks from the drug. Topical medications, preventing new growths, new generations of drugs that are as effective without as many side effects. I'm hopeful for the future, and I look forward for the advancements to come. Thank you.

John (03:22:45):

Hi, my name is John. I live in Ohio, outside Columbus, with my wife and two children. I was diagnosed with Gorlin Syndrome 40 years ago as a young teenager. The manifestations of my syndrome then and since have been BCC skin cancer lesions and OKC jaw tumors. I stopped counting my BCC skin cancer lesions years ago once I surpassed 1000 BCC biopsies and procedures, and I have had roughly seven to ten jaw cysts removed, including the loss of several permanent teeth. Treatments have included Mohs surgeries, surgical extractions, photodynamic therapy, and oral surgery. These experiences have challenged my morale and my quality of life. To date, our children have not shown signs of having inherited Gorlin Syndrome, but the potential that they might someday weighs heavily on my wife and me every day.

John (03:23:53):

Over the past 40 years, I've made six to eight visits each year to my skin cancer doctor's office prior to my participation in the Patidegib trial. Office visits usually involve three to five biopsies. The majority of these biopsies have come back positive, requiring Mohs surgery averaging 12 to 15 Mohs procedures a year or other forms of surgical removal. I usually go to work right after Mohs surgery the same day, not wanting to let my Gorlin Syndrome steal any more vacation time than it already does. Because Mohs is time sensitive, some years, my Gorlin Syndrome has consumed more than half of my paid time off for sickness or vacation. It has been such a part of my daily life that I often forget to tell my kids and my wife that it's a Mohs day. When I arrive home, they barely notice the bulky pressure bandages.

John (03:24:56):

I participated in three drug trials in the shared hope of discovering the miracle drug. In 2010, 2011, I was a participant in a vismodegib Erivedge drug trial. I found my complete hair loss and the unfortunate impact on food taste difficult but tolerable. Despite drug effectiveness and a significant decrease in my BCCs, I eventually withdrew from the trial because the middle of night leg cramps and resulting energy drain the next day outweighed the benefits. In 2016, I traveled back and forth to Ormond Beach, Florida where I participated the SUBA-itraconazole trial. The drug had a limited effect on my BCCs and eventually, I developed peripheral edema in my legs, ending my participation in the trial.

John (03:25:53):

When I started to hear about the Patidegib trial, I began to find new hope. What if the topical Patidegib gel offered the effectiveness of oral vismodegib Erivedge, but without the side effects of a systemic drug, so the pitch went. For me, for my children, for many others impacted by this disease, I volunteered to be a Guinea pig one more time and drove back and forth to Indianapolis over the course of two years. I'm confident that I was on drug, not placebo, the first 12 months of the trial as I haven't had a facial BCC since early in the study. For me, Patidegib was a life changer. Historically, the majority of my surgeries had been neck up. With the gel being applied exclusively to my face, my doctor visits and my need for surgery were mostly eliminated while on the trial medication. I had my life back. I understand that other participants enjoyed the benefits of Patidegib. The positive impact was incredible. But apparently, the statistics were not good enough to keep the trial going. This is devastating to me. So soon, I will return to more needles, scars, and disfigurement. This feels inhumane, particularly when I know there is something out there with no safety issues that can prevent my skin cancers from developing. I found myself daydreaming that I somehow got my hands on a supply of Patidegib. I've even fantasized about finding the recipe and making my own. All wishful, unrealistic dreaming, of course. But when your body has been cut on and sewn back together hundreds and hundreds of times, that kind of momentary imagining is marvelous. To know that I'm headed back down the road of surgeries, scars, and disfigurement is understandably disheartening. We are never cancer free, never in remission ever, but some of us could be.

Stacy (03:28:21):

Hi. My name is Stacy and my daughter, Rowan, was diagnosed with Gorlin Syndrome two and a half years ago when she was five when we started seeing our primary care physician about bumps growing on Rowan's skin. After a couple of years of doctor's visits for various odd things, a pediatric dermatologist biopsied one of her bumps and determined it was a BCC. Her diagnosis was confirmed with genetic testing. All of her other medical oddities, including uncorrectable bony abnormalities in her back and shoulder have all made sense under the umbrella of Gorlin Syndrome and now, we are monitoring her for the huge multitude of anticipated manifestations of the syndrome.

Stacy (03:29:04):

Far and away, Rowan's BCCs currently have the most impact on her, her life, and our family. Even with strict sun protection, Rowan wears a hat, high SPF sunscreen, UV clothing, and sunglasses every day with sunscreen reapplied at school. Rowan's BCC count is in the hundreds, more than I can count or keep track of. After her initial diagnosis, Rowan had surgery to remove 24 larger BCCs around her eyes and her neck. Then we tried imiquimod, an immunotherapy topical. It made her tired and grouchy like the flu, but did nothing to her BCCs. Eventually, it caused a sore in an area not being treated as too

much had absorbed into her system. And between that and the flu-like symptoms, which were significantly impacting her personality and joy in the world, we decided to stop using it.

Stacy (03:30:04):

After that, we tried daily topical FU treatments which burned off the top layers of her skin, but it was inconsistent and irregular in its effectiveness. Around her eyes, it burned off the skin which she was self-conscious about during school, but the BCCs grew back. On the back of her neck, the 5FU burned so far down that she now has scarring. The sores and peeling were incredibly uncomfortable for her and it was hard for me to continue putting it on her skin, knowing it was causing her so much pain. And the areas we put the cream on were treating such a small number of her BCCs, it seemed hopeless. How on earth was I supposed to rotate to all the affected areas of her skin, when she always have blistering and peeling skin?

Stacy (03:30:56):

Eventually we tried photodynamic therapy or PDT, during which our doctor applied a light sensitive medicine and then used a light source in the OR under sedation to destroy the top layers of her skin where the BBCs grew. It made her skin red and sore and her eyes swelled shut after each visit when we treated them. We had to keep her out of the sun for a few days after each procedure and she missed school and seeing her friends. Eventually her skin would peel and some of the BCCs would be gone. It worked better in some areas than in others, but also caused areas of her skin to change color. She had three sessions in about a year, but the BCCs were relentless and each time was an ordeal, including fasting, a full day of OR time and significant recovery time at home, including needing to stay inside and away from any sun for three to five days, plus limited time outside for two weeks so her treated skin would not burn.

Stacy (03:31:59):

Now, in addition to nicotinamide, a B vitamin shown to help reduce BCC growth and strict sun protection, we are using an off-label topical cream called sirolimus in a 1% solution, which seems to be preventing most new BCCs from growing and keeping her existing ones small in the areas that we use it. We can't use it on all of her body as too much could be absorbed by her body and cause adverse side effects, and it's unclear what the long term safety impact will be. But she hasn't had surgery in a year, which is a huge victory for us, but we know more surgery, more needles, more permanent scarring are in her future. Some days it is incredibly overwhelming that I start crying just getting her ready for school or swim class. BCCs grow everywhere, even on her labia. They're relentless. I wish more than anything it was easier to manage, and I know there will be other manifestations we'll need to address and manage as she grows. So this is just the tip of the iceberg. For her BCCs, I wish there was a topical treatment that didn't make her skin irritated and painful or make her grouchy and tired, that didn't need needles and anesthesia and OR time, and didn't result in permanent scarring each time. Thank you.

Meredith (03:33:31):

How do you eat an elephant? One bite at a time. I have used this metaphor as a useful way to break down managing my child's disease into bite size chunks, and it also serves as an incredibly apt visual reminder for what can happen to her appearance over time. Having Gorlin Syndrome means a lifetime of watching and waiting for a cancer that may never come or may come with an attack so brutal and vicious that there's never an end in sight.

Meredith (03:34:09):

My name is Meredith and I have a 14-year-old daughter. She is vivacious and joyful and she has wrestled with this disease for every day of her life. When she was born, she cried almost all the time. We didn't know why, but we suspected that it was related to the alarming growth of her head. We had discovered during a prenatal ultrasound that she had too much fluid in her brain and within a few weeks, we had her first specialist, a pediatric neurosurgeon. A few weeks after that, we had our first mother daughter photo, a prenatal MRI in which her tiny skeleton is seen curled against my spine.

Meredith (03:34:59):

By the time she was nine months old, we knew we had to do something and we had a hard conversation with her neurosurgeon about an intervention. The risk of doing nothing was that the fluid would put pressure on her brain and cause permanent brain damage. The risk of the intervention was that he could inadvertently cut the blood supply to her brain and cause permanent brain damage. We elected to move forward and felt very lucky that it was completely successful. We still do, but it was not the end of our journey. We noticed that she had other difficulties that were unusual. She was late to roll over, crawl, and walk. She needed a neck brace to straighten her head. She wore foot braces to assist with walking. She had an eye patch because her eyes had difficulty collaborating. By the time she was four, she had had two eye muscle surgeries.

Meredith (03:36:02):

We were vigilant about looking for other clues as to what was going on. And at one point when she was about a year old, we noticed hundreds of these invisible but palpable bumps on her sides and took her to a dermatologist for a biopsy. The results were inconclusive. By that point, we had maybe eight specialists for her and we went to two different genetics clinics, but no answers until she was five years old when we finally got a diagnosis of Gorlin Syndrome. We thought that would illuminate the path to caring for our child, but it didn't. For kids like mine who are born with hundreds of tiny basal cell lesions before the sun has kissed their skin for the first time, there are no clear answers.

Meredith (03:36:56):

We have a cabinet full of topicals that we have tried. Some work for a little while, some work a little bit, some work not at all, but none of them have been adequate to keep the tide of basal cells from overcoming her. When she was five, we asked her dermatologist to assist in every surgery by removing basal cells while she was still under anesthesia for something else. She's had probably 10 surgeries since she was five and in everyone has woken up with hundreds of little red dots all over her body, and it hasn't been enough to keep the basal cells from bubbling up.

Meredith (03:37:36):

When she was 11, we began a laser treatment in office. It was quite painful, so we offered her a gummy bear for each time she would let him laser her skin. And by the time we completed that treatment, she would walk out with well over a hundred tiny red, what appeared to be cigarette burns, all over her clavicle, her neck, down her sides, and fistfuls of gummy bears and it wasn't enough. When she was 12, we started PDT, another light therapy, and missed an entire day of school once a month so that she could go in to be treated and still not enough, more basal cells.

