James Valentine (00:13:44):

Good morning. My name is James Valentine and welcome to the Externally Led Patient Focused Drug Development Meeting for focal segmental glomerulosclerosis or FSGS. We're coming live to you from the Washington DC, Metro area, actually not too far from where the US Food and Drug Administration's headquarters are located in Maryland. To open today's meeting, it is my pleasure to introduce my cohost, David Feldman, Medical Project Director at the National Kidney Foundation.

David Feldman, PhD (00:14:14):

Thank you, James. Hello everyone. I am so happy to welcome you patients, care partners, and so many of you who are joining this EL-PFDD meeting on primary FSGS. We are thrilled that as of this morning, over 340 participants from 42 states and eight countries registered for this conference. Today's meeting was originally planned as an in-person meeting. However, the pandemic forced us to switch to a virtual format and even though we very briefly thought about holding off for an in-person meeting, it was clear that we could not delay bringing your voices to the FDA. Thank you for joining us in today's format and as you can see, we are – James and I – are appropriately separated from each other.

The National Kidney Foundation is proud to partner with NephCure Kidney International to host this EL-PFDD meeting, and I want to say how much of a pleasure it's been to work with Kelly Helm and Kristen Hood and Lauren Lee, all at NephCure in planning today's meeting. It's been a wonderful collaboration.

And now for a few thank yous:

First, to our testimony panelists for their dedication and courage in preparing the statements that we will hear today, and to our discussion panelists, who will add even more to today's conversation. A special thank you goes to our meeting co-chairs doctors, Laura Mariani and Suneel Udani whose talks will set the stage for much of today's discussions and of course, our sponsors. We are very grateful for the generous support from Boehringer Ingelheim, Cyclerion, Mallinckrodt, Retrophin, and Vertex.

This is an important meeting for the FSGS community. It gives you the patients and care partners a unique opportunity to speak directly to the FDA and the pharmaceutical companies that are currently developing treatments for FSGS. These are the two most important groups that will determine what treatments become available to you, and today you can help them by telling them what symptoms of FSGS are most important to you, what you're looking for in an ideal drug and what trade-offs you'll be willing to accept in a new treatment.

Importantly, you'll be able to voice your preferences regarding clinical trials for FSGS. To be clear, today, you can give input that can actually help influence the trajectory of drug development for FSGS and therefore, help bring to market drugs that matter to patients. During this meeting, we're going to ask you to let us into your lives. Please don't be shy. You are the experts in living with FSGS, so please call in and make your voices heard today. You can find the agenda for today's meeting by scrolling down on your screen and clicking on meeting program.

Finally, one last word to the patients and care partners: Today's meeting is the fourth EL-PFDD meeting on kidney disease that the National Kidney Foundation has hosted and in each of the previous meetings, the most common theme that emerged was that patients and care partners are looking for hope; hope for safe and effective drugs to treat their diseases, hope for a healthy life. Well, today's meeting represents that hope. The fact that five pharmaceutical companies are supporting this meeting means that scientists and senior leaderships of these companies recognize the importance of finding drugs for FSGS and believe it's worth investing efforts and resources into it. My wish is that you can take hope from knowing that these and other efforts are taking place around the world.

And now it's a real pleasure to introduce our first speaker, Dr. Aliza Thompson. Dr. Thompson is the deputy director of the division of cardiology and nephrology, which is in the Center for Drug Evaluation and Research at the US Food and Drug Administration, that's the FDA. This is the division that will review the merits of potential new drugs for FSGS.

And now Dr. Thompson will tell us how EL-PFDD meetings like ours fit into the FDA's function to approve drugs. Dr. Thompson, thank you very much for joining us.

Aliza Thompson, MD (00:18:57):

Thank you, David. Hello and good morning to everyone. I'm just going to get situated here. Fabulous. I'm here today with many of my colleagues from FDA to listen and to learn from you. This is a very difficult and challenging time, and I'm sorry that we can't meet in person, but as David noted, today is about hope and success. Because of important advances in science and because of your efforts and the efforts of the larger community, pharmaceutical companies are developing treatments for kidney diseases, such as FSGS. As David noted, we cannot delay this meeting. We, the FDA and our partners in industry, the companies that are developing treatments for FSGS need to hear from you.

We need to learn from you, so thank you for joining us today and for sharing your stories. I think it goes without saying, or at least I hope it goes without saying that patients, the people living with the disease should be at the center of the drug development process and yet, somehow as we developed this whole enterprise, we seem to lose track of this. Fortunately, we, as a larger community are working to address this. Some of you may already be familiar with FDA's efforts in this space, these efforts related to patient focused drug development. In the next few slides, I'll share with you the overarching goals of this initiatives. Next slide please. Right.

I think if you think about the overarching goals of patient drug development in this initiative, it really falls into two larger bins. One large component is really listening to you, all patients, the people living with the disease and learning from you all about what matters to you, but there's also another big bucket and that I'll refer to as the science bucket and that is how do we do this effectively? How do we do this in a systematic way? How do we systematically, effectively, consistently incorporate your voices into drug development and into our decision making? On this slide and something that we will ask you today, or you will be asked today, is to discuss what factors might affect your decision to participate in a clinical trial.

There's another part of this discussion that I want to highlight that I think is also something we need to engage with you all, and that is really about some of the challenges we face in designing trials that are intended to evaluate the efficacy of new therapies. For example, randomized controlled trials are often needed to determine whether a therapy is effective and depending upon the tempo of disease and by that, I mean how fast the disease progresses, patients may need to remain in their assigned treatment arms for a few years to determine whether a drug is effective and actually provide benefit to the patient. This is a challenging issue, but certainly one that we need to discuss.

Next slide please. Here again, we just highlight some of what we hope to understand from you today and what we hope to learn from you today about your preferences, about what might be acceptable tradeoffs for you in terms of risks versus benefits.

Next slide please. Great. As David mentioned, we've already had and been fortunate to have a number of patient focused drug development meetings related to kidney diseases. Often, I am asked how these meetings affect our decisions at FDA. How do they inform our decisions? I suspect that in the years to come, we as an agency and scientists outside the agency will study and attempt to understand and quantify the impact these types of meetings have on drug development, but really the best I can do at this point is to answer this question on a personal level.

Your stories, the stories that we hear at these meetings are powerful. Although you may see us as regulators and we are regulators, we are in fact people just like you. We have families and friends, we have people we love who have suffered from disease, and some of us have been patients and caregivers. I think many of us connect with your story on a very personal level. I think your stories remind us of the urgency with which we must act to address the obstacles to drug development, and they inspire us to do better. I think they speak to why many of us decided to pursue careers in medicine and why we decided to come to the agency. Simply put it is not enough to be able to diagnose the disease, to be able to tell a person the cause of their suffering, we need to be able to treat it.

Next slide please. In closing, successful drug development takes a village and obviously you, the patient, the people living with the disease need to be at the center of this process. As I noted before patient focused drug development meetings such as these are critical means to involve patients and to understand what is important to you, but I want to point out that these meetings are just one step in this process to truly accelerate drug development for FSGS. We need you all to remain actively involved, to essentially drive this process and to inspire and encourage others to be involved as well. Again, from the team at FDA, we thank you for sharing your experiences and stories. We are eager to hear from you and look forward to working with you in the years to come. David.

David Feldman, PhD (00:25:39):

Thank you Dr. Thompson for perfectly putting today's meeting into perspective. And now I'm very happy to introduce Dr. Laura Mariani. Dr. Mariani is a nephrologist and clinical researcher at the University of Michigan, where she is an associate professor of medicine in the division of nephrology. Dr. Mariani is an expert in FSGS and will present an overview of FSGS, the natural history of the disease and its treatment. Welcome Dr. Mariani.

Laura Mariani, MD (00:26:16):

Thank you so much for allowing me to participate in this important conference, where I'm going to tell you a little bit about the natural history of FSGS and its treatments. On the next slide, I'll just start off with my disclosures, which are listed here and then let's begin on the next slide was two patients. I wanted to share with you two patients that I took care of when I was training. The first patient is a 26-year-old man. He was born in the Philippines, completely healthy until around age 20 when he showed up with swelling in his legs. When he was diagnosed with FSGS, his kidney function was well-preserved. On steroids and then tacrolimus, his disease went completely away, but when he ran out of his medications or couldn't afford them, the disease came right back.

My second patient is also a 26-year-old. This woman is African American. She was born prematurely, but otherwise completely healthy. She was also diagnosed in her early 20s, but when she was diagnosed, her kidney function was already severely impaired. We did try immunosuppressant medications, including steroids, tacrolimus, and MMF. Unfortunately, none of them really changed her disease progression and when I left training several years ago, she was already starting dialysis. These patients obviously have a very different presentation and on the next slide, I think what's so frustrating is that both of them are given the same disease diagnosis, which is FSGS based on their biopsy.

These patients are asking me the same question, what disease do I have? How did I get it? Does it mean anything for my children? What will happen to me over time? What's the best, least toxic medication that we can try? While we're learning a lot and there are many researchers working on trying to find the answers to these important questions, honestly, there's much that's really unknown, and I think this is frustrating for both patients and clinicians. I want to tackle some of these questions and share with you

what we do know, and also be clear about places where we really don't have enough data. On the next slide, let's tackle the question, what disease do I have?

FSGS, really this is a pattern of injury on the kidney biopsy, and it means that some of the glomeruli have a partial scar, the glomeruli or the filters of the kidney. When the pathologists look at these biopsies, they often tell us not only where the scar is, but where it's located within the filter and the characteristic appearance – does that have cells or not. Unfortunately, this really doesn't link to biology, and that's why my two patients have such different courses. They can both have scars in their kidney, but it doesn't tell us the underlying cause. On the next slide, I just want to lay out a little bit how clinicians approach the question of “how did I get this disease?” We do know something about FSGS.

We know that there are certain genetic mutations, which can cause this pattern of scar on the biopsy. We know there are medications, infections, and other insults to the kidney, which can cause this pattern of scarring, but I know today, we're primarily talking about primary FSGS. For many patients, that means we don't understand the biology of what's causing their disease. For some patients, we think that they have a circulating factor that's causing the kidney to leak protein, and there's probably many different biological processes that can do this. The patient's like my two patients show up with similar symptoms. They show up with edema or swelling in their ankles and their biopsy can look very similar.

Unfortunately for many of these patients, that means that even if their kidneys do fail and they get a new kidney, the disease can recur in their transplant. On the next slide, I want to tackle the question about “what will happen to me?” Obviously, each FSGS patient is really different, and so there's unfortunately no data that we can say, "Oh, based on all of these different things, I can tell you exactly what will happen." When I sit down and talk to a patient, I go through all those individual factors, starting with what are all the things that we see on their kidney biopsy. We also go over all their clinical information, what other medical problems they have, their kidney function, how much protein they're spilling.

In some patients, we have genetic information that can tell us about how that individual is going to do. The biopsy can tell us a lot and so on the right, you can see this graph here that like I said, based on where that scar is, there are some patients that will tend to do better and some patients that will do worse. For example, that solid line are patients who have a collapsing lesion. The whole filter is collapsing down and while on average patients with that particular lesion tend to do worse, you can see from this graph that it's not everyone. It's not a hundred percent, so there are some patients that do really well and other patients who do lose their kidney over time.

On the next side, I wanted to highlight just another potential information you can get from a kidney biopsy of an individual person. We can tell something, not only about how the filters are damaged, but how the rest of the kidney is damaged. The interstitial is the space between the filters and if this disease has been aggressive enough, such that their scarring in between the filters, that's often irreversible. This study here from the Neptune cohort is that patients who had a lot of scarring, again that solid line, were less likely to have remission of their protein in the urine. On the next slide, while patients want to know “what will happen to me?”, a lot of the data that's out there is really what will happen to a group of FSGS patients.

Here what will happen to us and in particular, “will my kidneys fail?” On the left, this is data from the big Toronto Registry. It's about 280 patients with FSGS, and actually one of the predictors of whether or not a person will lose their kidney function completely depends on how much protein they spill over time. Again, you can see that solid line on the bottom. These are patients that even though they're treated, their protein does not go away and over time, over the years, you can see that more and more patients lose their kidney function over time. On the right, we can see a newer analysis that was published

looking at the same thing. Here is a group of studies, both observational and electronic health record data, where again, there were about 460 some FSGS patients here.

If you looked at four months after their biopsy, what their level of protein was, for patients who despite treatment had no response in their protein levels, the red line, you can see that just over two years, many of them had lost their kidney function. On the next slide, it seems that there's actually quite good data that the amount of protein you're spilling over time will tell me something about your risk of losing kidney function over time, but how likely is that to happen? How likely is it that a patient who's diagnosed with FSGS and gets treated will actually have complete remission of their protein? This is from the Neptune study. It enrolls patients at the time of kidney biopsy. Here, there's about 142 FSGS patients. And you can see overall a little less than 40% achieved complete remission of their proteinuria over the two years of follow up.

On the next slide, I'll show some data from a pediatric cohort. So, this is a large registered history of children with steroid resistant nephrotic syndrome. Of those who had a kidney biopsy, majority had FSGS. And again, in this group, you can see that about a third of patients were fully responsive to immunosuppression. Whereas a large proportion actually did not have complete remission of their proteinuria and were at risk of losing their kidney function over time.

So, on the next slide, the next question patients ask me is “what's the best least toxic medication?” And these are the recommendations from the international group of nephrologists that published guidelines in terms of treating glomerular disease. And you can see that the initial treatment for primary FSGS, although we don't completely understand the biology, is immunosuppression. And so the first line therapy is prednisone. This is a high dose and often I ask my patients to take at least a month and up to four months of high dose steroids, and then a slow taper over a six months total. An alternative are calcineurin inhibitors, cyclosporine or tacrolimus. These tend to work a bit more quickly, but really often require a couple months of trial before we decide if it's been effective or not.

If patients relapse their disease after those initial treatments are stopped, or if they don't respond to them at all, or when you try to taper the steroids, the disease comes back, there are some second line agents available. CellCept, Rituximab, ACTH, but really there's not a huge list of things to try that I would consider to be first- or second-line therapy. And so if those don't work, I'm often talking to my patients about clinical trials.

And then the last slide, I just want to highlight that medication toxicity is a real problem in FSGS. So even though we have therapies we can try, I'm often asking patients to take medications that make them feel poorly. And so, steroids can cause weight gain and mood changes, but all of these other medications can cause side effects. And I know our patients are going to tell us a lot more about what it's like to not only live with this condition, but also to take these medications.

And this table here is intentionally small, but I just want to highlight the many side effects. So this is a table from the FSGS clinical trial. It randomized 138 patients to CellCept and dexamethasone versus cyclosporine. These were children and young adults. And you can just see that actually there's many side effects patients are experiencing when they take these medications. So, we certainly not only need better understanding of the biology, but we certainly need better treatment options so that we can change how we're taking care of these patients. So, on the last slide, I'll just say, thank you very much for having me and I look forward to hearing from all of our patients.

David Feldman, PhD (00:37:25):

Thank you, Dr. Mariani for that excellent presentation and for very clearly setting the stage for today's presentations, for today's discussions. Excuse me.