Meredith (03:38:24):

At 13, she had her first Mohs surgery. The average age for first time Mohs patient is 68. She had three lesions on her lash line. For four hours, they repeatedly anesthetized her lid and scooped out diseased tissue while she watched. The next day, she returned for plastic surgery to repair the lid. She repeated Mohs again this summer to remove a piece of flesh from her scalp. Managing these basal cells occur simultaneously with managing jaw cysts, and the cruel twist is that you can't see the jaw cysts without imaging. The imaging requires radiation, the radiation fertilizes the basal cells in her face. She has had over a dozen cysts removed from her jaw from every quadrant and she's lost two permanent teeth. In my mind's eye, I see my daughter's joyful face transformed into one with shining scars spread like leopard spots that torque and pull her features and eat away at her nose and her eyelids and her ears. The ache of knowing a future I cannot protect her from is deep and penetrating. There is a morbid assurance of constancy that comes with this disease. There will never be a time when she can pause the march of cuts across her body. How do I prepare a child for that?

Larry Bauer (03:40:31):

Thank you so much, Meredith, for sharing your story. Thanks also to Rocki, Bud, John, and Stacy for sharing as well. So as I said, we're going to move into this next section which discusses treatments for Gorlin Syndrome. I want to remind everyone that we will be doing polling in a minute and to go onto their cell phone or their tablet and open up PollEV.com/Gorlin to participate in the polling.

Larry Bauer (03:41:02):

But before we go to the polling, I'd like to just review the discussion questions that we're going to use on this topic for the afternoon. So session two is perspectives on current and future approaches to treatment. We'll ask, what are you currently doing to manage you or your loved one's Gorlin Syndrome symptoms? Two, how well do these treatments treat the most significant symptoms and health effects of Gorlin Syndrome? Three, what are the most significant downsides to you or your loved one's current treatments and how do they affect daily life? And four, short of a complete cure, what specific things would you look for in an ideal treatment for Gorlin Syndrome? What factors would be important in deciding whether or not to use a new treatment?

Larry Bauer (03:41:46):

So those are going to guide our discussion later. But to start this off, let's go to a polling question for everyone. Once again, PollEV.com/Gorlin is what you open on your cell phone or your browser. And this first question is what medications or medical treatments have you used to treat Gorlin Syndrome? Select all that apply. A is imiquimod cream. B is 5FU cream. C is vismodegib. D is sonidegib. E is cryotherapy or freezing. F is laser therapy. G, curettage or scraping. H is Mohs surgical removal or biopsy. I is vitamin D. J is jawbone surgery for cysts. K is antidepressant or anti-anxiety medication. L is other medications or surgery. And M is if you've not used any of those treatments listed.

Larry Bauer (03:42:53):

So please once again, select all. If you've used several things, please click on each one that you have used or tried, whether it was successful or not, just that you've tried this to treat Gorlin Syndrome. And the answers continue to come in. It looks like people have tried many things on this list. Looks like G is out front, curettage or scraping for the BCC treatment, seconded by Mohs surgical removal or biopsy. And then also not surprising, we've heard a lot today about jawbone surgery for cysts. And then I think the rest of the treatments are fairly evenly spread out between the imiquimod, 5FU, vismodegib,

vitamin D, laser therapy. And only a very small number, there's only 1% of the responses that say that they have not used any treatment, which it would be very unusual.

PART 7 OF 10 ENDS [03:44:04]

Larry Bauer (03:44:00):

... unusual.

Larry Bauer (03:44:04):

Okay. So I think most of the answers are in... Actually the jawbone surgery for cysts has come out on top and the skin treatment, curettage and Moh's are coming in second. So can we move to the second polling question? Besides medications and treatments, what are you currently doing to help manage the symptoms of Golan syndrome? Once again, select all that apply. These are non- medical interventions, perhaps.

Larry Bauer (03:44:32):

A is avoiding sun exposure. B is sunscreen or sunblock. C is sun protective clothing like hat, long sleeve shirts or long pants. D is avoiding x-rays. E is having an annual brain MRI. F is pelvic ultrasound. G, stress management. H, acupuncture. I, CBD supplements. J, therapy or counseling. K, other. And L is I'm not doing anything to help manage my symptoms.

Larry Bauer (03:45:06):

Once again, please select everything from this list that you might have tried. And it looks like our top categories as the answers are coming in, are all related to sun exposure to try to prevent BCCs. So we see avoiding sun exposure, using sunscreen, and sun protective clothing is being pretty evenly at the top of the list. Next is avoiding x-rays once again to prevent the BCCs. But also high on the list with stress management. Which has been a, kind of an emerging theme today about the stress of having Gorlin syndrome.

Larry Bauer (03:45:54):

Well thank you for participating in the polling. I'd like us to go now to our Zoom panel. Thank you to all of you for joining. We really appreciate you taking the time out of your day to be here with us.

Larry Bauer (03:46:12):

So you just saw those questions. I would like to hear, would anyone like to volunteer to talk about what are some of the top medical treatments that you have tried for Gorlin syndrome? You could just raise your hand. Maria, I saw you raise your hand first.

Maria (03:46:32):

I beat you Lizzy. I've tried numerous things. I've tried topicals. I tried one oral drug. I don't like things that carry lots of side effects. So I've worked with my dermatologist for years. We've developed something of a system where I go on biopsy just to confirm, because the assumption is that's what it is. So we biopsy to clear. And so basically I get lots of biopsies and that's worked real well. But on the other hand, I'm never fully clear. They're always there. So the focus stays on my face because that's what's

present to everybody. So we make sure if we need additional Moh's treatment or whatever that focuses on the face. That's pretty much my routine.

Larry Bauer (03:47:33):

So Maria, you're saying that when they do the biopsy, they're actually removing the BCC completely at the same time?

Maria (03:47:39):

Correct. They just biopsy with a larger margin to make sure to get it all.

Larry Bauer (03:47:45):

And does it ever happen where they do one of those biopsies and it doesn't have clean margins and then it progresses to a Moh's procedure?

Maria (03:47:52):

Yes. Every once in a while.

Larry Bauer (03:47:55):

Every once in a while.

Larry Bauer (03:47:57):

My doctor is pretty good at knowing where things stop and start. It's a skill I don't possess, but she does. Thankfully.

Larry Bauer (03:48:05):

Thank goodness. Yeah. Thank you. Lizzy, your hand had gone up as well. Can you share with us?

Lizzy (03:48:14):

Yes. So at a young age, I actually... I'm so sorry. I'm Lizzy, I'm from Utah.

Larry Bauer (03:48:22):

Thank you.

Lizzy (03:48:22):

I am a person living with Gorlin syndrome as well as I have a mom who has Gorlin syndrome. One of my two brothers has it and of the two of us that have it, two of our oldest children on the each side have it. So I spend all the topics there.

Lizzy (03:48:48):

At a young age. I did have laser treatments done because for me, my skin cancers were on my face, for my brother most of his were on his back. I call that luck. So for me at a young age, I had laser treatments done over a hundred, right around my eyes. I want to say I was like 8 to 10 and I've had hundreds of most surgeries and excisions. And I even was part of the most recent partitive trial. And my philosophy there is if I can do anything to help the younger generation not have to go through what I have had to go

through, I'm here for it. Because the constant cutting, the dealing with that side of things, it takes this toll of your time.

Larry Bauer (03:49:53):

Thank you. Thanks Lizzy. Yeah, Erika.

Erika (03:49:59):

Hi, this is Erika. I'm a parent of an 11 year old who has Gorlin syndrome and her manifestations have been besides the physical characteristics, the jaw cyst and the BCCs are the biggest ones, but the jaw cyst have been kind of the main nuisance of lately. She's had four surgeries since she was four. The second to last one, she had five or six removed at the same time.

Erika (03:50:26):

As far as the treatment goes, I don't think I've heard anyone talk about the stint that people will put into drain the jaw cyst which again is an okay treatment if you're going to drain a jaw cyst once in your lifetime. But if you've got multiple jaw cyst and you're going to have that drainage and have your parent have to drain that it's pretty brutal. Sam has lots... She's lost a few adult teeth. She has had some speech issues because of the teeth and she's in speech therapy constantly. And just when they make some strides with her speech therapy, I'm like, "Guess what? She's got two more. So she's going back in again." So we've basically done the cutting, the surgeries, and then for the basal cells we've done cryotherapy mostly.

Larry Bauer (03:51:10):

Erika. I'm just thinking about the jaw cyst. Are jaw cyst always fluid filled or are they sometimes am solid?

Erika (03:51:20):

That's a great question. I remember going into the surgeries and I remember the doctor coming out and going ma, ma, ma, ma. And at that point he told me what they were. I remember some of them are liquid. He says that some of it they had to scrape away, but it's not solid. It's almost like a cyst filled. And depending on where they are.

Erika (03:51:40):

The ones in the front... Again, Lizzy you talked about winning the lottery. When they're on the front, you kind of win the lottery because you don't have to get so far back here where the post-surgical packing. If it gets loose [inaudible 03:51:55] blood, then they start drawing up blood. So you kind of want them to be up front but then the flip side of that is you don't want them to lose those adult teeth that are there. So it's either the best of the worst or the worst or the worst, but it's somewhere in that category in between.

Larry Bauer (03:52:13):

And you don't get to pick to choose where your jaw cyst are going to show up, right?

Erika (03:52:16):

No. And they come back. That's the thing. Let's say [inaudible 03:52:20] oh, he'll say we got everything. And guess what? In six months or a year going to have to go back in and get them back out again.

Larry Bauer (03:52:29):

Can you tell us a little bit about the stint? We haven't heard that before today. Is that a postoperative stint? They remove the cyst and then a stint is placed for drainage?

Erika (03:52:39):

It's before to drain the size of the cyst to make it so they do less damage when they cut it out.

Larry Bauer (03:52:49):

When do they put the stint in relationship to when they do the surgery? Is it like a day before-

Erika (03:52:54):

Months.

Erika (03:52:54):

Oh, months before.

Larry Bauer (03:52:56):

Weeks or months usually.

Larry Bauer (03:52:58):

Okay. And is that just at the doctors makes a decision whether to stint or not stint ahead of time?