So now we are at the core of the meeting, hearing from you and to lead us through the rest of the meeting, I'm really happy to introduce our moderator, Mr. James Valentine. James is an associate attorney at the law firm, Hyman, Phelps and McNamara in Washington, DC, where he assists the medical product industry and patient advocacy organizations in numerous matters, including issues on drug development and approval and clinical trial matters. And of course, all of these are things we're talking about today.

But here's the major reason why we're very lucky to have James as our moderator. Before joining Hyman, Phelps and McNamara, James worked at the FDA. And among other things, he was closely involved with the transition of the patient focused drug development, that's the PFDD program from within the FDA to the PFDD meetings that are now led from outside of the FDA, the externally led or EL-PFDD meetings, like our meeting today.

In other words, James knows these meetings. In fact, James moderated the National Kidney Foundation's last three EL-PFDD meetings on kidney disease. And he has moderated 26 of the 36 EL-PFDD meetings for other diseases that have been conducted so far. That's 70%. So, we're in the best of hands today. And it's a pleasure now to turn the meeting over to James.

James Valentine (00:39:17):

Thank you, David. And it's a pleasure to be with all of you this morning. So now that we've heard the clinical overview from a disease expert, as well as a colleague from the food and drug administration, now, as David said, we get to turn to the core of today's meeting, which is to hear from you, patients and their direct caregivers about the experiences of persons living with FSGS.

Patient focused drug development is a more systematic way of gathering patient perspectives on their condition and on available treatments. And as you heard from Dr. Thompson, your in person ... your input can help inform the agency's understanding of FSGS to inform drug development and review.

So far, FDA has held 26 of its own PFDD meetings. And as previewed by David, today marks the 37th externally led PFDD and due to the ongoing COVID-19 pandemic, it's the fifth fully virtual PFDD of its kind. Today's meeting is interactive. So I want to tell you a bit about what we'll be asking of you to do throughout today's meeting, but first let me explain the different topics that we're going to be addressing as a group. First, we'll be exploring the patient and caregiver experience with living with FSGS and its impacts on your daily life. In our second and third sessions, we're going to explore your experiences as well as your preferences about participating in clinical trials for potential drugs for FSGS.

And then finally, in our fourth session, we're going to bring everyone back together to explore the various approaches to treatment that you currently have, as well as be asking your preferences about future treatment and what it is that you would look for. So what will those discussions look like? Well, we're going to use a number of key methods to have you actively participate. And that's important. The success of today's meeting is contingent upon this community coming together and sharing their ... and having their voices heard and sharing their experiences. So we're going to be hearing from panels of patients and caregivers with FSGS to help set a good foundation for the discussion.

These panelists were selected to reflect a range of experiences of individuals with living with FSGS and the caregiver experience. We will then build on that panel discussion with audience discussion, with all of you who are tuned in live today. I'll be asking questions and inviting you to provide a comment. This can be done in one of two ways. We want you to dial in by phone and I'll be giving that phone number out throughout the entire program, as well as write in with written comments, which can be provided in the form that you see below the live stream today. You'll also see that we'll have a panel of members of the FSGS community on by Zoom that will also be participating in the discussion.

In addition to asking you to chime in live and share your experiences, we're also going to be using live polling questions throughout the day. We'll be asking you to pull out your phones or open up another tab on a web browser, go to a URL that I'll provide to you. And then you'll be able to see these questions throughout the day and provide your responses. And we'll get to see in real time the experiences of everyone that's following along. I also want to mention that today is not our only opportunity to have you provide input. There'll still be an opportunity to provide written comments for 30 days after this meeting using that same web form and importantly, all of today's input, as well as the additional written input will be summarized in a voice of the patient report, which will both be provided to FDA and made available for those researching and developing products for FSGS.

So before we actually move into our first set of polling questions, I want to go over a few ground rules for today's meeting. We encourage individuals with FSGS and their direct caregivers to contribute to the dialogue. So, that's over polling, dialing in by phone, submitting written comments. However, this is limited to individuals with FSGS and their direct caregivers like family members. Our friends and colleagues at the FDA, drug developers, clinicians and researchers are here to listen. So we ask that those parties stay in listening mode and not respond to the different questions we'll be posing to the patient community. Of course, views expressed today are inherently personal and the discussion may get emotional at times, it's an inherent part of sharing personal stories. So we ask that you please be respectful of one another. That is paramount. And to that end, I ask that you try to be focused and concise when making your comments, that way we can hear from as many voices as possible throughout today's program.

So without further ado, let's get to it. We're going to actually start with an initial set of polling questions that we have. So again, please pull out your phone, open up a web browser, open up a new tab on your computer, on your web browser and type in www.pollev.com/PFDD. Again, that's pollev.com/PFDD. That URL is at the top of the slide that you see now with the first polling question, which is asking you whether you're an individual living with FSGS, or you're the caregiver of someone with living with FSGS, like a spouse or a parent, maybe even a child of someone. So please respond to this. If you happen to be both a patient and a caregiver, please respond that you are an individual with FSGS.

And again, you'll be able to just stay on this webpage throughout the entire day. We'll be coming back to these polling questions throughout. So we're going to give everybody a few minutes here to get into the system. We want to be able to follow you and your responses throughout the day. So while this is one of the simpler questions I promise they'll get more interesting throughout the day, and we're just giving everyone some time to get into this system and answer this first polling question. As it stands, it looks like about 80%, just under 80% of our participants are individuals with FSGS primarily. And about 20% of our participants today are caregivers of someone living with FSGS.

If we can move to our second polling question. So here we want to know where do you, or if you're a caregiver, your loved one with FSGS, where do you live? Your options are A, in the US East coast – and that's the Eastern time zone – B, the US Midwest or the central time zone, C, the US mountain or the US West or the mountain time zone, D the US West coast or the Pacific time zone, E, Canada, F, Mexico, or the Caribbean islands or G, if you're outside of North America, including Europe and South America. We want to get a sense of where our participants today are, where you live.

So I'll give you just a few more moments to respond to this question. As it stands, it looks like about half of our patients and caregivers today are representing people living on the East coast, about just under a quarter representing the US Midwest, the next largest after that over 10% representing the West coast in the US but we do also have representation from the US West, from Canada, from Mexico and the Caribbean islands and from outside of North America. So very good representation from all regions. So, if we can go to our third polling question. So here, we would like to know if you're an individual living

with FSGS, your age, or if you're a caregiver, the age of the individual for whom you care or your loved one. So, what is the patient's age?

The options are A, younger than 18, B, between ages 18 and 29, C, 30 to 39, D, 40 to 49, E, 50 to 59, F, 60 to 69 or G, greater seven ... age 70 or greater. So again, please select your, or your loved one with FSGS's age. All right. Then, as it stands, it looks like we've got a good representation across the different age ranges. About just under a quarter of individuals in the 30 to 39 and the 40 to 49 age ranges, about a fifth of individuals under age 18, over 10%, both in the 18 to 29 and 60 to 69, just under 10% in the 50 to 59 age range and a few individuals representing those age 70 or greater. Then we go to our fourth polling question.

So here we want to know, do you, or your loved one with FSGS, identify as A, male, B, female, C, non-binary or non-gender conforming or D, if you'd prefer not to say. I'll give you a few more moments here to get in your response, as it stands, we're looking at about somewhere between 70 to 75% of our patients represented today are female, somewhere between 25 and 30% of our patients represented today are male. All right, if we go to our fifth polling question. So, here we want to know whether or your, or your loved one's ethnicity or race. The options are A, Caucasian, B, African American, C, Native American, D, Latinx, E, Asian, or F, some other race or ethnicity not listed above.

I'll give you a few more moments here to report in your, or your loved one's ethnicity or race. It looks like about 70, a little over 70% of our patients represented today are Caucasian. About a fifth of our patients represented today are African American, and then about a 5% each Latinx and Asian. If we could move to our next polling question. So here, we want to know a bit about your medical history or your loved one's medical history. So here we want to know what is the length of time since your diagnosis of primary FSGS. The options are A, less than one year ago, B, one to two years ago, C, two to five years ago, D, five to 10 years ago, E, more than 10 years ago, or F, if you're not sure the length of time since your diagnosis or your loved one's diagnosis with primary FSGS. All right, I'll give you a few more moments here. As it stands, it looks like our greatest representation – about 40% of our patients represented today – were diagnosed with primary FSGS more than 10 years ago, about 20 to 25%, both in the two to five year ago range and the five to 10 years ago range, about 10%, one to two years ago, and a little over 5%, less than one year ago. No one reporting that they're not sure. And if we go to our final polling question for this session, we want to know again, a bit more about your medical history. Are you, or your loved one, A, not currently on dialysis and have never received a kidney transplant, B, currently on dialysis and have never received a kidney transplant, C, a kidney transplant recipient in remission, D, a kidney transplant recipient with recurrent FSGS or E, kidney transplant recipient, and currently on dialysis that in other words, or for example, a failed transplant.

So please select a response that reflects your, or your loved one's medical history as it relates to kidney dialysis and transplant. So it looks like as any final responses are trickling in that about 60% of our group represented today are not currently on dialysis and have never received a transplant. We have a few individuals that are currently on dialysis, but have never received a transplant, 20% have received a transplant and are in remission, a little over 10% having a transplant, but with recurrent FSGS, and a little over 5% having a transplant, but are currently on dialysis, for example, because of a failed transplant.

TOPIC 1

James Valentine

So thank you so much for participating in these polling questions. It's great to have a sense of who we have with us today. That's going to help set the stage now, as we move into our first kind of real topic,

which is to hear from you all about your experience living with FSGS. We want to hear from you in this topic session about what symptoms and health effects of FSGS are having the greatest impact on you in your daily life.

We want to understand how those symptoms might vary, whether it's day to day, week to week, month to month, or even over the course of years. We also want to know how that translates into your life. What are the activities that you – are important to you that you're able – not able to do either fully or not able to do at all because of your FSGS? And finally, what is it that worries you about living with FSGS in the future? And to get us started on this topic, we have a panel of patients and caregivers. We have Bernadine, Christopher, Christine, and Jackie, who are going to share some of their stories related to those topics. So Bernadine, take it away.

Bernadine (00:55:55):

Hello, my name is Bernadine. Most people call me Dine. I'm 69 years old and have lived with FSGS for 36 years. I've had two kidney transplants and spent five years on dialysis. I'm happy to be alive. I was diagnosed with FSGS in 1984 when I was 33 years old, and my doctor found excessive protein in my urine. At the time of my diagnosis, I was a working mom in a failing marriage. I had attributed my exhaustion, intermittent joint pain and gloomy days to the stress in my life. When my ankles swelled, I assumed that I had eaten too much salty food. For more than 14 years my FSGS symptoms remain mild. My blood pressure and cholesterol readings stayed normal. And my creatinine and proteinuria levels were stable. I continued to experience fatigue, but lived a healthy, active life. I raised my son and built a successful career.

My nephrologist told me that my prognosis for avoiding kidney failure was good. He was wrong. One day in 1998, my doctor called with my latest lab results. I will never forget his words that day, "Ms. Watson, your creatinine level is ticking up." My nephrologist and I spent the next two years in a fierce battle with FSGS as my blood pressure, creatinine and proteinuria levels rose, my cholesterol spiked, and the edema in my feet got worse, my nephrologist fought back with the medicines available. On most days of the week, I felt close to normal. However, on one or two days, I was so fatigued I didn't want to get out of bed and so unable to concentrate that my work suffered. Once, I lost my train of thought in the middle of an important work presentation.

By early 1999, I was suffering from acute iron deficiency. My nephrologist told me that I would need a transplant or dialysis within a year. I was so anxious and depressed that I began seeing a therapist weekly. In 2000, I received my first kidney transplant from my older sister. The transplant alleviated some of my FSGS symptoms, such as fatigue and inability to concentrate, and my creatinine level returned to the normal range. However, I continued to experience intermittent joint pain and minimal edema in my ankles, especially after sitting for extended periods. I was told that my new kidney should last for 20 years, but by 2004, just four years later, I began to experience symptoms of FSGS recurrence, including almost daily bouts of fatigue, edema and lack of concentration.

In addition, I began to have symptoms I hadn't experienced before my transplant, such as shakiness and devastating diarrhea. I had just remarried and unfortunately, I was facing end stage renal disease. My depression and anxiety returned. A week before Christmas, 2004, I was rushed to the emergency room delirious from kidney failure. I spent the next five years on dialysis until I received a second kidney transplant in 2009. So far, my new kidney has lasted for almost 11 years. My creatinine readings are excellent. And according to my last labs, there's no protein in my urine. I still have minimal edema and intermittent diarrhea, which my nephrologist attributes to my anti-rejection and blood pressure medications.

I also continued to experience joint pain, which I'm told is probably arthritis. My greatest fear is that the FSGS will recur and I will lose the second chance at a healthy life. I watch my labs closely for an upward trend in creatinine or proteinuria. I'm also watchful for signs of the extreme fatigue, mental confusion, and edema that occurred before my transplants, when FSGS was raging through my body. Thank you for listening.

Christopher (01:00:17):

Hello. My name is Christopher and I live in Orange County, California with my wife for 17 years and my two sons Alexander and Christopher Jr. I'm 47 years old and I work as an executive sales coach. I was diagnosed with primary idiopathic FSGS 10 years ago, and it has been a struggle ever since – physically, financially and emotionally. In addition to not being able to receive an accurate prognosis for this disease, the therapeutic protocol has not changed for decades as there have been limited advances in understanding this disease or more accurately syndrome as we call FSGS.

Without an accurate prognosis, there is no understanding of how your life is going to change. Of course, planning for the future is almost useless. When you are told that you will almost definitely experienced renal failure, dialysis, and be in need of a transplant, but nobody knows if it will be five years, 10 years or 20 years, you are left with an overwhelming feeling of hopelessness. How can you plan for your retirement? How can you plan for your career? How can you plan to be around for the important events in your children's lives after such a prognosis?

With respect to career and financial matters, everything for me had to change. Being in a high visibility sales leadership role, I needed energy on demand wherever I was, that was going to change.

I now have to welcome the uncertainty of not knowing which days of the week I would have to completely shut down and do nothing but crawl from my bed to the sofa and watch TV. For eight hours straight I would experience muscle soreness and tingling, fatigue, and lethargy, and a mental fog that kept me in a zombie like state. I knew as soon as I woke up in the morning that I would be useless, which would happen sometimes three days a week. If I had work, I would have to push through the meetings, but later would be reprimanded for not participating enough in the meeting. Once a person in sales exhibits low energy and a lack of participation, they are doomed. I started to get pulled off of accounts, marginalized, and I even anticipated losing my job.

As I started to look for another job, I wondered what I would tell prospective employees. Yes, I have 25 years of experience, but on random days, I need to completely shut down at every meeting, I will need to get up and walk around for 20 minutes because of swelling and pain. And I can't really travel due to my low immune system and risk of stroke and the commute to the office is too long, so I'll need to work from home permanently. This was not going to be easy, but I had to try. I need a health insurance for all the expensive off-label treatments I would need.