Erika (03:53:09):

The decision usually is ahead of time. For Sam's last surgery, he was going in and he said that there's one that's so big that he if he can't get it, he was going to stint it during surgery, or put the drainage in it. I don't know if that's the right terminology. But he was able to get it all. So we were grateful that we didn't have at that time.

Larry Bauer (03:53:28):

Okay. Thank you, Erika.

Erika (03:53:31):

Thank you.

Larry Bauer (03:53:32):

Yes, Caitlin.

Julie Breneiser (03:53:36):

You're muted Caitlin.

Caitlin (03:53:38):

Oh.

Larry Bauer (03:53:38):

There you go.

Caitlin (03:53:40):

Sorry. Can you hear me now?

Larry Bauer (03:53:43):

Yes.

Caitlin (03:53:44):

I'm sorry. I'm Caitlin from Spring Branch, Texas. And I'm the second of three generations of Gorlin. My mother was very, very, very severely affected. She was a long term patient at MD Anderson Hospital in Houston, Texas. And because of my husband's career we have moved all over the country and lived in four states.

Caitlin (03:54:09):

So each time I had to go searching typically for a university setting, a teaching setting. Because forgive the pun, they're typically on the cutting edge of research. So my son and I usually go together as patients. And we've had a lot of different options to choose from. Topical medicines have not worked. Scraping, and burning, and freezing typically does not work. So I figured that's all for the same reason.

Caitlin (03:54:47):

Most all of our treatment has been most surgery exclusively. And the jaw surgery as well has been the same. Like Erika was saying, they've tried the draining and then removing, or just going in full blast in removing.

Caitlin (03:55:06):

My son was the poster child for air [inaudible 03:55:09] for several years. He did so well, never went for Moh's. He was constantly going for Moh's every three months, but now he's having some issues. So we're working through that with the University of Texas folks to see what we can do and then see what the next option for treatment is.

Larry Bauer (03:55:31):

It makes sense that you have to go to a university hospital, I'm sure to find the experts. Okay. Thank you very much for sharing that. We have a caller, Nicole from PA that we'll get to in just a second, but before we go to her, I would like to ask Dwayne, Dwayne.

Dwayne (03:55:51):

Yes, good afternoon. I'm Dwayne from Illinois. I do not have the syndrome. My 13 year old grandson does. So my wife and I consider ourselves an integral part our Gorlin team to work with our daughter

and her family and our 13 year old grandson. We've been with him every step of the way, he has manifested much of what you've been talking about today.

Dwayne (03:56:21):

He was born, he had an enlarged skull, before he was one year old he had to have three skull surgeries and plates installed in his head in order to handle the situation.

Dwayne (03:56:35):

And so as a consequence of that and continuing operations, we've been very involved in helping them through the situations that they had to deal with as he's progressed. Unfortunately, there were a lot of questions. We did not know what was going on. In spite of being in Chicago with great facilities in the children's memorial hospital, where he had his initial surgeries, he was not really diagnosed with Gorlin until he was eight years old. And he is now 13. And he's been dealing with the jaw surgeries and with the skin surgeries, of course, which mainly the BCCs are the prevalent thing that we're dealing with now.

Dwayne (03:57:22):

At one point he had 139 of them removed at one time. And I would use a term that I haven't heard today, but I've heard it in the past from others that the surgeries that remove these, the cutting, the burning and all of the things that are necessary to appropriate remove these BCCs are nothing short of barbaric.

Dwayne (03:57:49):

And I hope and pray that your attention and what you're doing today in bringing this out to the forefront with the public and with hopefully our friends, if the FDA will figure out a way to develop some topicals that will enable us to preclude from having them. And if not that then obviously in mercifully removing these BCCs without your heart... I know yours does too. When you see these young children that are being disfigured and burned and [mamed 03:58:30]. It's horrible. And I can't, but help think that if the appropriate amount of attention is brought to this rare disease that we will have some, if not permanent temporary solutions.

Larry Bauer (03:58:48):

Thank you [Dwayne 03:58:48].

Dwayne (03:58:48):

So I appreciate what you're doing.

Larry Bauer (03:58:51):

Thanks so much, Dwayne. Nicole's been waiting online. This is Nicole from Pennsylvania. Nicole, can you hear us here in the studio?

Nicole (03:59:02):

I can. Can you hear me?

Larry Bauer (03:59:03):

We can hear you loud and clear. Go ahead.

Nicole (03:59:08):

I'm Nicole from Pittsburgh, PA. I have Gorlin syndrome. I was diagnosed at eight years old and I'm currently 42 years old. And throughout my whole entire life, I've had mainly jaw cysts removal and Moh's surgery.

Nicole (03:59:23):

But when I think about treatment for Gorlin syndrome, it's really hard because of lot of my treatments have been unknown. So I mean by unknown is when I have a jaw cyst removal, am I going to have my teeth remaining? Am I going to have any Jawbone remaining? And a lot of times I've had jawbone taken away. Recently I've had some jawbone grafts done. I've lost six teeth permanently as a result, but no doctor wants to do implants on me. So either my teeth are completely missing in my mouth or I have removable partials in my mouth. And that makes it hard for my smile. And it's always been a fight with insurance because they consider it cosmetic in getting that covered.

Nicole (04:00:16):

For my most surgeries, it was always a treatment of am I going to come out with stitches staples or skin graft? I probably had about 10 skin grafts done to my nose alone to help me keep in normal. Or sometimes when he stitches me up, when he's done, he would test the extra tissue and call me back in because somehow he found more basal cell.

Nicole (04:00:43):

So it's very frustrating because you never know what's going to happen, what's going to be the outcome of it. Most recently a skin cancer has been found on me, a basal cell carcinoma. I should clarify, has been found on me in form of a lump underneath my skin. And I never knew that basal cell could be found as a lump underneath your skin. And it was a whole very scary process of finding it and my surgery scheduled for the day before thanksgiving.

Nicole (04:01:15):

And it's very concerning because how they going to treat it? Are they going to cut me open and stitch me up? Are they going to suck it out somehow? I have no, absolutely clue what's going to happen at this point. And under the skin's very scary too, because you don't know what's going to happen. You don't know what else is in there.

Nicole (04:01:34):

For myself also, I know this morning when I was listening off and on between watching children, I heard about the ovarian cyst. I had ovarian cyst. I was not diagnosed with them until 35 and I had to have a hysterectomy because of it. But my doctor believes I was misdiagnosed for so long because he said, he's never seen cyst like that. And so as a child, it would've been nice to have treatments, to be able to look at me more inside the body and help figure out what's going on there because I think that's a lot of times is the problems. We don't know what's going on underneath us.

Nicole (04:02:16):

Skin cancers are sometimes easy. Jaws cysts are sometimes easy, but they hide too. Because I had one hidden up in my sinuses. So I always would love some treatments to help detect things sooner than later or help take things away. Most of my skin cancers are on my face. So we keep doing the trials for the

gels. I would love to rub something on my face to make skin cancers go away. But I also don't want to deal with the side effects. I do not ever or wanted take air [inaudible 04:02:50] because of the side effects. But that's just me, so.

Larry Bauer (04:02:54):

Well thank you Nicole.

Nicole (04:02:55):

But that's my side.

Larry Bauer (04:02:56):

Yeah. Thank you so much for calling in. We really appreciate it. I just want to remind folks that if you too would like to call in, to get in the queue as a caller, please call from your cell phone (703) 844-3231. But now I'd like to turn to Julie to see if we've had any written comments come in on this topic.

Julie Breneiser (04:03:17):

We sure have. Let me start with Michael from Pittsburgh. He has written, "When my beautiful bride had her first most surgery to remove a BCC I was completely caught off guard and horrified as at the result. A small spot that looked like a bug bite ended up with a four inch suture line sneaking across her face. Despite trying to keep her head raised at night and apply ice packs, the swelling grew large and painful. There has to be another way." Excuse me.

Julie Breneiser (04:03:53):

Kate from Massachusetts writes, "Regardless of the time of day or evening I take [inaudible 04:03:59] I get really, really bad leg cramps at 3:00 AM. It keeps me awake for at least an hour. So those are some of the comments that have come in thus far.

Larry Bauer (04:04:09):

Thanks Julie. So I'd like to ask everyone to take out your cell phone again. We're going to do another polling question. This polling question is... If we could go to polling number three. Yeah. What are the biggest drawbacks to how you're managing Gorlin syndrome? And this time you can select up to three answers. So A, is that the treatments aren't very effective. B is the high cost or co-pays not covered by insurance. C is limited availability or accessibility of the treatments. D that they are disfiguring. E is side effects of treatment. F is pain. G is fear or anxiety about procedures, needles, or more scarring. H they require too much effort and or time commitment. I is other and J is not applicable as I am not using any treatments.

Larry Bauer (04:05:14):

So once again, you can select up to three of these possible answers And it looks like the disfiguring side effects is leading, followed by fear, anxiety around procedures, needles, and scarring, which we've heard numerous times today. There's high costs and co-pays not covered by insurance. We have 12% saying not very effective, and we have some folks talking about limited availability and requiring too much effort and or time commitment. So the biggest drawback that we're seeing right now is from the removal of BCCs and the disfiguring side effects.

Larry Bauer (04:06:21):

So if we could now return back to our Zoom panel. Thank you. And I'd like to put this question to you all. As you read that question about what are the biggest drawbacks or downsides to treatments? What were some of the first things that come to mind? Erika?

Erika (04:06:46):

Hi. I think one of the biggest downsides is that you're going to have to do it again. I think that the idea is like you're getting hit by a train every day. And I think it's the difference between a treatment option that's for a once in a lifetime thing versus something that's maintenance. If you have one Moh's surgery in your life, I'm sorry, that's awful, but you have one and that's one scar that's going to heal. But if you're going to have it 40, 50, 100 times, it's no longer a viable option. And I think that's what I'm excited about this panel for is opening up the fact that we need maintenance and we need to get to the root of the problem. And even if it's just figuring out the side effects of the drugs of the leg cramps, we just need little things to make these things less disfiguring and just less invasive.

Larry Bauer (04:07:39):

Okay. Thank you. Yes, Maria.

Maria (04:07:44):

Yes. I didn't say before. I'm from Pennsylvania.