And no one tells you this when you're diagnosed, but I will never qualify for life insurance for my family. I have no way of ensuring that they can survive after I'm gone.

My fears of not being energetic and engaged sales leader I once was, were realized in early 2020, when I contracted a fungal infection in my lung. After several stays in the hospital and a painful lung biopsy, I was told that if the infection reached my blood, my chance of survival was 50/ 50. This is another fear I live with every day due to being immunosuppressed. I'm worried that my kids will bring home germs that will get me sick, or I'm wondering when I travel to see clients, which germ is waiting for me. Because of these limitations and potential risks, I have had to change almost everything in my life. I'm transitioning from a 25-year career to starting my own business and that allows me more flexibility.

I have now put aside the notion of retirement. And my goal is really to build up a nest egg that now becomes my life insurance to support my family. All of the activities I once enjoyed such as long road trips, coaching my two boys in football, working out, et cetera, have all become impossible because of the unpredictability of this disease. Now my focus is on how much more time do I have left to function before stroke, infection, or renal failure diminish my capacity even more. I no longer think of life as a journey, but more as a race against the clock.

Christine (01:04:40):

My name is Christine. I am 46 years old and I live in Michigan with my fiance. I was diagnosed with FSGS in the fall of 2012 at the age of 38. I was on a fly-fishing trip in Denver when I noticed that my pants were getting tighter, that I had a lot less energy than normal and that my urine looked foamy. When I returned to Michigan a few days later, I found that I was 15 pounds heavier than when I left. Diuretics weren't working and by the time my kidney biopsy results came back six weeks later, I was carrying over 75 pounds of edema. In December of that year, my eGFR was 22. I was put on dialysis to help remove some of the excess water. After about a month, the prednisone started to take effect, my kidney function improved and I was taken off of dialysis.

I've had a few relapses since then, as we tried to find the right treatment. For me, a relapse means the onset of nephrotic syndrome. During the most recent relapse, protein spillage went from 97 to 880 milligrams per deciliter in about 10 days, although my eGFR has remained greater than 60, since 2013.

When nephrotic syndrome kicks in the edema sets in so fast, there is really no way to prepare for it. It feels kind of surreal, like waking up in somebody else's body. Imagine that your limbs are filled with memory foam and that every bit of pressure leaves a lasting indentation in your skin. When I have a relapse, my skin is stretched painfully tight and the simple movement such as walking to the bathroom are absolutely exhausting under that extra weight.

Wardrobe issues are always a challenge. Edema might accumulate in your abdomen one day or in your thighs and calves the next and finding ways to accommodate the swelling can be tough. During that first event, I went from a size two to a size 22 in about six weeks. And now I just keep clothing for every size in between just in case.

FSGS has had a dramatic impact on how I live my life. I was managing a microbiology lab when I was diagnosed. I was physically unable to keep up with the long hours and sleepless nights that, that job demanded. I was exhausted all the time and eventually made the decision to leave. I transitioned to a remote role with the same company, but the travel that was required was exhausting and exposing me to new illness with each trip. Every time I came home, I ended up with a new cold.

It's not just my work life that has changed. Being on prednisone has resulted in avascular necrosis causing pain and bone loss in my right hip. This has limited my ability to do some of the things that I love the most, like running, skydiving and martial arts. I've been told that I will need a hip replacement at some point. So for now, I'm just trying to take care of the one that I have.

When it comes to this condition, my biggest worries are the looming threat of a relapse and living life with a suppressed immune system. I've always been a very active person, but with the threat of a relapse, it often makes me hesitate to make plans too far into the future. Planning, something complex, like a long-distance backpacking trip or a scuba diving trip is difficult when you don't know if you'll end up getting sick again and be forced to cancel at last minute. I have recently started working on getting my private pilot's license, and I am concerned with how the progression of this disease will impact my ability to fly in the future.

My biggest fear is having to live the rest of my life on immunosuppressants. Obviously being immunocompromised during a global pandemic is a terrifying thing, but even outside of current events, living with immunosuppression can be daunting. In the past year, I've had bronchitis four times and I seem to catch a cold at least every other month. Getting sick that often can be a challenge when it comes to both family and to work.

My hope is that one day soon a cure will be found for this disease or at least a treatment that doesn't require immunosuppression.

Jackie (01:08:52):

Hello, my name is Jacqueline. I'm 19 years old and I was diagnosed with nephrotic syndrome on February 28th 2016. And then, later in June 2018, I was diagnosed with FSGS after my second kidney biopsy.

One of the biggest symptoms that hinders my life the most is swelling. When I'm swollen, it physically hurts to walk, stand or sit. No position is comfortable laying down, even then I'm still in pain.

Another symptom that impacts my life is all the side effects from my medications. I'm in drug trials for medications that aren't marketed for FSGS, they're for other types of diseases.

But FSGS, isn't like other diseases. Everyone who has it is dramatically different. They're affected differently and their experience is different.

Lastly, another symptom that affects me is pain. I have a very high pain tolerance. Everything I've had to endure thus far, from two kidney biopsies to hundreds of IVs and multiple chemotherapy infusions. The pain sometimes is unbearable, even with my tolerance. It gets so bad sometimes that I'll faint or have cold sweats, low blood sugar, and headaches. But I love to travel, seeing new places and experiencing all the world has to offer. When I go on airplanes, I swell so bad that I can't even walk. The amount of pain that I feel because of it is indescribable.

I had my Make-A-Wish trip last summer and I chose to go to Greece. There was no way for me to put my legs up during the plane ride. This negatively affected my experience on the trip because I was so tired to walk around the city and see all the scenery. I was so swollen on the plane ride back that I couldn't even walk off the plane. I had to sit in a wheelchair and people never truly understand because I look fine. I look like a normal kid with nothing physically wrong with me.

I don't really get best days. Every day, I experience negative effects from my symptoms, but if I am feeling better than usual, I still worry about being swollen or getting swollen. Once I start to swell, it's downhill from there. Even when I'm feeling fine and I'm excited do normal activities with my family and friends, I always have anxiety about suddenly not feeling well or getting dizzy, nauseous, or light-headed.

On my worst days, I can't even get out of bed due to the pain I'm in. It hurts to walk and stand and I can barely see out of my eyes because they are so swollen shut. I have migraines because of the pressure I feel on my face from the swelling, it's very unpredictable.

I could never really plan too far in the future because I won't know where I'm at or how I would be feeling. I have normalized many of the impacts as time has passed, but that is something I shouldn't have to do. I should have proper treatments, the proper medical care and proper medications that are for my specific disease and will actually work for me.

I've been fortunate enough that sometimes my body helps itself and goes into partial remission. I've never been lucky enough although, to have full remission, but the times that I have had partial remission, I've been blessed to achieve some of my goals. But, that can be ripped away from me at any

moment, because I never know when I will fall out of partial mission. I never know how long it's going to last for.

Every day, I wake up with the fear that I'm going to wake up swollen or I'm going to not feel well, and that I might need to go to the hospital. The fear of transplant is always in the back of my head. People seem to think, because they never fully understand, that a transplant is going to be my saving grace. In reality, if I could keep my native kidneys healthy, as long as possible, I want to be able to do that. Transplants don't get rid of FSGS. It is very likely the disease will reoccur.

The fact that every day my kidneys are slowly deteriorating scares me beyond belief. And the fact that no medication has worked for me and there's no medications for nephrotic syndrome is also very scary. It makes me wonder if there ever will be. One day I'm going to need a transplant, But until that day, I'm going to try really hard to advocate for myself.

James Valentine (01:13:11):

Wow, those were really incredible stories. Thank you, Dine, Christopher, Christine and Jackie for being so brave to put those statements together, to share today and really start us off on this important discussion of really understanding what it is to live with FSGS. We're understanding those daily symptoms and daily impacts. If you have symptoms and impacts, you would like to share with us, we would like to hear from you too. You can call in at +1 703-844-3231. We're going to be going through a number of different questions throughout this next hour. And so, if at any time you have something to share, please do call in again, that number +1 703- 844-3231.

I'd like to welcome our Zoom panel that we have today, that will be joining us here as well. But, to get us started and to get everyone else thinking about these issues. We have a few polling questions we would like to start off with.

So, if you can go ahead and pull out your phones, go back to that tab you might've opened, or if you just joined us and you weren't a part of the first set of polling questions, that's okay. This is polling questions for individuals living with FSGS and their direct caregivers. Go to PollEV.com/PFDD, you'll be able to follow along throughout the rest of today's program of the different polling questions that we have. So this first question is, how much does your FSGS or your loved ones FSGS impact your daily life in general? And so, please select the response that best reflects your experience, which is A, not at all, B, minimally C, moderately or D, a significant amount. So again, how much does your FSGS impact your daily life in general? (silence)

So, we'll give you a few more moments to get in your response here. As it stands, it looks like about over 50 percent are reporting that their or their loved one's FSGS impacts their daily life, a significant amount. Then, we're seeing approximately 20 percent are reporting, its impacts their daily life a moderate amount. And, about 20 percent also saying a minimal amount. We're seeing a smaller percentage, about 5 percent reporting that it's not impacting their life at all.

Can go to our second polling question. So now, that you've given us your general assessment, we want to hear from you about which of all of these different symptoms and health effects related to FSGS you or your loved one have experienced. So, please select amongst these options, all that apply, A, muscle and joint aches and pains including gout, B, bone or teeth problems, C, issues with eyes, D, high blood pressure, E, high blood sugar and diabetes, F, anxiety and or depression, G, brain fog, things like forgetfulness, poor concentration and losing track of time, H, being tired or exhausted, I, gastrointestinal problems, J, recurrent infections, K, swelling, such as in the ankles and face, L, some other symptom or health effect that's not listed on this slide or select M, if you or your loved one do not have any symptoms.

So, please select all that apply. We want to know all of the different symptoms and health effects associated with FSGS that you experience. I will point out, as you see the responses coming in, these percentages are a percentage of the responses, this does not reflect a percentage of people that are responding that have a particular symptom or health effect. This is the way that you'll see the percentages reported, anytime our audience is able to select more than one option to a question. So, this is our first time we're seeing this. So, you can think of this almost more as, of like a ranking looking at the bars. So, we'll give a few more seconds to get in your responses.

It looks like perhaps the symptom that is most experienced by our audience today is being tired or exhausted, followed very closely by anxiety and depression, swelling, and muscle and joint aches and pains, including gout, as well as I would say, high blood pressure and brain fog. So, we're seeing a lot of experience across the community with those, maybe in kind of a middle tier. We're seeing gastrointestinal problems, issues with the eyes, bone, and teeth problems. I would even put a recurrent infection in that middle grouping and other, so we'd be very interested to hear from you. Please call in and write in with what those other symptoms are. We really want to hear about those.

And then, in our final bottom tier, we see not a great deal of experience in this, our audience, say with high blood pressure, oh I mean, sorry, high blood sugar or diabetes. And, we see nobody reporting that they do not have any symptoms.

We go to our third question, here you're going to see the same set of response options. However, this question is different. We want you to select which three of those symptoms that you have that most negatively impact your daily life. So, which three symptoms of your FSGS or of your loved one's FSGS, most negatively impact their daily life and the same options as before?

David Feldman, PhD (01:19:28):

James, one thing that's interesting is that anxiety and depression is – lots of people are experiencing it, but it doesn't seem to be at the forefront yet at least, of impacting their daily life. I'm wondering if people are dealing with this better and what their strategies are, or if it's just that the anxiety and depression is not as severe as one might think about.

James Valentine (01:19:57):

Yeah. Although many individuals, it's seems to be in their top three, along with brain fog. And then, the number one thing being reported as a top three concern, or really a top three impact in daily life is, that being tired and exhausted. Other, maybe a second tier of issues being reported as top three is muscle and joint aches and pains, high blood pressure and swelling. However, every single other symptom and health effect here is in somebody's top three. And so, we really want to hear about this range of experiences. Why, when you were looking at this did you say yes? Whether it's something that was more common, like being tired or exhausted, or maybe something that isn't in many people's top three for you, but maybe for you it's issues with your eyes or recurrent infections. We want to hear during this audience discussion that we're going to move into, why it is you picked this as your top three.

And so, let's go ahead and get started with that. So, thank you for participating in these polling questions. We'll come to some others throughout. You'll see on our screen here, some of the members from your community, patients and caregivers that are going to be joining us today to be a part of this discussion. And I'd actually like to start with them for the discussion.

But before I do, I want to remind you in the audience; we want to hear from you. We want you to call in and you can join us at +1 703-884-43231. Again, that's +1 703-844-3231. We want to hear about – think about when you were looking at that polling question and made your choices. Can you share with us what you picked and why? Please join us and call in.

And, to get us started on that very question, we're going to go to our Zoom panel and I'd love to ask Katey, if she could tell us what she picked and why.

Katey (01:21:54):

Hi James, thank you so much for having me today. I'm speaking on behalf of my son, Reed, who was diagnosed just before his fourth birthday, as his caregiver. And so, the symptoms that I chose were definitely, I think what the majority of people had chosen, fatigue, muscle and joint pain and definitely anxiety and depression. As, he gets older, he's 10 years old now, I think the anxiety and depression is something that is definitely creeping in. And I can see more as a side effect of having this disease.

James Valentine (01:22:26):

Yeah. And can you tell us a little bit, why maybe relative to some of the other symptoms that he has, why you would say those are having a bigger impact on his daily life?

Katey (01:22:37):

Yeah. I think as he gets older, as he becomes kind of more aware of what his disease is and what it could mean for him, that's definitely where the anxiety comes in. He's definitely a very active kid and so, I noticed the fatigue much more when he's playing with other kids. He's usually the first one to be tired out.

JamesValentine (01:22:55):

Sure. And what kind of activities? Just to give us an idea of what that would be with other kids?

Katey (01:23:02):

Oh, he plays sports. So, he plays basketball, he does football, he does baseball. So, he's able to lead a very normal kid's life involved in sports, but there definitely is a difference of how long he can last compared to the other kids.

James Valentine (01:23:15):

Sure. Thank you so much, Katey. Like to maybe ask Jill to chime in on this as well. What symptoms have had the greatest impact on your daily life? And, if you can tell us a little bit about why those are the ones that you view as being most burdensome.

Jill (01:23:32):

Sure. So, I was diagnosed at the age of 14. And so, I would say that exhaustion and fatigue is definitely, probably the top symptom that I struggle with the most. On really bad days, it feels like I'm kind of pushing through mud to get everything done. And, I don't often have much energy left by the end of the day, so that's probably my most significant symptom that I experienced.

James Valentine (01:23:58):

Sure. And you said "On your bad days, that's what it feels like," How often? Is it a couple of times a month, a couple of times a week, how frequent are you experiencing those bad days?

Jill (01:24:11):

Unfortunately, it's most days. I would say it's rare when I have a day that I wake up and realize, oh this is a good day, I feel good, I have more energy. Unfortunately, those are rare and far and few between.

James Valentine (01:24:27):

Sure. And comparing those rare good days with those more common bad days. Are there certain things that you're more able to do on that good day versus a bad day that you notice?