Larry Bauer (04:07:47):

Thanks.

Maria (04:07:48):

I was one of the ones that chose limited availability because one of my preferred methods of treatment I was involved in clinical trials is photodynamic therapy PDT for short. But the most effective kind is using a red light, but the most available kind uses a blue light, which is not as effective. So you're faced with a treatment that is a little easier to tolerate, but if you can't find red light then it's less effective. So faced with those decisions. It's difficult.

Maria (04:08:26):

And then one other thing I wanted to mention, because this was a game changer. I have an adult son that has the condition. He has never had BCC, but he had a lot of jaw cysts. And one of the things that made a significant difference for him was a solution called [kanoise 04:08:44] solution. I don't know what the drug name is, but that was what I was told it was. And that made a huge difference. I shouldn't say stopped it, but made a huge difference in regrowth once his surgeon started using that.

Maria (04:09:01):

And then for myself with my treatment of BCC, another game changer was learning about subtypes of basal cells. Some are more aggressive than others and that would help me determine how to treat whether it was more aggressively or less aggressively. And I think anything that we can have in our tool belt that gives us options is a tremendous asset.

Larry Bauer (04:09:32):

Is there any way to know before biopsying whether it's more or less aggressive or does it take a biopsy to make that determination?

Maria (04:09:40):

It takes a biopsy to confirm. You can sort of tell. The majority of the ones that I get are the least aggressive subtype called superficial, which by its definition is just surface of the skin. And other ones have a significant look to them that dermatologists can tell a little bit. But pretty much it always takes a biopsy.

Larry Bauer (04:10:04):

Okay. And Maria, you had mentioned the red or blue light photodynamic therapy. Nobody's really talked about that. Can you just give us a quick overview of what is a photodynamic therapy session Like? Some of us have never heard of that, what is it?

Maria (04:10:21):

It's interesting because my experiences with it have been different. But I participated again in early trials of that, which is far different than what's been offered to me in doctor's offices, but was very effective.

Maria (04:10:34):

But basically you're putting a topical on the skin cancers that are going to be treated and that's left to absorb for a little while and then a light using for lack of a better term, a fiber optic cord to shine light on an individual tumor, a spot that's being treated. That was the way the trial was. Nowadays what the derms have for multiple reasons, that's why dermatologists have them are light boxes that are used to treat a variety of skin conditions. So it's the same idea. You put the medicine on the spots that you want to treat and shine the light box on that area and then the drug burns off those spots. It's not pleasant. It's not easy. You have to sit there for 20 minutes and the longer the lights on it, the more it hurts until eventually the medicine burns off and it gets a little better, but you got to go through a tough period. But you're able to treat multiple spots at one time. It's a game changer.

Larry Bauer (04:11:42):

Wow. Great. Thank you for sharing. Yeah. Lizzy.

Lizzy (04:11:49):

The biggest drawback for me, especially when I was younger was feeling alone. Now I mentioned that I have family members that have it, it's different. Just having a member that has it, that family member's there to tell you, you should be doing this, you should be doing this. But feeling alone because none of my friends had it. None of my friends knew anything about it other than what I told them and that I would show up with bandages and whatnot.

Lizzy (04:12:24):

For me, the biggest game changer with that was actually attending a few of the conferences most recently and getting to meet other women my age. A few of them have been instrumental. We talk, we Facebook message, just finding that support work group of people at one of the conferences I was talking with another Gorlin syndrome, young woman, I believe she's in her twenties, maybe early thirties. And her mom was sitting right next to her. Her mom wasn't affected by the syndrome. And she

and I were talking. And at one point I said to her, "If you ever need somebody to talk to I'm here." And right then her mom said, "Thank you. Thank you because you know more about this than I do." And I mentioned it to my mom afterwards and she said, what that mom did in that moment was tell her daughter, you don't have to talk to me about certain things if you don't want to, here is someone else that gets it, that knows it and that you can rely on for support in what you're going through.

Lizzy (04:13:36):

I mean, as my son battles this, yes, I would love for people to be right there and support him and he doesn't have that yet. But I think that fear and anxiety of going in and going under the knife, the fact that you can send somebody a message and say, today is the day. Today is the day is that I have to do this. And so many do it on our Facebook page and ask for help and support.

Lizzy (04:14:08):

I think overall for me, that fear and anxiety of going back in. Like Maria said, you don't know, you don't know until it's biopsied if it's the superficial or if it's the more aggressive and what plan of attack you're going to take. With these drug trials, my philosophy has still been the same. If I can help that next generation to not have to do what I've had to do, to not live with the scars that are visible. I mean, thank you to a computer screen that doesn't make them so visible, but they are visible. And they're that constant daily reminder that you live with this and you'll never be cancer free. We're never part of a cancer wards that you gain that group of people to be there and support you. You go into your dermatologist office and you go out. But that fear and anxiety of feeling alone even when you do have family members who have it is huge.

Larry Bauer (04:15:11):

Thanks Lizzy. Yeah, that just reminds me. I know at some cancer treatment centers when a person completes their cancer therapy, they have a big bell that they ring. They get a certificate, they go home, they take their picture. But what I'm hearing from you is that people with Gorlin syndrome never get to ring the bell. Yeah. Can I ask you Lizzy, how old were you when you first met someone with Gorlin syndrome other than a family member? Outside of your family?

Lizzy (04:15:41):

It was about two or three years ago, was all.

Larry Bauer (04:15:43):

Two or three. So that was a long time.

Lizzy (04:15:44):

Yeah.

Larry Bauer (04:15:45):

Okay. Great. Well, thank you. Yeah. Hi Dwayne. Go ahead.

Dwayne (04:15:51):

Yes, what Lizzy said, rung certain bell when she said being alone. I would bring up that when we finally discovered a few years ago what our problem was, our daughter-

Dwayne (04:16:03):

... finally discovered a few years ago what our problem was. Our daughter immediately hooked up with the Gorlin Alliance and received an insurmountable amount of help in discussing, in figuring out what was going on. And because of that, she was directed and found... We're fortunate enough to be in the Chicago area. She put together a very effective team of physicians to deal with the jaw, and the skin, and all the organs, all the things that can go wrong. And she also formed that same network of friends outside of it. So the psychological help that started with the Gorlin's Alliance, and then... Lizzy, don't be alone ever. Reach out. There are so many good people out there, such as the Alliance itself and others who are willing to help, because the mental drain of this disease is devastating.

Dwayne (04:16:57):

When you asked earlier, Larry, about the consequences of what's happening, the thing that entered my mind was whenever... I know that we have good doctors, and unless it's really a bad forecast of a certain thing that's wrong, the thing that enters my mind as a grandparent and a close member of the group is the damage and the frustration and the hurt that my daughter and her family, her husband, and Cole himself go through. It's very frightening for them. And having that group of people that they know they can rely on is important. So Lizzy, don't ever be alone.

Larry Bauer (04:17:39):

Thank you, Dwayne. Thanks for sharing that. We have, in just a minute here, I see we've got Kaylene from Massachusetts who's holding on a call. But just before we get to Kaylene, Kathlyn would you like to weigh in on this topic of what are some of the drawbacks or downsides of the treatments that you've tried for Gorlin syndrome?

Caitlin (04:18:00):

Yeah. Thank you.

Caitlin (04:18:02):

One of the most recent ones is, some insurance companies will limit you to the number of Mohs surgeries you can have... or number of basal cells, I should say, to be removed by Mohs surgery in one day. And they want you to come back the next day, if you have two or three more for the second, third, and so on. I have a real problem with that, because if you can go in and get two or more taken care of in one day, I mean, that makes more sense. But at any rate, I agree with Maria about the severity. And so what that insurance problem brings us is to look at the severity of the basal cells that have been biopsied. And then you have to choose, because of your insurance restrictions, which ones will be done, when, and how long you wait, and those kinds of things. So that's the problem right now, at least in our situation.

Larry Bauer (04:19:08):

It seems incredible that someone would have to ever pick and choose that way.

Caitlin (04:19:12):

Right.

Larry Bauer (04:19:12):

Yeah. But thank you for sharing that.

Larry Bauer (04:19:15):

So if we could now go to our caller. Kaylene from Massachusetts, are you with us?

Kaylene (04:19:22):

Yes. I'm with you.

Larry Bauer (04:19:23):

Hi. Kaylene.

Kaylene (04:19:24):

Hi.

Larry Bauer (04:19:25):

So we're just having a discussion here about some of the downsides of Gorlin treatments. Yeah, go ahead.

Kaylene (04:19:32):

So my name is Kaylene. I am 22 years old and I was diagnosed with Gorlin when I was two. It runs in my family, my father and his side of the family also have it. However, my condition has been more severe in regards to the manifestation than the rest of my family. And basically, when I was four years old, it was when it really started to affect me. I was diagnosed with a cardiac fibroma. And when I was diagnosed with this fibroma, it was a shock to my family because it was the first time I had ever been diagnosed with something major that was Gorlin syndrome related. So at the age of four, my parents were forced to find a cardiac surgeon for their young daughter to remove this fibroma, and I only had a 50% chance of living at the time. It was in 2004, so not a lot was really known about the syndrome and it was very rare.

Kaylene (04:20:45):

So a lot of places refused to do the surgery, which was really difficult on my parents. And luckily, we were eventually able to find a surgeon who would do this type of surgery, but it was very emotionally draining for my parents, very emotionally draining for me. I know, when I was four years old, I was so desperate to be able to help myself get through it that I literally wanted to go down to the blood bank and give blood to myself when they were trying to find blood for me, for the surgery. And to this day, it still affects me. I have a scar on my chest as a result of it, and it's not cosmetically the best car to have. And it affects me in regards to being able to wear certain things. So when you're 22 years old, a lot of people like to wear things that are a little revealing, like v-necks and things like that, I don't have that opportunity to be able to do that and feel comfortable in my own skin.

Kaylene (04:21:50):

And even to this day, I can remember being four years old and just being so scared about that surgery. Most people don't remember when they were four years old, but that was just such a traumatic experience, just having to go through an invasive surgery like that. And until there's a way that we can

find a better treatment option or a cure for these cardiac fibromas, especially for these young children who have to go through it, I'll never stop advocating for better treatment because no four year old or anybody should have to ever go through that.