Jill (01:24:43):

Yeah. I think on the good days, I have more energy to get maybe all the things on my to-do list done as well as play with my young child. Enjoy some activities that I like to do. Where on other days, just maybe getting through a workday kind of does me in.

James Valentine (01:25:03):

Sure. Well, thank you so much, both Jill and Katey for getting us started here. I'll just do a reminder that you can call in and share your responses. We actually have a few people who've already called in, in the queue. I'll just remind you that you can call in at +1 703-844-3231. You can also write in if you have a comment that you want to share. There's a little form that's underneath the live stream that you're following on the webpage today. You can scroll down to that and add a written comment, and we'll be trying to share as many of those as we can as well. But know, that if we don't get to your comment, we will still consider it in the voice of the patient report, which is the summary report for today's meeting.

So, I'd like to go to the phone and we have Acacia from Grand Rapids, Michigan, who has a few symptoms that she would like to share with us. Acacia, are you with us? Acacia, are you with us?

Acacia (01:26:05):

Hello.

James Valentine (01:26:05):

Hi, welcome. We'd love to hear about some of the symptoms that you experienced and the impact that they have on your daily life.

Acacia (01:26:16):

I think some of the symptoms that I experienced that have a lot of impact on my daily life would be, I experience migraines a lot, GI issues, fatigue, a lot of abdominal pain.

James Valentine (01:26:39):

Sure. And how frequently are you experiencing some of these things, migraines, GI issues, abdominal pain. Is this a daily occurrence or is this a little bit less frequent than that?

Acacia (01:26:54):

I think it's definitely daily for GI issues. Migraines, I get them probably a couple times a month. Abdominal pain, pretty much every day.

James Valentine (01:27:11):

And, what does that mean in your daily life? Are those daily GI issues and abdominal pain, is that having any impact on what you're able to do in daily life? Or how would you describe maybe its impact on your quality of life?

Acacia (01:27:28):

I think it definitely has a big impact. Definitely being a teenager and having these symptoms, I feel like I miss out a lot on things. I've been out for a couple days, definitely for school, with GI issues and migraines, where I miss out on a lot of things that my friends are able to do. And so, I think that definitely affects my life a lot. And, definitely transitioning into college more, I have a lot more on my plate. And, managing that with all of these symptoms, I think it's very hard.

James Valentine (01:28:07):

Sure. How often would you say you've had to miss school due to any of these issues? How frequently?

Acacia (01:28:15):

I missed a lot of my eighth grade, just because that's when I was getting my transplant and first got diagnosed. And then, a lot of my senior year also, I had to miss for the symptoms.

James Valentine (01:28:32):

For the symptoms. Okay. Well, thank you so much for calling in and sharing that. These are exactly the kinds of things that we want to hear from you all, to hear about, so thank you, Acacia. We have another caller that Kent from Kerrville, Texas, who also would like to share some of his symptoms and the impacts that they're having. Kent, are you with us?

Kent (01:29:00):

Yes, I'm here.

James Valentine (01:29:01):

Hello Kent.

Kent (01:29:05):

Yeah, I was just wanting to mention that I've had FSGS diagnosed for over 33, oh actually over 38 years. And I've been transplanted for over 33. And, I say that just to offer hope to people out there with FSGS.

My diagnosis was by biopsy, but one of the things that I noticed that was not mentioned in the symptoms was cardiac issues. I've had multiple cardiac issues. Although, I've run the gamut, my age is 70 right now, and I was in the 2 percent bracket, on the age when they asked about ages. So, as you progress through this, as you do have to remember that cardiac issues become very important. So, you don't want to miss symptoms of cardiac problems, such as chest pain, fatigue. The fatigue may not just be from kidney disease, it can be from a cardiac issue. And I didn't want that to go unchallenged because cardiac issues are major with kidney disease.

James Valentine (01:30:12):

Sure. And can you maybe just tell us a little bit specifically about your cardiac issues? When in your 33-year disease experience, maybe since transplant, have those arisen, what does that look like?

Kent (01:30:32):

Yeah, one of the things that I have is arrhythmia. I've had sino-arrhythmias and a lot of PVC, so I'm on medications for cardiac rhythm issues. And also, I'm on medications to lower cholesterol because I've also had a stent put in one of the major arteries in my heart, which they call the widowmaker, the left anterior descending. That had to be stented because it was 95 percent block. So, none of this goes without saying that kidney disease is also complicated and, or is part of heart disease. And those symptoms can come on early in life.

James Valentine (01:31:21):

Sure. Well, thank you so much Kent, for joining us today and sharing those experiences. I want to do a check in with David, who's been monitoring the written comments that have been coming in online, to see what symptoms are being reported by those submitting web comments.

David Feldman, PhD (01:31:41):

Right James. Ashley, from Medina, Ohio is writing about her daughter who was diagnosed in 2015. Her most significant symptoms were swelling leading to sepsis, extreme protein spilling and a blood clot in her right renal vein. That's the vein that leads blood out from the kidney.

Michelle from the Philippines, says that "Living with FSGS is very difficult." She's had a stroke twice and my blood clot... Sorry. “My blood pressure is always high. My energy is always low and I also developed anemia and have lost a lot of weight.”

James Valentine (01:32:31):

Sure. Well, thank you for sharing those. And please keep writing those in. We want to hear from as many voices as possible today. It's helping paint this picture of what are the common things that are experienced. And we've also heard from some less common symptoms and health effects. I want to go to a phone caller, then I'm going to come back to our Zoom panel here in a moment. We heard from Acacia about some of the symptoms that were driving her to miss school. We have Lisa from Massachusetts, who also has some experience with her daughter missing school, but for some different symptoms. So, I would love to hear from you, Lisa. Are you with us?

Lisa (01:33:16):

Yes, I am. Thank you. So, I wanted to talk about the severity of the exhaustion that people deal with. My daughter was diagnosed in 1998, she's now 24, post-transplant with recurrence. And at the time of her transplant and dialysis, she was at the high school level. And due to her fatigue, she was not able to finish high school. And now, as an adult, she is, on a good day, able to work part time. So, the fatigue is a huge issue for my daughter. It just breaks my heart that she so desperately wants to live what we would call a typical life, but because of the disease, the side effects of medications, she's not able to do that.

James Valentine (01:34:11):

Sure. And you mentioned that on good day, she can work part time. Can you just tell us, what that looks like a little bit?

Lisa (01:34:20):

So, she's fortunate enough to work for her dad. And so, he understands the disease. On a good day, she is able to work about four hours in the afternoon, early evening. Most days she sleeps about 14 hours,

wakes up very croggy and typically is easily exhausted. She tries to exercise; however, her fatigue gets best of her.

James Valentine (01:34:49):

Sure. Well, Lisa, thank you so much for calling in and sharing your and your daughter's experience with FSGS. I now want to move us into a little bit of building on what we were talking about. We've been asking you to share your symptoms and health effects that have had the biggest impact on your daily life.

Sometimes it's hard to know maybe exactly which symptom might be driving a particular impact; and so I want to frame this discussion a little bit differently and ask, of the activities that are important to you, which of those can you not do or not do as fully because of your FSGS? And it may, because of one the symptoms is really driving that, or it might be because of the constellation of different topics. And so, I'd like to maybe have Karlene start us off and share if there's any. What are those activities, that in your life are limited by your child's experience with FSGS?

Karlene (01:35:51):

Sure. Yeah. So, my son is four years old now. He was diagnosed about two years ago with FSGS. And really with a toddler – because of the extreme swelling and the immunosuppression and the constant fear of being hospitalized, going to the ER, ICU – It really affects our decision making day-to-day, about what activities he can do. Like, playing on the playground where there's lots of germs, attending preschool, where there's a lot of germs and something could worsen his nephrotic syndrome and FSGS and cause him to go straight back to the ER. He's been hospitalized so many times that we constantly have this fear of, will that activity cause him to go back to the hospital.

And so, yeah, just general socializing – being around a lot of people – is affected. And because of the uncertainty, we have challenges just on planning in general, right. Like, we feel uncomfortable traveling; will there be a children's hospital nearby if something happens and he needs to go to a hospital? Is it a good children's hospital nearby? So, these sorts of things limit us a lot. And then, there's the day-to-day of eating with a very restricted diet, below sodium. He's on a plant-based protein diet because he has a side effect to the tacrolimus, which is a metabolic acidosis, so things like that.

James Valentine (01:37:39):

Sure. And Karlene, you mentioned so many aspects of day-to-day anxieties and needing to plan, but even when traveling, is there a particular example or story that you can think of, of where that impacted something that was important to you and the family?

Karlene (01:38:01):

Well, we've just in general, haven't traveled honestly. So, whether it was a wedding, for example, wedding on the East coast, where we, I think a normal family, all of us would go. But, because we're uncertain, we just send one representative. I mean, that's typically what we would do for an occasion like that. Just to keep our son kind of more, less likely to be susceptible to as many germs.

James Valentine (01:38:35):

Sure. Wow. So, thank you so much for sharing that. I want to bring in the full audience here and go to our second set of polling questions on this topic. So, if we can go to polling question number four. We want to ask you, so again, pull out your phones, open up that tab, go to PollEV.com/PFDD. We want to

hear from you about, which of these have you experienced while coping with your FSGS? And, if you're a caregiver, have the person you care for, your loved one experienced. And the options here are, A, depression and, or feelings of hopelessness, B, anxiety and worry, C, low self-esteem, D social isolation, E, difficulty with family and friendships, F, difficulty with relationships outside of family, or G, none of the above. So, please select all of these that you or your loved one have experienced while trying to cope with FSGS. I think some of these, you can see were just highlighted in some of what Karlene was sharing with us. We want to hear from you.

All right and I'll just remind you, that the percentages you're seeing are percentages of responses, not the percentage of individuals that have responded for each of these options. So again, this is like a ranking, using the bars and as it stands, it looks like the thing that has been most experienced of these other impacts of FSGS is anxiety and worry, followed very closely by several of the others, depression and, or feelings of hopelessness, social isolation and low self-esteem. We see difficulty of relationships outside of the family and still many people, but just maybe lowest of the rank, difficulty with family relationships. None of our participants in the meeting today have said, that they have had none of these impacts. So, I'd actually like to – we have a phone caller who wants to speak to this exact issue. So, while we have this up, I'd love to hear from Amanda, from Chicago, who shares some of these experiences. Amanda, are you with us?

Amanda (01:41:07):

I am.

James Valentine (01:41:08):

Welcome.

Amanda (01:41:11):

Thanks. I just wanted to comment on my experience with anxiety and depression. So, I actually have a transplant now. I've had it for six years, but I'm 30 and I was diagnosed with FSGS when I was 14. And in regards to the question that was posed a little bit previously about anxiety and depression and it being low; I think that's because it's not necessarily on the forefront of our minds because the other symptoms that we're experiencing are so severe. So, we have our attention focused on that, such as, getting the tremendous amounts of edema, trying to deal with the pain. I'm not focusing on how to necessarily fix my anxiety. And it's also really hard to talk to doctors about anxiety and depression when they're trying to fix those other symptoms.

And it can seem like it's not as important to fixing anxiety and depression and it can almost feel silly. And again, I just wanted to comment on that hopelessness that a lot of FSGS patients feel because that anxiety and depression seems to be linked to the fact that there's really no treatment and there's not necessarily or really a way to fix the symptoms. And you don't even know what's going to happen after you get your transplant with the FSGS. I have anxiety still six years out because I worry about my FSGS coming back. I get nervous every time I get labs and look at those protein values and say, now is it coming back again? What are we going to do about that?

James Valentine (01:42:46):

Sure. And have the things about your condition, about your FSGS, have those things that are driving anxiety or depression changed over the years that you've had FSGS? Is it different now than it was before? Or has it always been that same worry that's kind of been driving that?

Amanda (01:43:07):

The worries have mostly been the same. When I was diagnosed when I was 14, no one really told me what was happening to me. So I always had to guess and I was often worried that this was a death sentence. I also wasn't informed what dialysis meant. So I worried about dialysis every day of my life. My FSGS took quite a slower course than I have seen with other people. It took me eight years for my kidneys to fail. But again, even after transplant, that's supposed to be a very helpful and an awesome experience. And indeed, it was, but the worry and anxiety doesn't go away because FSGS can come back in your transplant and then what do you do?

James Valentine (01:43:48):

Right. Now, thank you so much for sharing that. So helpful to hear about that. And the kind of psychological impacts of a disease like this are so important for us to hear. So thank you so much, Amanda, for being brave and sharing that.

I want to go to our final polling question and then we'll come back to the audience discussion. So we want to know which of the following statements is true for you as related to living with FSGS. Select all that apply. The options are A, your general daily function is limited by FSGS. B, you miss work or school more than you're comfortable with. C, family stress is common. D, others don't know what it's like to live with FSGS. E, you cannot participate in sports or other physical activities that you enjoy. F, you cannot participate in other hobbies, other than those physical activities that you enjoy, or G, none of the above applies to you or your loved one. So please select all that apply. We'll give you a few more moments here to get in your responses.

All right. So it looks like a major experience of our participants today is that others don't know what it's like to live with FSGS. And so, we definitely want to hear about that. What does that mean? How has that impacted your daily life? How has that impacted your relationships? Very important for us to understand that.

We see pretty much all of the other effects being rated high, are being selected by many people. And then maybe hobbies being the one thing that's reported by many people, but not quite as much as those other impacts. It does look like there may be a small number of people that have not experienced any of these as well. So if we can go back to our Zoom panel, I'd love to go to Dan. On this topic what have been the impacts in daily life that you've experienced as a result of your FSGS and have you share any of those that stand out to you.

Dan (01:46:26):

Sure. Probably the biggest one that I've had is just lack of energy. I used to have jobs where I was very physical all the time, whether I was a mover moving furniture, or I used to work in infrastructure jobs and everything. When I first got diagnosed just a year beforehand, I could easily put my wife in my hand and lift her up over my head. Right now, I'm at the point where it takes probably any and all energy I might have, just to lift her up at all in any way. It just robs you of everything that you used to do. When I'm planning out a day, I need to plan in advance sometimes two, three days. If we're going to be going to a party where I know there's going to be a lot of walking around or doing anything, I know I need to rest for two days. Usually sleep as much as I can the day before, just to try to make sure I have enough energy budgeted out to go through everything that I need to on that one day.

James Valentine (01:47:35):

Sure. And so, you mentioned that there's certain physical activities. You mentioned the example of lifting your wife up with one hand. Is the reason you can't do that the same as the reason you need to

budget out your activities through the whole day? Is that because of the fatigue? It's too tiring to do that?

Dan (01:47:56):

It's too tiring do it, but also just my entire muscle mass has just completely shrank because I cannot be active enough to keep it up.

James Valentine (01:48:06):

Sure. That's very helpful. You mentioned that fatigue is kind of ever present. Are there good days versus bad days? And what does that look like for you?

Dan (01:48:19):

A great day for me is being able to take a two, three, four mile walk with my wife and the dogs. A bad day is having to take everything I have to go around and just do basic daily cleaning of the house.

James Valentine (01:48:36):

Wow. Well, thank you, Dan so much for sharing that. So important to hear. I want to check in with David to see on the topic of impacts on activities and quality of life, what those that have been writing in have been saying.

David Feldman, PhD (01:48:52):

Right, James. Maybe we can go back to symptoms before we go into impacts. Lillian writes about something that I think is very important and we hear about a lot. "The hardest part for me was that people around me, even the doctors made me feel like I was crazy because they said my symptoms were not related. And people around me said that I was just overreacting because I look normal." I've heard that a lot. In terms of impact, Melanie from Loveland, Colorado writes that, "The most bothersome problem is the destructive nature of this disease. It's destroyed my native kidneys and my transplanted kidney. FSGS has devastated my life, by completely turning it upside down. I have spent the last 10 years trying to manage it so I can manage my life and have some sense of normalcy."

Amanda from Westminster, Maryland writes, "The symptoms that affect me most have been fluid retention and anxiety. These symptoms affect my life in several ways." She talks about a relapse that made it... "So I had to miss a lot of activities until we got things under control. The fatigue made it difficult to participate in any activity, big or small. Fluid retention was so great. At one point, I thought my skin was going to bust open. I carried 40 pounds of fluid. It took a concoction to get most of it off. Carrying so much weight was tiring and exhausting. It ruined my body as in ways pregnancy never did." And she talks about... "And then an anxiety attack that landed me in the ER. I was afraid to leave the house because I had been cooped up so long. And then I got to the point where I didn't want to be home, because I had been there so much. Anxiety is still an issue."

James Valentine (01:50:53):

Wow. Yeah. Thank you much to each of you that shared those written comments. Again, so important to hear the different ways that FSGS has impacted your lives. One of the things that we saw in the polling questions was the one of these, we put up a number of the different ways, kind of outside of the direct symptoms that FSGS has impacted your lives. And the thing that was reported most frequently, was that others don't know what it's like to live with FSGS. So we actually have a caller who wants to speak to

that topic. We have Jackie from Texas who wants to add some of her experience around that. Jackie, are you with us?

Jackie (01:51:36):

Yes. Hi.

James Valentine (01:51:38):

Welcome.

Jackie (01:51:38):

Thank you. Yeah. I just wanted to talk about the comment that said yeah, people don't know what it feels like to live with FSGS. So I was diagnosed at 16, going through high school and all that. I got a lot of mixed comments about all that, but then after I started showing less, I guess that I'm sick. So I walk around looking like a pretty normal person. I don't look like I have very many issues, but a lot of even my closest friends have told me comments like, "Oh, you're still sick." Because I'll be taking my medicine in front of them. And they'll just say things like, "Oh, you're not over that yet." And it's kind of trying to explain to them that it's not something that just goes away is really difficult. Because it's hard to tell somebody, "Yeah, I don't look sick. I don't really feel that sick. But at the same time, if I miss this medicine it's not going to be a great experience for anybody."

James Valentine (01:52:37):

Sure. And how has that either made you feel or how has that maybe impacted those relationships with those friends?

Jackie (01:52:46):

So at first I had a very different way of seeing my diagnosis. I was kind of shamed, I guess. I felt very secluded, but I think I've been sick for over 10 years now. So I think I slowly just started to accept it. And so now I accept different questions people have, and I'm a little bit more open with it. And I think having that control over the narrative and how people see it has really helped me to just kind of being okay with these types of questions and these comments where I'm just like, okay, yeah, it makes me feel singled out. It makes me feel insecure at the same time. It's a good thing that I don't look sick. Right? So I've been having to kind of change the way I see things and the way I even interact with those types of comments.

James Valentine (01:53:35):

Sure. No, that makes sense, and I'm glad to hear that and thank you for sharing that story. I'd like to now go to our Zoom panel and just see if with a wave of hands, if anyone has a symptom or activity that we haven't mentioned yet that you experience that you would like to share with us. Yeah. Dan.

Dan (01:54:05):

Yes. Sorry about that. Basically, dovetailing off the previous caller with friends and everything, the friends that I have that don't understand what's going on with this, they have a hard time understanding that sometimes I need to break plans last minute because of the tiredness. But then at the same time, I have other friends who go the other direction, where if they wake up and they have a cough, they tend to want to stop plans or they just give me a call. "Hey, we're letting you know, we woke up this morning,

not feeling a hundred percent. Are you still... Do you mind? Do you want to take the risk? Do you want to do this or that?" That's one thing we haven't really gotten into. Those who understand it, are definitely on our side. It's just getting it out to everyone because nine out of 10 of us look completely normal on the outside. There's nothing to this that makes you look sick.

James Valentine (01:55:05):

Sure. You mentioned that those that do understand it – that's great to hear that they proactively reach out and get your input. Have you had any experience where, for those that don't understand the disease, where that's maybe had some impact on your relationship with them, or maybe some other impact on your life?

Dan (01:55:31):

I've got a couple of friends who are convinced that with my diagnosis might – I got it because like the previous caller a little while ago from Texas – he was saying that the cardiovascular issues. My family has a history of not making it out of our forties. My brother just died a little while ago. I got diagnosed because my wife forced me to go to a cardiologist. And that's when we found everything in blood work. And then the swelling at the same time. But I have friends that are convinced that somehow this is catchy and they don't want it. So I have not been around them at all. There's a couple that have written me completely out of their lives because of it.

James Valentine (01:56:16):

Wow. Thank you so much for sharing that, Dan. So one of the things that I had asked earlier was, wanting to know how things have changed over time. Whether that's kind of day to day, week to week, month to month or over the years. We actually have a caller who wants to share a little bit about her patient experience. And that's Missy from Wisconsin, who I'd like to welcome. So Missy, are you with us?

Missy (01:56:47):

Hello.

James Valentine (01:56:48):

Hi, welcome.

Missy (01:56:51):

Thank you. I can talk about over time because I'm one of those long haulers. I'm a 22-year patient. I was diagnosed at 29. I was a newly hired teacher. I was in a new engagement and marriage when I was diagnosed. So my first doctor told me, "You're going to be hooked up to a machine or dead in five years." So that was an awful way to start. But I had a lot of symptoms over time. I've had various degrees of fatigue. Like other people have stated I've had good days. I've had atrocious days. I worked through 18 years of this disease. And my appearance, I think was the greatest thing. I could fake it throughout the workday with the exhaustion and edema. I'd wear giant dresses and all the compression were underneath.

I tried to make up and haircuts, so it didn't look like my hair was falling out. But I would go home at the end of the day and literally, there were days I crawled into the house to lay on the couch with the fatigue. Diet changes are really different with dialysis and initial prognosis. It was really hard to get low

sodium 20 years ago and then high protein post-transplant and all the different changes. It's so difficult to be social when you're diet restricted.

James Valentine (01:58:27):

Right. One thing that you had mentioned that you had experienced also that we haven't heard a lot about. So I just want to maybe probe on this specifically, is brain fog. And I know we had a number of people report that in the polling question, but do you mind sharing a little bit about your experience with that particular symptom?

Missy (01:58:52):

Yeah. And it really changed over time. I have little sense of what's normal. I searched for words, even though I'm an educated person. I can't remember names of kids in my class at times. I see a kid more than their parents in general, and I see them six months later and I have no idea what their name is.

James **Valentine** (01:59:16):

Right.

Missy (01:59:17):

It was really difficult – well, teaching – to search for words or stammer. It frightened kids at times when my appearance changed and I couldn't think straight. Some parents asked me, "What is going on? Are you pregnant? Are you sick? Is this contagious? Are you going to die?" But I have a great deal of difficulty thinking through work. When I finally was on dialysis, I think that's when the brain fog was the worst. Even now, I guess I search for words. But I gave up on teaching because I just couldn't think on your feet and literally be on your feet all day.

James Valentine (02:00:00):

Wow. Thank you for being willing to share that. So important to hear that. It's a big impact. And so thank you so much for calling in and sharing that, Missy. I want to quickly check in with David on any other impacts in daily life. And then I'm going to take us to our final discussion question.

David Feldman, PhD (02:00:22):

Right, James. Amanda, from Tampa writes, "When I was diagnosed, I was so exhausted that I could not continue to work and had to take medical leave. I was sleeping 20 hours a day." Ken from Robinson, Maryland writes, "I am tired and exhausted at least half the time. My energy levels change on a daily basis. Anxiety and depression on a daily basis also."

James Valentine (02:00:52):

Sure. Yes. So, starting to see some here, are those recurring themes. So, I want to build on everything that's been experienced with this disease. And we've heard a little bit about this already with some of the anxieties and worries, knew about further progression or recurrence. But we want to hear just generally about what it is that you worry about for your future or for your loved one's future, living with FSGS. Whether that's some of those things that have already been mentioned, but any other worries that you have in addition to that. So again, if you want to call and share any of your worries, you can dial in at +1 703-844-3231. I'm going to go to our Zoom panel here to get us started on this question and ask Katey if you can share with us some of your worries.

Katey (02:01:47):

Yes. Thank you, James. As a parent, I definitely have many worries of what's going to happen for my son in the future. He hasn't had to have a transplant yet. So, what does that mean if he does, will FSGS come back? We've tried several different medications and what are those long-term effects that we might not be aware of that might happen as he gets older? Definitely for us, we fear that we're going to run out of different medications to try. We've had success with some medications, but I feel if things start to flare up here again, what else can we try? Because we've tried a lot of different things. So there's just a lot of unknown with this disease. And I think that's where a lot of the anxiety and depression can come in.

James Valentine (02:02:29):

Sure. Thank you, Katey. And Jill is a person living with FSGS. Maybe you could share with us any worries that you have for the future.

Jill (02:02:40):

Yes, some of them are similar to what Katey said. I am experiencing symptoms from being on certain medications for many years. And so I worry, I continue to worry about what that means moving forward. For me right now, probably the biggest fear I have is being on dialysis and having to rely on a machine several times a week to live and what kind of quality of life that will be for me. I have a young five-year-old son at home and I worry how that will impact my ability to have the energy, to keep up with him as well. So that's my biggest fear right now.

James Valentine (02:03:18):

Sure, and both you and Katey have made some mentions of worries related to treatments and what might be available or might not be. I think we're going to get a much better understanding of what it is that your worries relate to; a little later in the program, we're going to get a lot more information about individuals experiences with those treatments. So I think we'll even better understand where you're coming from. So I would like to thank our Zoom panel for joining us today and for all of your input. I want to go now to a caller that we have, who wants to share some of her feedback, or her experience rather about worries for the future. So on this topic and that's Nicki from Illinois. So Nicki, are you with us?

Nicki (02:04:08):

Hi. Yes, I am.

James Valentine (02:04:11):

Welcome.

Nicki (02:04:14):

Thank you. Yeah, so basically, I recently graduated from college about a year ago and this is kind of the time of your life, where you're planning. You're planning your life out and what used to be so black and white for me, is now just a puddle of gray. I'm thinking, in a few years I would want to get married, start thinking about having children. But I have to keep monitoring my labs and praying I don't have to go on a treatment that could risk my fertility or the current treatment I'm on – I might have to go off of to have a child because you can't be pregnant on it. So the question is, what's going to happen with my disease?

If I have to go off of this medication, what are going to be the future ramifications? Will I make it into my thirties, without my kidneys declining or having to get a transplant? And the idea of a transplant scares me, not just because of the entire process, but if I'm taking a kidney from a family member, what if it fails immediately? And then I took a kidney from them and as you can see, it's just a huge – I feel like everyone kind of goes through that. So thoughts of panic, where you just don't know.

James Valentine (02:05:27):

Sure, sure. And that's many things that are really kind of weighing on your mind and worrying you. So I can imagine that's a lot to manage. Have you found that having these worries has impacted your quality of life today?

Nicki (02:05:49):

Yes, because I've always been a planner. I always have the next month, the next year planned out completely for my life. And because I can't do that anymore, I feel like I can't make long term decisions about what's going to happen with my job. Where can I live? There's a lot of guilt, I would say about something you can't control. Like my current significant other. I almost feel guilty because I can't promise him a future where I can be healthy. I can't assure that I can give him a potential child down the line, the life that I ideally want to give. And I think the concern really comes from hurting those close to you, right? Because you can't promise them this perfect life anymore because it could go one way or it could go the other.

James Valentine (02:06:35):

Sure. Well Nicki, thank you so much for sharing that. Very insightful and powerful to hear. We have one other caller, will be our last caller that we have time for today. Or not today, but for this session, rather, who is Sarah from Boston, who also wants to share some of her worries related to FSGS. So Sarah, are you with us?

Sarah (02:07:04):

Yes. I'm on the line. Can you hear me?

James Valentine (02:07:05):

Yes. Welcome.

Sarah (02:07:09):

Great. Thanks. My name is Sarah. I live in Boston, Massachusetts. I've had FSGS for 20 years, which is quite some time. I'm fortunate enough that I have not had a transplant, but I have tried a host of different drugs. Prednisone does not work for me. So I'm Prednisone resistant. That has a whole host of symptoms I won't spend time to talk about, but it was a very horrible experience. I faced a lot of nausea, throwing up round face, gaining a lot of weight and it didn't work for my disease. But I do take an ACE and ARB and I eat a lot of proteins still. Even though it's kept me in pretty good shape and due to the protein in my urine, I know that that's slowly but surely deteriorating my kidneys. And as somebody who is a woman with FSGS, I would like to have a family one day.

And so of course the treatment that I do take to lower the protein, you cannot take if you want to conceive a child. There is currently no treatment on the market for women who are of age of conception, who want to continue on their medication. That's one thing. And then the second thing is

just a symptom of knowing that your kidneys will deteriorate if there's no treatment that really focuses on reducing that proteinuria and that causes fatigue and other issues. If you have an increase in protein, you'll get edema, which I face and that's really concerning to me.

James Valentine (02:08:35):

Sure, sure. And so same question that I had for Nicki. Do these worries have an impact on you today in terms of your current quality of life?

Sarah (02:08:46):

Yes, it really impacts my quality of life. My ability to go through life. I'm married, my husband and I, we want to conceive a child. It's terrifying to one, not have a treatment for FSGS after 20 years. And then the worry of, do I get off my medication and hope that my disease doesn't progress at the risk of wanting to have a family? And just more generally speaking, even just the risk of not knowing, right? What if I don't get off my medication, and for some reason, this medication doesn't really target protein? I take ACE and ARB and why is there no treatment out there that really focuses on reducing my protein?

So it's a constant worry every day. I say I have a silent disease because you can't see it. And I can look at my urine, I've had it for 20 years. I know when there's more bubbles, that means I have more protein, but I walk around not knowing whether or not it's going to progress. Or when a treatment is going to be available. And so, I really called to action from this group that it affects my quality of life. Not just biologically, but mentally, everyday worrying whether or not I'm getting worse.

James Valentine (02:09:52):

Absolutely. Thank you so much, Sarah, for joining and sharing all of that. So, to close out this first discussion, we have several more to come. But to cap us out on this discussion of worries, related to living with FSGS, I'm going to see what has come in on the web.