Larry Bauer (04:22:31):

Thank you, Kaylene. Yeah. It sounds like the downsides for that intervention, like you said, they continue even into your adult life. So thank you for sharing that. We had not heard too much about the treatment of cardiac, the myoma that you have and so it's important that you shared that.

Larry Bauer (04:22:50):

I see, we also have a caller, Martha, from Massachusetts. Martha, are you on the line?

Martha (04:22:58):

Hi. Yes. Hi, this is Martha. I'm calling in from Boston.

Larry Bauer (04:23:02):

Thanks.

Martha (04:23:03):

Hi to Erika, Erika and I know each other.

Martha (04:23:06):

I just wanted to call in and say that I'm 60 years old and I was diagnosed as a teenager. I just wanted to say that I just recovered from... so that's my fourth cyst surgery on my sinus that I've had in last five years, I went 18 years with no carotid cyst at all. I've had plenty of basal cells throughout, but the cyst seemed to give me this huge break, and I have no explanation other than perhaps hormones, menopause. That would be a topic I'd love for us to take up at another time.

Martha (04:23:39):

But the one thing I want to say is my cyst that I just had taken out, I had a drain in for 15 months, and I know we touched on this topic. And the reason he put it in this time was because when it came back, it came back bigger than the last two times when that same exact cyst had been removed. So it just got bigger and bigger, it was right up near my occipital lobe near my eye. So he was concerned about some eye potential damage if he removed it when it was that big.

Martha (04:24:09):

So after 15 months, he took it out. I waited a few weeks. I had the surgery. And what he also did is he stuffed it with a packing of Efudex. And I think this is becoming more popular as to preventing the recurrence of carotid cysts, and not to say that it worked the second time because that's exactly what he did. He did put the packing in the second time and it came back bigger, but that's just another medication that people are experimenting with in the use of non-recurrence.

Larry Bauer (04:24:42):

Okay. Thank you. Thank you so much for sharing.

Larry Bauer (04:24:45):

And we have, I see, one other caller on the line. It's Lorna from Hawaii. Aloha, Lorna, can you hear us here in the studio?

Lorna (04:24:55):

Hi, there. Yes, I can.

Lorna (04:24:57):

Can you hear me?

Larry Bauer (04:24:57):

We can hear you clearly. Please go ahead.

Lorna (04:25:00):

Oh, okay. So just touching on the subject of, in regards to the OKCs, so my son had his first one removed at the age of seven. And at that time, it was the size of a golf ball. And he did too have the drain tube installed after it recurred. And at that age of seven, to have something like that put in... It kept falling out a few times. The doctor wanted it to be in for a couple of months, I think, before he went back in. And we would have to go back in, have him get it stitched back up into his gums. And then to irrigate that thing every day as a parent... I mean, to a seven-year-old, that was just really crazy to do. And so now he's still dealing with that same cyst, now he's 15 years old and it tore through his sinuses, [crosstalk 04:25:58] teeth, so when he smiles-

Larry Bauer (04:25:59):

So Lorna, he's had the same cyst problem for eight years?

Lorna (04:26:05):

Yes. At age seven, that's when the first one presented. And then he was diagnosed with Gorlin syndrome the day before Thanksgiving when he was 12 years old. So then everything started to make sense. Like since I was pregnant from him, weird things... It was in my third trimester, the first ultrasound that they had, something looked funny with his head. They were concerned for hydrocephalus and they kept watching that. And so as soon as he came out, they have to do a CAT scan to check. And then just now the puzzles are being put together for me as a parent, because I could never understand all these strange things why were they happening? But yeah, so we-

Larry Bauer (04:26:57):

Who finally put the picture together? It sounds like your son had seen a lot of different people, but who finally pulled all the pieces together and came up with the Gorlin diagnosis?

Lorna (04:27:09):

So yeah, his oral surgeon had actually... Once he went in to take out the recurrent cyst on top of several other ones like on his lower jaw, but this big one was where his sinuses are in that maxillary area. So he didn't say anything after he took... He took it out and we were in the car, driving home. He called me and he was like, "I think you should have him see his primary physician and have him tested for something called Gorlin syndrome." And I was like, "What is that?" And he was like, "It's just like skin

cancers, and sometimes they get these OKCs, and stuff like that." So thankfully, he had opened that door for me because I had no idea. So he got genetically tested and so did my whole family. So I have two other children and my husband, we all got tested. So he's the only one that's affected.

Larry Bauer (04:28:07):

At what age did he first develop a BCC, if he has?

Lorna (04:28:13):

If I recall, ever since he was a baby, an infant, like months old, I would see these small spots on his body. But to me, it looked kind of like.... you know hen you get goosebumps?

Larry Bauer (04:28:27):

Yeah.

Lorna (04:28:27):

They were very, very small and I would see it like on his torso area. So I never thought anything about it. And then when he was that little, just a few months old, he would get these really big like boils on weird parts of your body that you wouldn't see it, like on his thighs or sometimes it would be in his torso area and stuff. And just there's no rhyme or reason, I took him to the doctor and would point it out. And sometimes I thought it could be like a mosquito bite or something. But they would just come and go sporadically.

Larry Bauer (04:29:01):

Okay. And they never biopsied one?

Lorna (04:29:06):

No, she would just treat it with mupirocin like Bactroban ointment, and then it would go away. So right now, he just had a BCC that was taken out of his scalp this week. And then on top of that, he had that one boil looking thing appeared on his arm and on his neck, so I showed her. Because he hadn't had it in a while, so I asked her to look at it and I said, "This is what I was talking about when I mentioned when he was little." So she looked at it and she was... It's kind of hard, so she's now treating him for staph, but she didn't think to biopsy. I'm not sure why. Well, he's a wrestler too, so she said it could be from that. So right now he's on antibiotics for it. And hopefully, that takes care of the problem.

Larry Bauer (04:29:57):

Yeah. Well, thanks for tuning in today. And thanks for calling, Lorna. We appreciate your input.

Larry Bauer (04:30:03):

Julie, do we have any written comments coming in about the difficulties or drawbacks to treatments?

Julie Breneiser (04:30:10):

We do, Larry.

Julie Breneiser (04:30:12):

Clara from New Jersey has written about some OKC surgery, jaw cyst surgery that she has. And she's written, "The most painful thing for me was an ongoing nerve damage done from one of these cysts." She says, in her whole mouth, she has pain and burning all the time. She also states that she has many leg cramps that cause her terrible falls and injuries throughout her body. She says, "I'm living in fear and continue to worry about not being able to take care of my body's daily needs."

Julie Breneiser (04:30:46):

Another couple of comments are from... One is from Kyle in Pennsylvania, "Each procedure is painful and makes me nervous, yet the symptoms keep coming back and I have to go through it all over again. Each time there is surgery, there's also swelling and pain."

Julie Breneiser (04:31:07):

Another comment, "The decades of wounds, scars, lost teeth, pain on Erivedge and other treatments result in lost hair, lost beard, and have all created an overall fatigue in me."

Julie Breneiser (04:31:20):

So those are the comments we have related to treatment failures and downsides at this point.

Larry Bauer (04:31:26):

Okay. Thank you.

Larry Bauer (04:31:29):

So is anyone on the Zoom panel... Anything you want to add after hearing all of these stories? Anything come to mind about the downside?

Larry Bauer (04:31:38):

Lizzy, go ahead.

Lizzy (04:31:42):

Somebody just mentioned it, and I think it was one of the callers, about the fact that they appear and then they kind of go away. I think it's important to know that with BCCs, when they go away, they're really just going under your skin to grow more. So I've had some that I can find them and I book my dermatologist appointment, and I go in and see my dermatologist, and they're not there again. And my dermatologist says, "This doesn't really look like anything. What are you talking about?" And advocating for yourself is super hard. My dermatologist is my uncle, I love him, but I've gotten to the point that I say, 'No, I strongly think this is a BCC and you're going to biopsy it."

Lizzy (04:32:36):

I have numerous scars, one on the back of my hand that didn't even look like a BCC. It was just a raised bump. And I convinced him to biopsy it and it came back as a BCC, and he said, "Wow, I was surprised." When his office staff calls... because I've worked there.... They say, "So you want to hear the good news or the bad news first?" And my comment to them always is the same, "Was I right on all of them, or was he actually right on one of them?" Because nine times out of 10, he will think that some of them aren't and they say, "Wait, he didn't think it was?" And I say, "Yeah, because they grow out and then go back down."

Lizzy (04:33:17):

I had a few on my face that I had mentioned to him just before starting the Patidegib trial. And he said, "No, those don't look like it." And I said, "Well, will you biopsy it?" And he said, "No, I don't see the need to do that right now. It doesn't look like it." And while I was on the trial and I was going in to see him about other spots, because I told him this is the area you cannot operate in. He would say, "Well, I'm really concerned about this spot." And I said, "Well, you weren't a year ago when I said this is a spot that needs to be biopsied."

Lizzy (04:33:50):

I think so often a lot of us, and I don't know if anybody on the panel would agree that we have to advocate for ourselves. We have to say, "You need to do this." And it's hard. It's hard knowing, like Kathlyn said, that you can only do so many surgeries at once. You can only do so many biopsies at once because of insurance purposes. It's hard. And so the fact that they're trying these trials that could possibly help us, especially in the facial field, is huge.

Larry Bauer (04:34:31):

Lizzy, I have a question about what you just said. You said sometimes that they're deeper under the surface. But if they go to biopsy one that you indicate, like there's something there, but it's deep, you might not be able to see it from the surface. What's the difference in the biopsy procedure? Is it a needle biopsy that they just go deeper? Or what is the difference between getting a surface biopsy versus a lesion that you say is embedded under the skin?

Lizzy (04:34:59):

So my experience with that is, if it's something that's more raised on the skin, they can do... Now, I'm going to forget the medical terminology.

Larry Bauer (04:35:09):

It's okay.

Lizzy (04:35:09):

But they can do a sort of a scrape biopsy that basically just... Shave biopsy, that's the word I was looking before.

Lizzy (04:35:15):

Maria's agreeing with me.

Larry Bauer (04:35:16):

Okay, great.