David Feldman, PhD (02:10:11):

Right. So, Elaine from Henderson, Nevada writes about her 10-year-old son who has APOL1 associated FSGS. APOL1 is a genetic risk factor that's found in African Americans. Very important risk factor for FSGS. "We don't know what the future holds. Safe treatment options for FSGS patients are needed and thorough screening of at-risk populations are needed. So treatments can start early and hopefully prevent the need for dialysis and transplant." Very important concept.

Brandon from Colorado Springs writes that his daughter Macy has suffered from recurrent FSGS and has really endured a very difficult medical journey. "Our biggest concern is how will all of this affect her future? Will she have access left for drug treatments as an adult? Will there be a treatment when her FSGS returns after her second transplant? And when will antibiotics no longer work for her? Will her mental health hold up? Will she live to have a successful future?" All very difficult things to, for any patient and certainly parents to be dealing with.

Alyssa from Canada writes, "I live alone. So I fear not having the energy to take care of myself in the future. I also live hours from my specialist. How will I get to the appointments? Friends can help, but I don't want to be a burden on my friends."

We also have some other comments on symptoms that we did not get to earlier. Pam from Maryland writes about her daughter with" low blood pressure. She's only eight years old." And then Ken from

Robinson, Maryland writes, "I'm tired and exhausted half the time, anxiety and depression." James, I think we already got to this one.

James Valentine (02:12:30):

Sure.

David Feldman, PhD (02:12:31):

So these are very difficult experiences for people to deal with.

James Valentine (02:12:39):

Absolutely. And really appreciate. Now we heard a couple of different worries there and from some of the written comment or so. Including worries about even being able to get to see a healthcare professional, which is so important for them monitoring in this condition. So now we're going to move into our second topic for today, which is to start to get your input on participating in clinical trials in FSGS. And so to give us a little bit of some background about the challenges of conducting clinical trials in this condition, we have a presentation that's going to get us started from Dr. Suneel Udani.

Dr. Udani is a clinical nephrologist in the community practice, Nephrology Associates in Northern Illinois, which is in the Chicago Metro area. He's also an associate member of the University of Chicago section of nephrology, where he teaches glomerular disease to nephrology fellows. So I welcome you, Dr. Udani, to lead us off in this conversation on clinical trials.

Suneel Udani, MD (02:13:47):

Welcome everyone. Thank you all for joining us today. It's obviously difficult times. So I very much appreciate you spending your day with us. Needless to say, everyone in this room clearly recognizes how critically important the discussion for today is, and the desperate need we have to move our field forward. Along those lines over the next 10 minutes or so, I'll share some perspective on challenges in clinical trial design for FSGS. In the hope that it can help future trials succeed and ultimately achieving our goal, which is to bring the best treatments to our patients.

These are my disclosures. Next slide. So our discussion of course is centered around what's most important, our patients. And along those lines I've presented here a case vignette of a patient that presented our practice that represents, I would think a fairly typical case of primary FSGS that many of the clinicians and investigators in this room have encountered before.

Young African American man with a strong family history of kidney disease, including nephrotic syndrome who presents with a nephrotic syndrome as well as renal dysfunction. The kidney biopsy demonstrates fairly typical findings of primary FSGS. And he's seen in the community nephrology clinic and started on the standard care, Prednisone, one milligram per kilogram per day for four months. And unfortunately like many others, he has no clinical response, but develops significant steroid side effects. So the question really becomes, how do we design a clinical trial that is not only appropriate for this patient to enroll, but that will also help us positively intervene on future patients like him.

Next slide. As we walk through challenges in the clinical trial design, we're really going to walk through each step in a clinical trial and to discuss the challenges in each step.

First, the inclusion criteria, we'll talk about some of the challenges of defining FSGS as a whole. And we'll talk about the treatment itself and how the issues of equipoise come up. And lastly, we'll talk about how we assess global trial outcomes and limitations in each of those potential assessments.

Next slide. The fundamental challenge really is how do we define FSGS as a disease entity. As a field, we've really agreed that FSGS is really a pathological lesion rather than a disease. It's simply what we see on light microscopy. Over how that lesion got there can always be little more of a challenge and not always be an easily answered question. A recent review proposes four distinct archetypes of disease with different processes that lead to the final lesion of FSGS. Again, without much debate, we can all agree upon this classification. Furthermore, most of us can recognize that bottom blue circle, the hyperfiltration- mediated or adaptive FSGS as we consider secondary FSGS, yet top three circles pose more of a challenge.

Interventionally, they're all classified as primary FSGS, even though as you can see, they represent very different disease processes which require at least to some degree, different therapeutic approaches, but because they share some aspects of clinical presentation, they can be difficult to distinguish.

Next slide. With this categorization in mind, how do we define primary FSGS with respect inclusion criteria? To define primary FSGS specifically excluding genetic causes depending on a drug proposed mechanism. Which of these categories would our patients best fit into?

What criteria would allow for his inclusion to a trial? Ultimately, we're trying to strike the balance between a broad enough criteria that allows for entry of individuals who may respond to treatment but not so broad that include others that are highly unlikely to benefit. Since we do not always know how to place individually each category, this obviously becomes difficult. The additional challenge of course, is that this is an ultra-rare disease with small numbers. The more we subcategorize, the smaller numbers get, the harder it becomes to recruit patients and draw conclusions about intervention with any statistical validity.

Next slide. Of course, the challenge that's top of the disease definition is even individuals with similar pathogenesis can present a variable fashion. So the question is, where in their presentation they opt in for a clinical trial? Should it be the time of diagnosis? Specifically, should it be prior to a trial of steroids?

Certainly, if we're ever to display steroids as first line therapy, of course we should, but would clinicians and patients buy-in? If not before a therapeutic trial of first line therapy with steroids, how far after? What is the risk of waiting and when do patients pass that point of no return where any intervention is highly unlikely to be effective? Is there a GFR criteria which will best represent that? That becomes even more difficult because most patients with FSGS present with a decreased GFR at the time of diagnosis. Other subpopulations post-transplant and pediatric populations bring up their own potential issues. Trials of large excluded post-transplant FSGS, one could argue this is the most pure form of the permeability factor of primary FSGS. Including them may explicitly inform us about how to better care from native disease.

Pediatric patients have their own unique characteristics with regard to pathogenesis and clinical presentation. So how do we account for those in our inclusion criteria and what do we use as the definition of a pediatric case? Time of first diagnosis or age at the time of the study?

Next slide. Moving on to the actual intervention itself, we know that there must be a comparator group to the experimental arm and this should really be the standard of care. Are we coming back to our patient? I would suspect that the standard of care would be even up for debate. What the comparator will be will undoubtedly influence how likely the clinician will be to endorse a trial for their patients. Most clinicians and patients are very reluctant to refer or enter a trial with a placebo arm as the comparator, even when they're not sure what the best next step would be or there's a clear standard of care. Clinicians and investigators must truly believe that there is a concept of clinical equipoise where the patient's just as well off receiving the comparator even if it's a placebo as the experimental therapy.

We can try to get around this by having instead of a placebo, an active comparator as a control arm. Once again, depending on what this agent is, will influence whether we believe it as truly equipoise. Lastly, even if individuals who may receive a placebo and they still continue their 10 milligrams of prednisone that they've been on forever because below that dose, they have a full-on flare. What about other long term agents? How do we not blunt the impact of experimental therapy without putting patients at risk for a serious decompensation?
Next slide. The rare nature of FSGS further complicates trial design as a conventional model. The randomized controlled trial is best suited for diseases that are more common. We have large numbers and looking for a small effect size that can yield statistical significance. With rare diseases, especially those with the heterogeneity of FSGS, it's more difficult. Other trial designs listed here may be better suited for rare diseases. For FSGS, specifically novel trial designs such as the shared control groups and umbrella and basket designs, which can allow for multiple agents and larger groups of individuals to be studied at the same time may be optimal. Unfortunately, these have not been widely adopted as of yet.

Next slide. FSGS presents some rather unique challenges with regard to drug therapy because the affected organ is the kidney. How the kidney is affected can impact how the drug is handled by the body. On the one hand of the drug is cleared by the kidney and there is renal dysfunction or impaired renal clearance, the drug is likely to last longer in the system. So it would be a good thing with regard to therapeutic effect, but may also expose a patient to an unforeseen risk. Adversely, if a drug is protein bound, the patients having lost a protein in the urine, the drug is likely to not last long in the system, which will of course have impact on this therapeutic effect.

[inaudible 02:21:12] the pharmacology of a drug, how a drug is handled by the body is initially studied in healthy subjects and then extrapolated to the target population. We try the same approach in FSGS. However, this could yield either very dangerous outcomes or very wasteful process. Therefore, the pharmacology and specifically the pharmacokinetics, how long a drug lasts in the system must be considered specifically for this disease state early in the drug development process to prevent any of these unintended outcomes.

Next slide. Lastly, the challenge of course is measuring success and how do we determine which outcome is the most important. Conventional outcomes have centered around proteinuria. While we're going a little more and more liberal with this, the question of how much proteinuria reduction and for how long, meaning is it good enough to have the proteinuria reduction for as long as the patient's on the drug or does it require a more sustained response, that still remains a question.

What about soft outcomes such as diuretic requirements and other complications of nephrotic syndrome? Most clinicians would argue these are not soft with regard to day-to-day care and are quite meaningful. Most importantly, what do patients feel as important to assess and grade a drug on the first success. Certainly, drug toxicity, but what other aspects? These have been until late, largely excluded from design in our clinical approach, which is probably a part of the reason that we still think 60 milligrams of prednisone for four months is an acceptable standard of care.

Next slide. As I wrap up, I realize I've posed many challenges without offering corresponding solutions. The truth of course, is that we don't have easy solutions to these challenges by leaving with these simple recommendations for trial design moving forward. Start with a more precise disease definition, with specific attention to different populations, pediatric versus adult, native versus post-transplant, genetic versus non-genetic. Do not deter people with the concerns that they or their patients receive a placebo Be rational but not restricted with previous therapies and you could call it medications.

Recognizing that FSGS is a rare disease, utilize non-traditional study designs to maximize both the number of patients that can be part of a study and the number of drugs that can be studied in a given period of time. Assess the effect of renal disease on pharmacokinetics early. Let's focus on what's

important to patients and clinicians and consider non-traditional methods to assess treatment effect. Lastly, we need a broader education campaign to clinicians that are first seeing these patients thinking about clinical trials early, rather than when we're looking for salvage therapy. Better design trials will certainly encourage that participation early. With that, I thank you again for your attention and hope you all continue to stay safe and well.

TOPIC 2

James Valentine (02:23:50):

Thank you Dr. Udani for that overview of the challenges in conducting and designing clinical trials in FSGS. While certainly we are not going to be able to tackle all of those here today, we do want though to have a discussion with you, individuals living with FSGS and your caregivers about what is important to help ensure that patients are going to be willing to participate in trials that they're designed in a way that are the types of trials that you all would accept and be willing to join and be willing to stay in once you've joined. And so, to help inform that discussion, what I have here is a number of the questions that I'm going to be asking about. And what I want you to do is think about, across any of these questions, if there's anything you would like to share, we have a shorter 30-minute discussion period for this.

So, I'm going to encourage you at this point if you want to call in about any of these topics, you can call in at +1 703-844-3231 as well as I want to remind you that you can write in and help answer any of these questions using that comment box that's under the live stream on the webpage that you're following along today. So the questions that we think are important to understand – clinical trials that can help support drug approval – we want to know from you what information is important for you when you're trying to consider participating in a clinical trial.

Which types of trials are you more likely to enroll in? Is it one that studies how a new drug might manage your underlying cause of kidney damage in FSGS but it's not necessarily studying symptoms or the disease progression? Is it a trial that studies if and how well a new drug will reduce symptoms, or is it maybe as a third option, a study that helps to evaluate whether a drug actually reduces the progression of FSGS?

So, a few different potential focus – ways that the studies could be focused – would that impact your decision to join a study? A third question is what would be most important in deciding whether to participate in a trial? We want to ask you about different factors that would be important to you, whether that's the frequency of having a 24-hour urine analysis, whether it's the amount of travel or the distance of travel to a study site, the number of biopsies you might be asked to contribute, or the frequency of study visits. And finally, some questions maybe about the drug itself in the medication. Does the type of medication, whether it's a pill or an IV infusion, or maybe an injection, or maybe the frequency of needing to take the medicine influence whether you would participate in that drug trial.

So whichever of these may be most important to you, we want to hear from you about this, but to get us started, I want to first get a sense of what our experience with clinical trials is as a group today. So if we could go to our first polling question. So here we want to ask you, and again, this is the time to pull out your phones, go to that other tab that you have. If you're just joining us, if you're a patient or a caregiver, we'd like for you to go to PollEV.com/PFDD, and you'll be able to follow along with the polling questions for the rest of today's session.

Here we want to know what is your experience and perception of clinical trials for a new drug with FSGS or if you're a caregiver, what is your loved one's experience with and perception of clinical trials?

Your options are A, you're currently participating in a trial. B, you have in the past participated in a trial and you would do so again. C, you've participated in a trial but you would not do so again. D, you have not participated in a trial but that's because didn't know of the opportunity. E, you have not participated in the trial but it was because you were not eligible for that trial. F, you have not participated in the trial even though you were aware of the opportunity and eligible. G, you would never enroll in a trial or H, you're just not sure about whether you would participate in a trial.

So please select the response that best reflects your experience and perception of clinical trials. We'll give you a few moments here to get in your response, think about this.

So it looks like as it stands, we have about a third, little over a third of our participants saying that they've not participated in a trial, but it's because they weren't eligible. So we would like to hear from you about what it was that made you ineligible and whether that impacts whether you would be willing to try to participate in a study again. We see about a third of our participants have participated in a trial and would do so again. So I'd love to hear about your experiences in trials and why it is, what about that experience would make you want to do so again.

About a fifth of our participants saying that they have not, but it's because they didn't know about the opportunity. So we would like to know, what of those different factors I mentioned would make you more likely to participate in a trial. About 10% are not sure. And so, even for that, we want to know what makes you unsure. And then a small percentage have said that they've not participated even though that they were aware of it and not eligible. And even for you, we really want to hear for you what made you choose not to participate in a study.

So with that, I'd like to welcome our Zoom panel for today. And I'd like to start off with those discussion questions that I had. What is it that would be important for you to know in order to participate in a study? Which type of study might you be more willing to enroll in, or are there any particular factors that would make you more likely? And of course, please let us know if you have clinical trial experience or not.

So maybe we can start with Kayla on this. What would be important for you when thinking about participating in a clinical trial?

Kayla (02:30:19):

I think one of the most important things for me personally as a patient and a potential parent to a child that has also the mutation as well is that, what type of medication, what symptoms are they expecting? How far am I going to have to travel to go get this treatment? How many biopsies? Is there going to be more intensive testing for me? There's already a lot of needle sticks with lab work and your analysis, how much extra is it going to require and what are they expecting the outcome to be at the end of the day? Is it going to prevent protein loss? Is it going to protect the kidney? There's just a lot of variables within that.