Lizzy (04:35:16):

A shave biopsy, where they can just go in and shave that top layer of skin off and go on and biopsy it. Whereas, if it does go deeper, and if it isn't as visible, and you can run your finger over it, there's nothing there, it's more deep. They have to do what's called the punch biopsy, where they take a little punch and work its way in to pull it up so that they can snip it off. And then you have to be stitched for that.

And usually, in a week, you find out, guess what? Now that stitch gets to come out and I get to have surgery all over again.

Larry Bauer (04:35:46):

Okay. Thank you. Yeah, the punch biopsy... Do they give you anesthesia, some kind of local anesthesia?

Lizzy (04:35:52):

Yeah.

Larry Bauer (04:35:52):

Yeah. Okay.

Lizzy (04:35:52):

Yes, yes. Every time.

Larry Bauer (04:35:54):

Erika? Yeah.

Erika (04:35:57):

Hi, just building on what Lizzy says, you have to become your own expert on everything. And I grew up saying... I grew up, that you trust your doctors and whatever they say is law. And after speaking with the support group and speaking with Julie and everyone else, I've had altercation... Not altercations, it's too strong of a word. But I've been in doctor's meetings where they've wanted to do a procedure that was completely against a Gorlin's protocol, and they'd have called in somebody else. And I've said to them what the procedure should be. And then this one doctor looked at me once, he goes, "Are you a medical professional?" Because I knew so much about what should happen. And I looked at him, I said, "No, are you?"

Larry Bauer (04:36:34):

You said, no... You should have said, "Kind of."

Erika (04:36:38):

And then I switched doctors after that and they didn't really make a stink because it was just so amazing to me. And as an educated person with a support group me, and these were the options in 2017, at one of the best children's hospitals, scares me that you had to fight to get something done. And these kids can't speak for themselves.

Erika (04:36:59):

And just in closing, I think that for my own... Like from Samantha, one of the scariest things for me is... And Meredith talked about it and another mom talked about it... is that watching your kids lose their smile. And when is that point when they realize their smile is actually scary to people instead of invoking that they're happy. So to me, that's the scariest and the hardest part about the whole procedures is they lose their smile and when you see the light go out of their eyes, and they don't even want to smile anymore. That's my biggest fear.

Erika (04:37:37):

I made it through the whole thing without crying, except for the past half an hour. I'm going to mute.

Larry Bauer (04:37:41):

Thank you. Thanks, Erika. No, thank you for sharing that. That's an important part of the story.

Larry Bauer (04:37:47):

So we're going to move now to the last segment of the program, thank you for everybody hanging in with us. I'd like you to take out your cell phone one last time and go to the PollEV. com/Gorlin, and we have two final questions for you. The first one is, which aspects of your condition would you rank as most important for a possible new drug or medical treatment today? And you can select up to three of these. So what are your top three?

Larry Bauer (04:38:21):

A is, prevent the need for more surgery to remove BCCs. B is, prevent BCCs from developing at all. C is allowing a person to go out in the sun without concern for causing skin cancer. D, reduce the recurrence of jawbone tumors in a non-surgical way to eliminate them. E, treat the underlying cause of the disease. F, prevent genetic transmission to children. G is, prevent brain tumors. H is slowing or stopping progression, and I is living longer, and J is something other. So these are which aspects of your condition you'd rank as most important if we were to develop a new drug? What symptom or aspect of Gorlin would you like to see treated? And you can choose three.

Larry Bauer (04:39:16):

So as the answers are coming in, it looks like prevention of BCCs developing is in the lead, which is linked very closely to A, to preventing the need for more surgery to remove BCCs. And then I see preventing genetic transmission to children, treating the underlying cause, and reduce the recurrence of the jawbone tumors, those are all ranking high. And we get some responses for allowing a person to go out in the sun, and also for slowing or stopping progression.

Larry Bauer (04:40:05):

Still a few more people answering, but it's slowing down. And the prevention of BCCs is still the lead, and the preventing the need for more surgery to remove BCCs.

Larry Bauer (04:40:24):

Okay, thank you. And then let's go to our next polling question.

Larry Bauer (04:40:29):

This one is a little different, a little shift. This is about looking at a new treatment that might be developed. So, would a preventive treatment that reduces new basal cell carcinomas by only 30%, not a 100%, and it had no challenging side effects, would this be an improvement on your current options? So A is yes, or B is no. So this is a prevention treatment and it reduced basal cell carcinomas by 30% from what you currently have.

Larry Bauer (04:41:10):

And I don't see anything moving, and I think that the reason for that is because it's pretty clear. Yeah, I think we're at a 100%. So let's go back to our Zoom panel then. So it looks like pretty much unanimously everybody has said that a reduction in 30% would make a difference.

Larry Bauer (04:41:36):

So I go back to the panel and I'd like to put the question out there, what would you all like to see in a new treatment for Gorlin syndrome?

Larry Bauer (04:41:45):

Show of hands, anyone would like to contribute?

Larry Bauer (04:41:47):

Lizzy, go ahead.

Lizzy (04:41:51):

I mean, I think we all wish that that number was a 100%, but 30% gives us hope. I mentioned earlier that I had laser treatments around my eyes when I was young. My uncle who's my dermatologist, he was at the time in Ohio doing his residency, had a doctor there that wanted to me to come in and do a full facial skin peel and re-graft all new skin on my face when I was a child.

Larry Bauer (04:42:22):

What? Wow.

Lizzy (04:42:23):

And my mom told my uncle at the time, "That's why you're in Ohio, and we're in Utah. We aren't coming to visit you." And just knowing, I think it gives us hope. It's the reason why I did the Patidegib trial. It's the reason why I'll do trials going forward to give us hope, to find something that helps. Like Nicole that called in, I'm not in a place myself where I feel like I could do the average. I couldn't. Being a mom trying to combat all those issues, I met people at the conference that were going through that and hearing all their issues they were having, I deal with my own depression and anxiety already. I don't need to stack that on top of it, but to know that there could be hope. 30% is somewhat of a low number, but as you saw, that graph didn't move. I think we all stand behind each other and beside each other more so as a team that we are here for whatever improvements there can be.

Larry Bauer (04:43:38):

Okay. Thanks, Lizzy.

Larry Bauer (04:43:42):

Dwayne? Can I call on you Dwayne? What would you like to see for your... Short of a cure, like if we can't cure Gorlin syndrome, but we could help it, what would be the greatest help to your grandson?

Dwayne (04:44:01):

Everyone is interested in hope for the future. I really feel that what you folks are doing is so critical and I hope the FDA really takes this to heart and realizes that even though this is a relatively rare problem in our society, it is substantial in the lives of the people that are affected by it. And I'm appalled by the fact

that we dealt with enlarged skull, skull surgeries, eye problems, all kinds of things in the Chicago area with a very sophisticated network of physicians of which we turned now loving a group of them that are taking care of Cole. However, the fact that they didn't know about what's going on is appalling to me. And so God bless Julie and you and the Alliance, we've got to get this out in order to get people's attention, in order to get support, to get money and to get support for finding a cure.

Dwayne (04:45:13):

And so I think I'm just more interested in the general approach right now. All of these things need to be... I don't know how many times I would tear up listening to the heartbreaking stories that we saw today, and we need solutions to this. And one of the things that bothers me, and I know that the Alliance has touched on it and had people talking about it is, this is a genetic problem. And we seem to, now with computers, have broken into the world of genetics. I would hope that as a group and some scientists who would look to see if there isn't a genetic patch or something to get to the heart of this problem. That's my biggest hope.

Larry Bauer (04:46:02):

Thank you, Dwayne.

Larry Bauer (04:46:02):

Kathlyn?

Caitlin (04:46:09):

I agree with Dwayne 100%. One of the things that I've seen over the years in the progression of the disease, starting with my mom, myself, and my son, the level of the medical community that knows absolutely negative nothing about this disease. So I even had a recent experience last week with a specialty physician who admittedly didn't know anything about it. And her treatment for my problem at the time was totally wrong. And my dermatologist had my back and said, "Look, if you ever have an issue, you come to me. I'm the one." I think, like all of the panel has said, we need to be the best advocates for ourselves and our children, and even talk to physicians, like Erica. I have had physicians where they say they knew about Gorlin. So I would quiz them, "Okay, what are three major manifestations?" They couldn't answer my question. So I would politely go to somebody else.

Caitlin (04:47:09):

The main thing is the medical community needs to know about this disease. We talked in the last session about being livers, not survivors, and so they need to understand that the world does not revolve around leukemia, lymphoma, and breast cancer, and the cancer world. That we're a very strong part of that because we never get rid of it. So I am constantly telling physicians what they're dealing with because they admit that they have never seen.

Larry Bauer (04:47:44):

Yeah. Thank you, Kathlyn.

Larry Bauer (04:47:47):

I see, we have a caller, Tom, from Massachusetts. He's in the queue. And just before we get to Tom, Maria you've had your hand up. What would you like to say?

Caitlin (04:48:00):

I agree with Dwayne, the genetics-

PART 9 OF 10 ENDS [04:48:04]

Maria (04:48:03):

I agree with Dwayne, a genetic fix obviously would be at the top of the list, but they make scary sci-fi movies out of stuff like that. So that's always a little scary. Aside from that, obviously from all that we've heard today, there's such a variety of expression of symptoms that at least having options is such a valuable thing. It's hard to label just one because you want to help yourself and you want to help somebody else too. So that would be my two thoughts on that. Thank you.

Larry Bauer (04:48:44):

Thanks, Maria. And Erica real quick, before we...

Erika (04:48:47):

Sorry, just real quick. I think that Gorlin is a rare disorder, but we grow tumors everywhere. But everyone in the world at some point in their life is going to grow a tumor. So any cures that we come up with, any treatments, everyone will benefit from in their life, even if it's just once. We're the Rosetta Stone for tumor growth. And I just want to... If you can fix us, you can fix anyone else. Thank you.

Larry Bauer (04:49:11):

Thanks Erika. Okay. If we could go to our call line, and we've had Tom from Massachusetts on hold. Tom, are you there?

Tom (04:49:22):

Hi, can you hear me?

Larry Bauer (04:49:23):

We can hear you clearly. Tom, go ahead. We're on this topic of hopes for the future.