James Valentine (02:31:05):

Yeah. Out of all of those, are there any things that would be deal breakers for you – make it so you would say, this is just too much for me to accept in order to participate in a study?

Kayla (02:31:17):

The amount of biopsies required. I've seen somewhere there's initial, middle, and end biopsies. That's quite a lot of invasive testing. I didn't have a great experience with my initial biopsy that diagnosed me and I'm not sure that I would be able to handle that multiple times.

James Valentine (02:31:36):

Sure. And can you maybe just give us a little bit of an idea of what that experience was with the biopsy?

Kayla (02:31:41):

Yeah. So my FSGS is actually genetic. So I watched my mom go through it. We didn't even know the mutation existed until in May of this year. So it was kind of an emotional issue for me at that time and then also the pain level was not what they had let me know at the time. It was supposed to be, "Oh, you'll feel better in a couple of days." Weeks later, I was still in pain from that biopsy. And it's just something that I wouldn't choose again if I had to.

James Valentine (02:32:11):

Sure. Well, thank you so much Kayla. And maybe Eftihia, if you could share any of your thoughts again, anything that might be important for you to know or think that would be an important consideration or factor to decide.

Eftihia (02:32:26):

For us, I'm a patient parent. My daughter is six and I think the biggest thing for us would probably be the why. Like, why is this trial going to work? What case studies are there to prove what this is going to help? That's a big thing for us.

James Valentine (02:32:42):

Yeah. And so for you, is it more important that it be trying to manage the underlying cause or is it reducing symptoms or reducing progression? Which of those would you have her and would she be willing to participate in a study for?

Eftihia (02:32:57):

I think the underlying cause would be the most important thing for us so that we could kind of figure out how it started and then from there, I feel like you find out a lot more information on how to stop it.

James Valentine (02:33:11):

Sure. Well, thank you so much for sharing that. So, the first question I asked was about what would be important information. I believe we've had some web comments come in about, with some people reporting what would be important for them to know. David, can you let us know what that is?

David Feldman, PhD (02:33:29):

Yeah. So, Amanda from Westminster, Maryland, said that she wanted to “know as much information as I can about a trial. What side effects and what the outcome that it would be expected like full or partial remission?” Another Amanda from Illinois, “it's important for me to know what is the purpose of the trial, how it will help me and patients, how it might make my FSGS better and if it can be, the agent, the drug can be used for recurrence of FSGS in transplants. I'd also like to know how safe it is and I like to be informed along the way of what is happening in the study.”

James Valentine (02:34:15):

Wow. A lot of really good inputs there.

David Feldman, PhD (02:34:18):

Right. We have one more from Nikki in Detroit. She says that "the fear of taking part in a clinical trial is that I would be placed on a placebo. If you're joining a clinical trial, it's because you are desperate for a new treatment to save your life. If you are in the placebo group, then you are not receiving any hope of disease control or remission, at least anytime soon. That is terrifying."

James Valentine (02:34:45):

Wow. Yeah. Thank you all for writing in there. I know we have someone who actually has experience in clinical trials that has called in – Becky from Massachusetts – and would like to share both the positive aspects, but maybe some things that would be important for considering whether to enroll another trial in the future. So Becky, are you with us? Becky, are you with us? All right. Well, while we're trying to get Becky there on the line, I'm going to come back to our Zoom panel here and again, try to see about some more perspectives on participating in studies. And so I'd like to go to Cheryl and see what your thoughts are. What are your preferences around studies?

Cheryl (02:35:36):

Good morning. My personal preference would be actually any of those choices, but in particular, perhaps focusing on the ones that would slow disease progression.

James Valentine (02:35:56):

Sure. And you know, so when you're thinking about that, would you be willing to participate in the others or is it just that would be your preference amongst those different options? Would you say if something was there to help address fatigue or address edema or something like that. would that be of interest to you?

Cheryl (02:36:16):

Yes possibly, depending on what the overall goal is and what kind of medication.

James Valentine (02:36:27):

Okay. Thank you very much for that. So I want to expand this and get us thinking about a lot of different factors that you might consider. So now that we've heard some of those, if we can go to our polling questions, I have a couple more for you about some different things that might be important.

So if we go to our second polling question, here we have a list of factors. So I'll read through this but I know there's a lot to consider here and we want you to think about which of the following factors related to a test drug in a clinical trial, which three of these would you rank as most important to your decision in participating about a trial? And if you have thoughts about any of these, we'll encourage you again to call in +1 703-844-3231 or write in using that web form under your live stream.

We want to hear about the selections that you'll be making for us here. So your options are A, whether you might get the placebo or be assigned to placebo and get the sugar pill, so to speak. B, whether you need to stop your current treatment in order to participate. C, potential side effects from the new drug. D, how the drug is taken, whether by mouth, IV, or injection. E, in earlier trials, whether the drug's been shown to be effective for specific benefits that are most important to you or meaningful to you. F, knowing if you can make the commitment to participate in the trial. G, the frequency of the exam appointments. H, the distance; the amount you have to travel to get to the trial site. I, the length of time that the trial would go on. J, whether a kidney biopsy is required. K, negative things that you've heard

about clinical trials. L, whether your nephrologist has recommended enrolling in that trial, or M, some other consideration that you rank as most important to your decision about participating in a clinical trial.

So please select your top three things that you view as most important, or if you're a caregiver that you view as most important for your loved one.

All right. So it looks like final responses are just trickling in here. We, again, these are the percentages of responses, not the percentages of people that responded. So it's, again, a ranking.

It looks like the thing that's in most people's top three is the potential side effects from a new drug. So I'd love to hear about what side effects it is that would make it so you would consider not participating in a trial. After that, we see whether or not you need to stop your current treatment and or whether you might get placebo being the next top choices followed by whether in earlier trials, the drug might have been shown to have some benefit on specific things that are meaningful to you, how far you'd have to travel, and whether your nephrologist recommends it. And however, every single option here is in somebody's top three.

So lots of potential areas for feedback. We'd love to hear from you. If we can go to our third and final polling question here, we heard this comment come up from one of our Zoom panelists. so we want to ask you about it. Would you enroll in a clinical trial if it required how many kidney biopsies? And we'll ask you to select the greatest number of biopsies that you would be willing to accept within a one-year period. A, you would only enroll in a trial if it had no kidney biopsy. B, you would enroll with one kidney biopsy within a year only. C, you would go up to two kidney biopsies in a year or D, if you'd be willing to participate in a study with three kidney biopsies within a year.

All right. So it looks like of our participants today, a little over 40% of you would only enroll in a study with a maximum of one kidney biopsy per year. We see about a little over a fifth of you would be willing to enroll in a study with two per year and a similar amount little over one fifth of you would be willing to enroll in a study with three per year, and over 10% of you reported that you would only enroll in a study if there is no kidney biopsy involved.

So thank you for this. We very much want to hear your inputs on why you selected that about those burdens as well. But I want to start off, we have a couple of phone callers, one who has experienced participating in trials and another, who has not been able to get into a clinical trial. So I'd like to start with Becky from Massachusetts. I think we lost you a little bit earlier. So Becky are you with us?

Becky (02:41:54):

I'm here now.

James Valentine (02:41:55):

Welcome.

Becky (02:41:58):

Thank you. So I was able to participate in a clinical trial and I had a wonderful experience with it. I think some of the positive things about clinical trials is it gives you an opportunity to really get to know the doctor. You get a lot closer attention with them. You're seeing them sometimes weekly sometimes every other week. So you really get to understand your medical history at a much deeper level than I think you do just going to your nephrologist, monthly or every six months, depending on where you are. So that was a really positive experience for me. And while the clinical trial did not work for me, I would definitely consider participating.

Again, some of the big things for me are the convenience factor, given that I'm a working mother with two young kids. So needing to make sure that I can actually get to the site for the drug is really important. And then again, some of the things like the biopsy, because then I'm down and out for a couple of days, or the number of 24-hour urine that I have to participate in because I don't know that people putting together these trials understand what a pain that is to do if you're working or in and out of the house throughout the day.

James Valentine (02:43:18):

Yes. Do you have any for you, at least personally, any specific recommendations or thoughts about how many 24-hour urines you could do in a study or how many biopsies and given that you mentioned that they are so burdensome?

Becky (02:43:38):

Yeah. I mean, for me personally, I think one biopsy in a year is enough. If it was a situation where I thought the drug was really helpful and my doctor really thought it was going to work for me, then I think I would probably be willing to flex there and do two. Three sounds absolutely crazy when I think about that. And in terms of the 24-hour urines, I mean, it's not something that you want to have to do on a regular basis. If it's something that you had to do three times throughout the trial, then that definitely feels like something that wouldn't deter me from participating. But if you told me I had to do it every week or even every month, that sounds like a lot.

James Valentine (02:44:26):

Okay. Sure. Well, I'm glad to hear that you had a positive experience in the study and felt like you got really high-quality care, but really also appreciate your feedback on making sure that these studies aren't too burdensome. So really appreciate it Becky.

I'd now like to go to Lisa also from Massachusetts, who wants to share about her daughter's experience not being able to get into a clinical trial. Lisa, are you with us?

Lisa (02:44:54):

Hi, yes. So, yes. Hello. My daughter prior to transplant was not able to be in any clinical trials because there were not any clinical trials. She was one of the first patients at Boston Children's to try the medication program for Tacrolimus. And at that point we were so desperate to find something that would help her proteinuria. So my push would be to get the information about clinical trials out to nephrologists. Many patients are not responding to the current treatments and we need a focus on new novel therapies. So I would say, make sure that information is getting out, that there are clinical trials available and getting that in the hands of patients and caregivers.

James Valentine (02:45:49):

Sure. And anything else, say if your doctor did have a clinical trial to share with you, is there anything that you've thought about, from maybe what we posed in that polling question, that would be most important for considering a trial even say post pre-transplant?

Lisa (02:46:09):

I would say the side effects of the medication, looking at studies using the medication would be very important and also-

James Valentine (02:46:20):

Any specific side effects that come to mind when you're thinking about that?

Lisa (02:46:26):

I would say anything that affects my child neurologically, because I think a lot of the medications they have right now are affecting my daughter that way as far as a tremor goes headaches, fatigue.

James Valentine (02:46:40):

Okay. Sure. Well, thank you so much Lisa. It's an important message for us to hear about the need to make sure that information about studies is getting to doctors so that patients can actually participate in these. I'd like to now go to our panel and thinking about that polling question and that array of factors, love to hear what you selected and why you selected that as being most important. Gianna, would you like to get us started here?

Gianna (02:47:11):

Sure. I am a two-time kidney transplant patient. So thinking about that definitely makes me very cautious when looking into clinical trials or thinking about clinical trials because most of the time there are no prior trials with a kidney transplant patient even in them. So, obviously someone needs to start somewhere but being the first person to be the transplant patient within the trial definitely makes me very nervous. And then the side effects recently, my symptoms are mostly bone issues and in some of the trials that have been presented to me, some of the side effects could be broken bones or jaw health issues.

So it seems a little conflicting to me and I don't know if it's necessarily worth it, but I would like to know if there are less risky trials for people with transplants. I definitely worry about the biopsies although one biopsy I would probably do within the year, but I know there's a slight chance that biopsies can also cause strain to the kidney. And with this being my second transplant, I'm really unwilling to take a lot of risk, but I willing to take the risks that might be able to show that any type of progression could be slowed or the underlying cause of this can be found.

James Valentine (02:48:50):

Sure. Very clear feedback there Gianna. I really appreciate it. I want to give on our Zoom panel, Curtis, the last word on what factors were most important from your perspective?

Curtis (02:49:04):

For me, it would be the amount of biopsies. Like Gianna, being a kidney recipient you kind of want to keep what you already have and don't want it damaged. And also, I would go by what my nephrologist would be saying and how his recommendations would come in as far as what the trial is all about. Whereas I would like to help with trying to slow down the progression of kidney disease and also the underlying factors, especially within the African American community. There are still some cautious things that I would have to look at and really need to know the information about it.

James Valentine (02:49:58):

Yeah. And that's a really good point Curtis. Is there anything you think that is specific that would be important information for the African American community from your experience or from others, that

you want to put out there as being a place where we might be able to be a little bit more sensitive and provide important information?

Curtis (02:50:21):

Well, the biggest one, as it was stated I think in the first panel was the APOL1characteristic that is really high in people of color and especially the African American community. And finding out why that particular type of gene is affected more in people of color than anyone else. And also, African Americans are three times to one as far as getting kidney disease. So what are the underlying causes of that outside of high blood pressure and diabetes. So trying to look into more things like that.

James Valentine (02:51:10):

Okay. Well, thank you so much, Curtis. And I want to thank our Zoom panel for all of their contributions to this discussion. I want to be respectful of our lunchtime, our lunch break. I know we're a couple of minutes over, but I do want to make sure that we get in maybe a couple or top two or three web comments that have come in. So David.

David Feldman, PhD (02:51:29):

Right. So, Jen from Minnesota writes, "There seem to be very few trials for patients who have already had a transplant. I'd love to participate in the clinical trial, but I am not eligible due to transplant."

So that's a common problem.

Erica from Washington, whose daughter was in a lipid apheresis trial, and to determine whether or not they wanted to enroll, she says, "We mainly looked at how very similar patients responded to different treatments and both the low side effects and success with a few very similar patients, made us willing to give it a try." So they looked into the evidence. So evidence is important.

James Valentine (02:52:18):

Sure. Great. Well, really appreciate all of the feedback from everyone on this. We're going to continue the discussion on clinical trials when we return. We're going to talk about a very specific type of trial used to help support a special regulatory pathway. So we're going to give you some background on that when we returned from our break at 1:05 Eastern Time. So we're going to break now for just a little under 30 minutes.

TOPIC 3

James Valentine (03:18:37):

Hi, this is James Valentine, and welcome back to the Externally Led Patient-focused Drug Development meeting for FSGS. Hope you had a nice lunch break.

We've covered a lot of ground this morning, talking about both understanding the burdens, symptoms and impacts on daily life of FSGS. And started the conversation around your preferences for participating in clinical trials for drugs for FSGS. And that brings us to where we are now in today's program, where we're going to talk about a special type of clinical trial, that relates to a specific FDA approval pathway called accelerated approval.

And so we're going to start out with a presentation on this topic by Dr. Kimberly Smith from the FDA. Dr. Smith is a nephrologist, and a clinical team leader for products being developed to treat kidney diseases

within the division of cardiology and nephrology at FDA. The same part of FDA that Dr. Aliza Thompson, who spoke this morning, is from. So it's my pleasure to welcome you. Dr. Smith, take it away.

Kimberly Smith, MD, MS (03:19:43):

Thank you, and I appreciate being here. I enjoyed all of the discussions earlier this morning, and the efforts that you've made to keep this discussion moving forward despite all of the challenges of doing this virtually rather than in person, where I can see all of your faces while I present. And so, I've been asked just to give a brief introduction to the accelerated approval pathway for new drugs, since this may be unfamiliar to some of you. For those of you who joined the IgA nephropathy meeting about a year ago, many of these slides may look familiar to you, from the talk that Dr. Lisa Thompson gave at that meeting. So thanks to her for sharing these slides with me.