Tom (04:49:31):

Thanks. Thanks, Larry and Julie and the FDA for doing this all today. I've had Gorlins for over 30 years, and my wife has been a caregiver for that whole time, and our daughter is 21, also has it. But I would say that unlike the amazing people who've shared their incredible stories of resilience today, to this point, I've had only a mild case of Gorlins and knock on wood so far, our daughter has as well. And what that means is for me, I've had over 500 basal cells removed in those 30 years. And I go in for surgery three or four times a year to try and keep it a mild case with my derm surgeon. But again, very thankful for the GSA for having these get togethers. And especially with the mental health, just having someone else to talk to is important, but actually it's some of those conferences I've heard before something that I haven't really heard touched on much today. So I just wanted to bring it up quickly and just mention it.

Tom (04:50:37):

So the FDA's aware of this as well. But one of the things that I've heard from a lot of people at these conferences is the fact that this Gorlin Syndrome affects people's ability to go to work. And you've kind

of heard some of that today from cases where the disease is so disabling, whether it's the brain, the speech, the site, or whatever that they can't work. But another thing is that even if people are not disabled to the point where they can't work, it still can be very difficult to get a job or hold a job because they need so many surgeries or treatments which often involve travel because a lot of times they don't have these medical resources near them, and there's a frequency of those treatments and travel as such that there aren't enough sick days and vacation days for them to cover that.

Tom (04:51:24):

So it becomes a real catch 22 in that the expense of the treatment and the travel when you don't have a job and no salary, and you don't have insurance coverage is really a huge, huge burden on top of all the other burdens that people have talked about today. So as far as any possible treatments, the cost is just such a huge factor in all of that too.

Larry Bauer (04:51:49):

Yeah. Thanks so much, Tom, for calling in. I have to say though, that I am completely struck by you saying that you have a mild case of Gorlin Syndrome and you've only had 500 BCCs removed. That just it's stunning, nothing less than stunning. Julie, any comments from online written comments?

Julie Breneiser (04:52:08):

Yes. I've got a few written comments, and they really put the hopes for the future in a nutshell, quite nicely. One from Sarah in California, my hope is future prophylactic medicines that will be 100% effective without debilitating side effects. Another from Colorado, until there is a cure, I wish there were topical treatments that would shrink and prevent my skin cancers without an ugly, irritated reaction. And another one that has come in relates to having treatments that are topical similar to the Erivedge and Odomzo. So basically a hope is the topical version of the Hedgehog inhibitors, people like that idea. So by and large putting these together, there are four of them. Topical treatments without side effects would be impactful for them.

Larry Bauer (04:53:14):

Would be impactful. Okay, thanks so much for those written comments. I'd like to go back to our Zoom panel. At this time in the program, we're going to say goodbye to you. So Lizzie, Erika, Dwayne, Kevin, and Maria, thank you so much for being with us today and for being on screen the whole day and contributing to this important meeting. We appreciate it so much. Your contributions will be lasting and we just want to say a thank you to you all. So you're free to leave at this time. I'd like to continue with, we have a couple other people on telephone calls. I see that we have Charlotte from Texas. Charlotte, can you hear me?

Charlotte (04:54:00):

Yes, I'm here.

Larry Bauer (04:54:05):

We can hear you Charlotte.

Charlotte (04:54:05):

Are you there?

Larry Bauer (04:54:05):

Yes, we do. Go right ahead, Charlotte.

Charlotte (04:54:07):

Okay, well, I'll try to keep this short. I was regarding Mohs and the PDT I was diagnosed back when this was being started. And as I've gotten older, I guess my age and the length of having the Gorlins, the treatments have become less effective. Like in Mohs, they had told me at one point when I was in my late thirties, that they might have to take my scalp off because of the different ones I had on my scalp, unless I tried a new treatment called PDT, which is a photodynamic treatment. And I went and had that done. I had to drive to Dallas to have that done. And that enabled me to keep my scalp and my hair rather, my hair and all that for a good 20 years. Of course, with Erivedge, I'm losing that now.

Charlotte (04:55:01):

And on the MOS treatment, when they first started the MOS on me, I'll say right here, I'm 71 now. But when they started all this, I was in my thirties. And when they started the Mohs, they could go in and they trace, they take it off by layers and follow the roots until they get all the roots. And then it's a clear area. And that can take half a day, can take a whole day when they're doing it. But as I've gotten older, they've told me that when they go in to do Mohs treatment to take a basal cell out and they start following the roots to get rid of it, they run into roots from other basal cells that are crossing over into the same area. And if they have to go chasing those basal cells, then they'd be all day trying to clear the scalp area.

Charlotte (04:55:50):

So I'm hoping that they will come up with a cure or a treatment in the younger generation, so they don't have to get to a point where it's almost like I'm on the borderline of things metastasizing because of the root systems of the basal cells. And I'm thinking I'm trying to be positive about the DNA. I think they're on the right track with the DNA. I think if they can magnify and get into more detail looking at the DNA, they'll find something where the nutrients maybe that are being blocked from the muscles that are causing the muscle cramps. They'll be able to track it down more precisely to where it only interferes with the basal cell and doesn't affect the muscles or anything else. And that's just my thoughts.

Larry Bauer (04:56:40):

Thank you, Charlotte. May it be so. These are all wonderful ideas and great expression of hopes for the future. We have one final caller I'd like to go to today. This is Christie from Ohio. Christie, can you hear us here in the studio?

Christie (04:56:56):

Hi.

Larry Bauer (04:56:57):

Yeah. Hi, Christie.

Christie (04:56:58):

Hi.

Larry Bauer (04:56:58):

We hear you. We hear you. Go ahead.

Christie (04:57:00):

Hi. It's great to hear you. I'm so proud of all of our advocates today, our peeps, Julie, Jean, for putting the whole thing together and all the presenters. I'm so proud of you for going and moving from affected individual to an advocate. And we've advocated today for people you will never know, but they're going to get and receive a much better idea of what their condition encompasses. I'm always been fond of moving from the having a specific treatment at a certain age, and then really looking at the whole body of work that has to go on. But one thing we didn't talk about much today is genetic counseling and reproductive health. That is so important to consider when people are wanting to have alternatives to having their own biological children. And those are tough decisions, but my son who's 47 has chosen never to have children because he does not want to pass this gene along.

Christie (04:58:04):

Even though I passed it to him, because I'm affected as well. One thing I'd like the FDA to know is keratocystic odontogenic tumors are not your run of the mill dental cyst. There's a lot of other dental cysts in the general population, but these are specific to this condition and are much more invasive and much more difficult to control. Sometimes they're not recurrences, but new occurrences because there are sister cysts that are lying there dormant, waiting to ignite. So that was something also that didn't get brought up, but you couldn't have made me prouder today. I'm so pleased with all of you, and thank you to the FDA for hearing our voice and our soul.

Larry Bauer (04:58:48):

Christie, thank you so much. I couldn't have said it any better. Those were the perfect closing remarks for our meeting today. And now we're going to move into hearing summary remarks. The summary remarks are going to be given by James Valentine. It's my great pleasure to introduce James who has this impossible task of trying to summarize everything that we heard of today's meeting. James is an associate attorney with Hyman, Phelps and McNamara. And some of you may know James from other externally led patient focused drug development meetings where he's helped plan. And he's been the moderator like I'm doing today for about three fourths of all the externally led patient-focused drug development meetings that have been held to date.

Larry Bauer (04:59:31):

Prior to joining the firm where he works. James worked for the US food and drug administration, the FDA in the office of the commissioner where he facilitated patient input and benefit risk decision making and served as a liaison to stakeholders on a wide range of regulatory policy issues. And just before James starts, I'm signing off as your moderator. And I just wanted to say a great thank you. It's been a pleasure and an honor for me to be the moderator, to have helped Julie in the planning of this meeting. And I have nothing but wonderful wishes for the future of people living with Gorlin Syndrome. And I hope that this meeting is an important step forward for your community. So now we turn to James with a summary. Thank you.

James Valentine (05:00:18):

Thank you, Larry. And thank you to Julie and to the Gorlin Syndrome Alliance for having me. So I've taken down lots of notes today, and I'm going to do my best to summarize what I've heard from you,

individuals living with Gorlin Syndrome and your care partners. So let's start in the morning. In the morning, we asked you to share what it is to live with Gorlin Syndrome, the symptoms and daily impacts. And what did we hear from you? Well, we heard about diagnosis. We heard that even with genetic testing availability, there can still be a lengthy journey to diagnosis. One person wrote in that it wasn't until age 32 that they got diagnosed, and this was recently despite having multiple clinical signs and symptoms. We also heard that this diagnostic journey exists for many despite first signs and symptoms occurring in infancy often. And several participants shared that they actually had treatment prior to ever receiving their diagnosis.

James Valentine (05:01:20):

But then getting to symptoms, we heard that Gorlin Syndrome has multiple impacts on people living with it, everything from reporting enlarged head, cataracts, arthritis, scoliosis, and other bony issues, cleft palate and lip, jaw bone tumors, ovarian cysts. And that's just to name a few. And you reported that each of you are living with many of these symptoms. It's not just that you have one of those. And just listing them doesn't even begin to impress upon the significant impacts that you said and reported that they had on your lives. A couple of notes that I jotted down. Bob discussed jaw bone tumors, leading to dental problems, including the loss of teeth and actually a speech impediment. This discussion of jaw bone tumors was a recurring issue. We heard John discuss that as a result of these tumors, he only has 16 remaining teeth subjecting him to need large amounts of anesthesia for the removal.

James Valentine (05:02:22):

Two women shared their experience with ovarian cysts and another symptom of Gorlin syndrome. Both were large, described as the size of a grapefruit in one case and a football for the other, making them appear pregnant and at least in one case causing the ovary to not function. And that's even before we get to the cancer. So with cancer, we heard that basal cell carcinomas are the number one most burdensome impact of your Gorlin Syndrome, both from the polling and the prominence with which this symptom was discussed. You are not cancer survivors, but you are chronic cancer livers and not liver as in the organ, as Julie said. We heard about not just a handful or even tens of BCCs, but your counts when reporting them were always in the hundreds. We even heard from Beth that her son who's just 13, has already had over a hundred BCCs.

James Valentine (05:03:22):

I noted that Alice reported that she experienced between four to 500 BCCs in the 35 years she's lived with it. And Bud and John, both shared that they've had over a thousand BCCs. This translates to tremendous burdens of treatments for these BCCs, which I'll get to in just a few moments. It's also malignant cancer. We heard Brandon share the stark reality of living with chronic cancer. He experienced two life threatening Gorlin Syndrome related malignancies. We heard this from several others as well. Cancers like medulloblastoma, pelvic osteosarcoma, and glioblastoma again, to name a few. The symptoms didn't just end at these physical symptoms, but you told us how Gorlin has a psychological and emotional impact on your lives. Kevin described the psychological impact of being repeatedly subjective to pain associated with these multiple manifestations and how this was exacerbated with treatments. Several speakers shared how children are forced to struggle with "the real sense of mortality." One patient sharing that her son wakes up in the middle of the night with anxiety fearing death.

James Valentine (05:04:38):

We also heard about the impacts that living with Gorlin has on your daily lives. We shifted into that discussion and perhaps not surprisingly, we heard that the number one impact on daily life was the limited ability to participate in outdoor activities. The sun was described by you as your enemy, limiting what you can wear and what you can do. If you do want to do something outside, I heard from you that you have to plan around when and where there will be shade. Many activities are limited with several symptoms making physical activities and participating in sports difficult. Children were described as not being able to keep up with their siblings and their peers when it came to these physical activities. Several participants described how any one or more of these symptoms, not to mention the time seeking treatment related to them, resulted in missing work and the difficulty in maintaining a job.

James Valentine (05:05:35):

For others, this limits their ability to plan financially as well as for their future or to retire. The impacts extended into social life. I heard that Gorlin Syndrome poses barriers to your social relationships and activities. Some examples that I took down in my notes were that these impacts include being self-conscious about smiling, bullying due to the large head size, feeling ostracized due to bandages and bloodying, visual impairment making conversations or navigating social settings difficult. This also included psychological and the emotional weight of this disease, both on those living with the condition, as well as their caregivers. Comprehending what the rest of your lives will look like, one parent shared that her young teenager wakes up in the middle of the night, anxious that he doesn't want to die. And that risk of death is real. We heard from Rocky sharing that her husband's passing as of a result of metastatic BCC.

James Valentine (05:06:41):

As for future concerns, what we heard, which was supported by the polling question is that your number one worry is the uncertainty of not knowing how Gorlin will progress. We heard from a number of people describe this as things like a ticking time bomb or living on top of a volcano. Many of these impacts are compounded given that Gorlin is a genetic disease. So we heard that both parents and children are living with the condition and trying to cope with both individuals. And finally these impacts were described as not being limited to those living with Gorlin, but also their children, their parents, siblings, and other family members who both share in the exhausting nature and trauma of the condition, as well as the restrictions it places on activities in daily life. So after we heard all of that from you in the morning session in the afternoon, we asked you to share your treatment experiences and how well they were working.

James Valentine (05:07:40):

What did we hear? Well, first we heard that the most common treatment approach is jaw bone surgery persists given the high rates of this symptom and lack of alternatives. We also heard about draining cysts as an alternative to this. And that can last many months, one person reporting the drainage needing to be in for 15 months. The negative result of the jaw bone surgeries is the removal of teeth, the impacts on speech that can require speech therapy, as well as importantly, the social impact of losing one's smile and how that really negatively impacts self-esteem.

James Valentine (05:08:20):

If these cysts are close to the eyes, we heard that it can even risk damaging your vision. But beyond that, most of the treatment approaches we heard about were focused on treating and preventing the BCCs. This included lifestyle modifications like avoiding sun exposure, using sunscreen and sun protective

clothing. However, we heard that this was not enough to stop the formation of new BCCs. We heard that each of you have tried several therapies both now and in the past. The most common is Mohs and surgical removal, as well as scraping. Beyond that we heard the top treatments include other therapies that were polled about. And many of you have tried. We heard that these treatments have mixed effectiveness that varies greatly from person to person in the short term, but universally the long term progression of the disease is ever present.

James Valentine (05:09:14):

Nothing cures Gorlin. Stacy talked about the astounding volume of BCCs that her young daughter has had, and the variety of treatments that they've tried. The only one with a consistent impact had been an off-label topical that had significantly stunted the growth of new lesions and did not have side effects. Another example is Maria mentioned that red light phototherapy had been helpful to treat her tumors. Several of you shared experiences participating in clinical trials. This makes sense to me, given the unmet need that you shared with us. So you resort to trials for potential useful treatments. And I also heard that it was important to help the next generation. Some of these experiences have actually resulted in treatment benefits for you. For example, John spoke about how he, "had his life back" while in a recent trial that was closed because it did not meet its endpoints.

James Valentine (05:10:11):

And this devastated him. For him during the trial, he was able to avoid needing annual visits. And now he's back to 12 to 15 visits annually for the surgical treatment of dozens of BCCs at each appointment. I heard that regardless of what the type of treatment was, when you did experience fewer new BCCs, that this led to an important improvements in your quality of life. Most spoke that avoiding MOS and surgery was the greatest benefit for having fewer BCCs. This to me was put into context from what all of you shared about the downside of Mohs and surgery, pain, permanent scarring, and disfigurement, especially on the face, head, and other parts of the body, the need for risky anesthesia, especially for kids. All of those risks were made worse by the fact that this is needed chronically as well as multiple rounds within a single visit, often needed to get clear margins, compounding the time burden, the pain and the anxiety. Despite these negative consequences, you have to continue to undergo this treatment option hundreds of times.

James Valentine (05:11:28):

So frequently that one person shared it's done so commonly that he no longer even tells his family when it's Mohs day, because it's so routine. This translates to a lot of lost time. I noted that Alice estimates that 40% of her life she's been in recovery or treatment. Another person estimated that they used 50% of their paid time off for treatment. Some specific drug side effects that were noted as most troublesome included, hair loss, pain, fatigue, and leg cramps at night. Ultimately at the end of the day today we asked you what short of a cure you're looking for from a future treatment.

James Valentine (05:12:12):

The one thing that was heard loud and clear there and was reflected in the polling was that you were looking for preventing new BCCs, as well as the ability to prevent needing more surgery to remove those BCCs. And in a follow up polling question, it was unanimous that preventing just 30% of new BCCs would be an important improvement over available treatments today. And in discussing that polling question, you acknowledged that this is a small percentage, but still would reflect an improvement.

James Valentine (05:12:48):

In discussion, these desires for future treatments was often described as being avoiding, "being cut" as well as the associated anesthesia, needles, and scarring. I also lost track with the number of times different people requested in a future treatment, if it could be topical, or if it could avoid the side effects of oral drugs. So with that, if I missed something important, I do apologize, but know that this is only the start of our work to summarize what was heard today. I truly hope that you walk away feeling heard. We know our colleagues at the FDA and at drug development companies, were listening. And as someone who previously worked at FDA, I know how valuable this input is. So now to close our meeting, I'd like to send it back to Julie in the studio.

Julie Breneiser (05:13:42):

Thank you, James, for the wonderful summary. This has been a powerful day of hearing personal stories to help understand Gorlin syndrome and its impacts. I'd like you to go away with three things, remember three things. Number one, individuals with Gorlin Syndrome have a lifelong cancer burden. We are never cancer free. Number two, every organ system in the human body may be affected by this rare genetic disease. And three, most individuals with Gorlin syndrome have a tremendous number of basal cells during their lifetime, many over 1000. Thanks to the brave presenters who willingly shared their struggles and stories today.

Julie Breneiser (05:14:33):

I believe that you can now feel the weight of this disease and see the gaping holes in our medical care from diagnostic delays to lack of treatment options. For us, there is no break, no remission, no walking away, no ringing the bell. We need safe, effective treatments with less scarring, pain, and disfigurement to prevent and manage the endless flood of basal cell carcinomas. We also need help to treat and reduce the 40 plus percent recurrence rate of the jaw cysts the odontogenic keratocyst that can result in loss of permanent teeth, facial numbness, and disfiguration. Additionally, our community would like to have safe FDA approved treatments for each of the 60 different possible manifestations of Gorlin syndrome.

Julie Breneiser (05:15:28):

You've heard how we feel and seen how we look. Most of us are resilient by necessity, but worn down over time by the unceasing nature of our disease, the needles, cuts, pain, disfigurement travel, ordinary outdoor activities, even sunlight shining through a window upon our skin can create a toxic exposure that negatively impacts our enjoyment of each day. We spend our lives on high alert for the next malignancy. Finding employment conditions compatible with maintaining baseline medical care and minimal UV exposure can be difficult to impossible for those with high numbers of basal cells and other manifestations that we and our children endure. Starting at birth affected individuals are ill-equipped to protect themselves from the exponential growth of lesions and multitudinous manifestations. Some do not survive the ravages of our cancers. As you saw, even an improvement of 30% would be a meaningful outcome to the Gorlin Syndrome community.

Julie Breneiser (05:16:40):

For example, bringing the total lifetime number of BCCs from four digits to three digits. That's significant. Thank you to the FDA staff who tuned in today and to Will Llewellyn from the FDA patient-focused drug development staff who guided us through the process. We're grateful for your help. Thank you to Dr. Sally Lewis from the FDA, for your perspective on the externally led patient-focused drug

development meetings and to Dr. Joyce Teng from Stanford University for your very educational clinical overview of Gorlin Syndrome. Thank you to the Dudley Digital Works media team. None of this would've happened today without my GSA staff, Colleen, Kathy, Jean and Joanne, who worked incredibly hard behind the scenes to plan and execute this meeting. Thanks, team GSA.

Julie Breneiser (05:17:35):

Our next step will be to compile all the information from this meeting into a voice of the patient report. There'll be a web link for the next 30 days for affected individuals and family members to submit additional comments. So if you didn't get a phone call through, if we didn't get to it, or if we didn't get to your comment, please send in the comment, and we'll will do our best to get it there. The video and report along with the list of supporters will be publicly available on our website Gorlinsyndrome.org. Everyone in the Gorlin Syndrome community, particularly the presenters are owed a tremendous amount of gratitude. Many of us minimize or deny our problems, but in this setting, you've shared what goes on behind closed doors, the bad, the ugly, the pain, the anxiety. Thank you again for going to those dark places and telling your stories. The impact of this meeting is going to be felt for years to come. Please take care, everyone.

PART 10 OF 10 ENDS [05:20:00]