Next slide. So just a brief outline of my talk. I'm going to start with the two approval pathways for drugs in the United States, followed by just some introductory information on what we refer to as surrogate endpoints, and then some other aspects of the accelerated approval program that you should probably be aware of, to inform your discussions later this afternoon.

Next slide. So there are two main approval pathways for drugs in the United States. The one that most people are familiar about are referred to as traditional approval. That's approval that's based on either a clinical outcome or clinically meaningful endpoint, which is something that a patient actually feels a measure of how they function or a measure of some other important clinical outcomes. So we often refer to this as how a patient feels, functions or survives. Important examples in the kidney disease space would be for instance, kidney disease progression to kidney failure, would be the one that I think we heard a lot about earlier today. That's a major fear and a major concern for a lot of patients with kidney disease.

Traditional approval can also be based on a validated surrogate endpoint. We'll get a little bit more into what a surrogate endpoint is in the next few slides, but these are surrogate endpoints that have a fair amount of evidence to support that if you show an effect on one of these measures, that's really likely to predict a fact that a patient is likely to care about, on an important outcome or clinically meaningful endpoint.

The other pathway that I think people are often less familiar with is the accelerated approval pathway. This is a pathway where the approval is based on a surrogate endpoint that's reasonably likely to predict clinical benefit but may not have evidence to support it to the level that it would be enough for traditional approval. This pathway is a little bit unique in that often times the drug can be approved and can reach the market, but there is an opportunity to resolve any uncertainty related to the effectiveness of the drug or to verify the clinical benefit in the post-marketing setting. So after the drug was approved and providers can actually prescribe the drug to patients, there may be additional studies ongoing to confirm that there is a benefit to patients.

Next slide. So what are the requirements for accelerated approval? So the product must be for a serious or life threatening disease or condition. I think we would all agree based on the testimony this morning, that FSGS would qualify for that. And it also must provide a meaningful advantage over available therapies. Given that there are no approved therapies for FSGS, I think we would all agree that FSGS would qualify on the basis of those criteria. As I mentioned, you may have to do a post-marketing confirmatory trial to verify and describe the effect on an end point that would be important to patients. And if at the end of that trial, the benefit is not confirmed, the drug can be withdrawn from the market, or if that trial did not demonstrate that there was enough of the benefit to outweigh the risks associated with the drug, there is the potential for the drug to be withdrawn.

Next slide. So what are surrogate end points? These are end points that are used in trials as a substitute for a direct measure of how a patient feels functions or survives. But it's something that we would expect to predict those important outcomes. And that expectation is based on a variety of sources of evidence. This could be epidemiologic data, looking at associations between various markets and outcomes, the effects of other therapies and knowledge of the pathophysiology of the disease, the basis for the disease or other evidence. It's typically a marker, like a laboratory measure; proteinuria or creatinine, or estimated glomerular filtration rate would be examples. Could be radiology images or some sort of a physical sign. And then we think about these on the basis of how strong the evidence is to support them.

So I mentioned that a validated surrogate endpoint would have a fairly high level of evidence, and that could be used to support full approval or traditional approval, meaning that no further studies would be needed in the post-marketing setting, at least from an efficacy standpoint in terms of the benefit, or there are reasonably likely surrogates. As I mentioned, those are endpoints that would have a level of evidence. So it's not quite good enough for traditional approval, but would support accelerated approval. And then we also have this concept of candidate surrogate endpoints, meaning you have something that may or may not be about one of these other pathways, but is being investigated for that, maybe further study is needed. Next slide.

So what are some examples in the kidney space? So at the FDA we have, and many of you are aware of this, we have accepted effects on serum creatinine or glomerular filtration rate as a basis for traditional approval. These are laboratory tests, but I think we all understand that if you have a substantial decline in kidney function, that does predict progression to end stage kidney disease and other important clinical manifestations of kidney disease. For some diseases, we've also accepted effects on proteinuria. So if you take somebody who has a lot of proteinuria and you put them into complete remission or near normalization of the proteinuria in some diseases, we believe that that is enough to support full approval, enough evidence of benefit.

Other examples are hemoglobin and hematocrit to treat the anemia associated with kidney disease. You're on phosphorus to treat elevated phosphorus and dialysis patients, and then serum potassium to treat elevated potassium associated with kidney disease. So all of these would be markers that are not direct measures of important manifestations of kidney disease, they are laboratory tests, but that we believe they predict an important outcome and they have formed the basis for a traditional approval historically.

Next slide. So we also have surrogate endpoints that we have accepted as a basis for accelerated approval. So I mentioned that a substantial effect on proteinuria, meaning complete remission or normalization has been accepted as a basis for traditional approval. Some sort of a lesser degree we've accepted as a basis for accelerated approval, meaning you're decreasing proteinuria and it's sustained for a period of time, but maybe you didn't quite shut it off or break it down to near normal. In Fabry disease, there are histologic findings in the kidney deposition of compounds and that has been used on histology findings as a basis for approval. And then total kidney volume for patients with Autosomal Dominant Polycystic Kidney Disease. Next slide.

So what are some challenges when you think about surrogate endpoints? The disease processes are complex and drugs can sometimes have effects beyond those that are intended. So it can be difficult for those reasons to identify a surrogate that we believe predicts the treatments effects on clinical outcomes reliably. We also have examples even in nephrology community and nephrology space of markers that identify patients at risk, but don't actually predict the treatment’s effect on important outcomes. And there are examples when what we expected didn't actually turn out to be the case.

Whenever we're using a surrogate endpoint, we're not actually measuring the clinical outcome directly, the clinical benefit directly. So there's uncertainty that we may not have the whole story. And then even if we do believe that changes in a marker will predict the clinical benefit, how big of a change do you need to see for that to actually result to me in the outcome you expect? If you see a small change, is that enough? How big of a change do you need to see? Next slide.

And then I mentioned that you need to be able to verify the benefit after accelerated approval in many cases. And for that to occur, patients may need to stay in the trial and in their assigned treatment arm, meaning either the study drug or the placebo, the non-active drug, including standard of care or whatever else is background therapy for the population. And they may need to do that for two to three years to verify the benefit even after the drug is on the market. If the patients decide once the drug is marketed to leave the trial or to leave their assigned treatment arm, it's possible that even if the drug is effective, the trial isn't going to show that and that can make it difficult to interpret the findings once the study is completed and to determine whether there truly was a benefit to patients. And so this is, I think, a key consideration when we start to think about these programs. Next slide.

And I believe That was my last slide. So I appreciate your attention and I look forward to the discussions this afternoon. I'll turn it back over to David and James.

James Valentine (03:30:08):

Great. And thank you so much, Dr. Smith, that was incredibly helpful overview of both surrogate endpoints and also how they fit into trial designs to support accelerated approval and what else needs to be done to confirm clinical benefit after a product's been approved under accelerated approval, and that's going to be the topic of this discussion. So I really appreciate you spending the time with us on that.

If I could get our discussion questions put up here. I actually, this is going to be kind of the prompt so to speak, a case study that we're going to help get you to give us some input on your considerations for participating in clinical trials that could be able to support accelerated approval and continue to support them once the drug is approved.

So what we want you in this situation to do is consider – you're considering to enroll in a clinical trial where you have a chance of being given either the potential medication for FSGS, so the new drug that's being studied, or standard of care treatment. That might be things like prednisone or an ACE inhibitor along with placebo. And you won't know which you are getting, whether you're going to be on the new drug or the standard of care treatment arm of the study. In that study, the trial is going to be evaluating whether the medication lowers protein in your urine, also known as proteinuria, in the first phase of the study. If the trial does show that proteinuria is lowered enough, the medication will be approved under accelerated approval as Dr. Smith just described.

However, that study continues on to verify that the medication slows the loss of kidney function. So, patients who are enrolled in the trial must remain in the trial in that assigned treatment arm, whether that's the investigational or new drug or the standard of care treatment arm for an additional one to two more years. And so, in this situation where you're considering whether to participate in this trial, we want to know what factors would motivate you to participate in the study in the first place.

And then once the drug is approved under accelerated approval, and we need that one to two more years of a time where you're still staying in those treatment arms, what would motivate you to stay in the trial during that extension phase? Because as Dr. Smith described, that information is really important in order to verify that the effect on proteinuria actually does translate into an impact on something that's important clinically, which in this case would be showing that the medication slows the loss of kidney function over the course of one to two more years.

And so if you have thoughts about this, we're going to encourage you to call in the phone number. Again is +1 703-844-3231. If you're just joining us, we welcome patients and their direct caregivers to call in and help us understand your views, your perspectives on these questions. We also encourage you to write in any responses that you have related to these questions in that comment box that's underneath the live stream that you're following along on.

But to get us started, we actually have a couple of polling questions, try to get the wheels turning around these issues. And so we're going to go to our first of two polling questions that we have related to these accelerated approval clinical trials.

So, in that proposed trial that I just described, we want to know, how long would you be willing to stay in your assigned treatment arm during the post-marketing extension phase? So just to remind you, this is when after the drug has been approved based off proteinuria and we're following the effect of the drug for an additional, at least one year, to see whether it helps slow the loss of kidney function.

So, if you can go to your cell phones, open up your web browsers, go to PollEV.com/pfdd. For those of you that participated throughout the morning, it's the same website, and let us know how long you would be willing to stay in the extension phase. Your options are, A, one year, B, two years, C, three years or D, you would not be willing to stay in the treatment arm for any period of time during the extension phase. I'm going to check. I don't see any responses coming in, so I want to make sure that the question is activated for you all. Okay.

So again, thinking about once that drug is approved, how long would you be willing to stay in your assigned treatment arm during that post-marketing extension phase? The options are A, one year, B, two years, C, three years or D, not willing to stay in your treatment arm for any period of time after the extension phase. I see, we just needed to refresh here in the studio to see the responses coming in. So thank you all for answering this question. So we'll let you think about this a little bit more. And as you're thinking about this, we want you to think about why it is you're making this choice. Because we want you to call in, we want you to write in to explain why it is you'd be willing to stay in a study, even though you don't know if you're on the new drug or if you're on the standard of care group for these additional years while the drug has been approved under accelerated approval.

So it looks like most of our results have already come in. So what we're looking at is about just under 40% of you say that you'd be willing to stay in the study for two additional years. About the exact same number right now at least are saying that you'd be willing to stay up to one additional year. And about 20% of you saying that you'd be willing to stay in for an additional three years, while about 5% of you said that you would not be willing to stay in the treatment arm for any period of time during this extension phase. So it's very important to know, and again, we're going to be asking you to help us understand why you chose these responses. So we can go to our second polling question.

So now we want to try to understand what of those different types of measurements, and this is regardless of whether it's for traditional or accelerated approval, that you would consider relevant to you and your FSGS. And we want you to pick the top three of those measurements. Is it A, the protein leakage in urine, like proteinuria. Is it B, kidney function, which is measured by GFR. C, blood in the urine or hematuria. D, swelling, including edema. E, fatigue. F, measures of depression and anxiety. G, measures of brain fog, like forgetfulness, poor concentration or losing track of time. H, general quality of life. I, delaying time to dialysis or transplant or J, some other thing that if measured in a clinical trial, you would view as relevant to your FSGS. So please select here, your top three.

I'll remind everyone because our participants can select more than one option; what we're seeing is the percentage of responses, not the percentage of people picking each response. So it's a ranking type exercise in terms of the bars. We see what you think about this just a little bit more here. I know it's a lot

to consider, what measures you would say are relevant, which of these outcomes are relevant to you and your FSGS in a clinical trial.

As it stands, it looks like the top choice is protein leakage in the urine and the measures of that. Close behind that is kidney function as measured by GFR. And then we see a little bit lower, delaying time to dialysis or transplant. I think that is echoing some of the comments we heard earlier in today's sessions. We do see swelling, edema and general quality of life getting a fair number of responses as a top three measure that would be relevant as well as fatigue. However, all of the different measures that are listed here have been selected by some of our participants as being kind of a top three most relevant measure for you. Nobody selected that there something else that wasn't listed that would be relevant.

So hopefully this has gotten you thinking a little bit. We really want to understand, again, what would really motivate you to participate in these clinical trials? And so, like with our previous discussions, we're joined by a number of members of your community on live by Zoom. And so here we're asking what factors would motivate you to join a study? And then what would motivate you to stay in that study once the drugs approved under accelerated approval during that extension phase? And are those things the same or are they different in terms of those motivators?

So perhaps we can start with Diane to share what would motivate you. If you want, you can share even what you responded to that polling question to help frame for us what you'd be willing to do. So, Diane, welcome.

Diane (03:40:17):

Yeah, hi everybody. For me, the top motivation would be in the view of my first nephrologist. There's quite a few studies that would be possible to participate in over, say, a two or three year timeframe and the selection of which one to participate in is really important. I want to be sure that the one I choose to do has the highest probability of positive impact, not only on myself, but on research moving forward. And this is such a big decision that I'd actually seek a second opinion of another nephrologist that I greatly trust. It's that critical of a decision to me.

James Valentine (03:40:56):

Sure, And maybe if I can probe a little bit specifically on that period of time after the drug is approved. So in this hypothetical study, we're saying the drug would be out on the market but you would be still randomized either to drug or to standard of care. And that information is important so we can actually confirm whether the drug works. Is that something you'd be willing to participate in?

Diane (03:41:28):

Again, it would be something I would discuss with my nephrologist and it would very much depend on how my experience had been to date. Had the clinical trial required that I stay at the same level of other medications, just to give an example, say 10 milligrams of prednisone over the course of the trial and they wanted me to stay on that for a couple of new years, I think that'd be a deal breaker. I think the ability to be flexible at that point about the treatment, if it is indeed coupled with another drug that I've been taking, would be really important.

James Valentine (03:42:02):

Sure. And Jill I see you nodding your head. Is there something you'd like to add to that?

Jill (03:42:08):

Yeah. I am pretty open to trying many different options of treatment because I've tried so many and I'm running out of options. And so, I would try a clinical trial, but the fact that prednisone is one of the options really makes me take a real second thought about it. Because I'm sure many of us have been on prednisone before and I don't know that I could sign on for a year or two of being on prednisone. The answer to the question I felt like really depended, because it depends on so many factors and so for that particular example, prednisone really throws a wrench into it for me personally.

James Valentine (03:42:52):

Sure. And totally appreciate that. It all depends on the specifics, the devil's in the details. So hearing from you, both of you on what those considerations are, that's exactly what we want to hear from everyone today. So we actually have a couple of phone callers who have chimed in about their willingness to participate in this type of study. The first one that we have is Nicki from Illinois who has some thoughts about this. So Nicki, are you with us?

Hi Nicki, are you with us?

Nicki (03:43:27):

Hi, yes.

James Valentine (03:43:30):

Hi Welcome. We'd love to hear your thoughts about this.

Nicki (03:43:35):

Yeah, thank you. So yeah, I actually answered to the extended treatment, I said I was not willing. And my reason being is because ideally, I would love to say, I could do a year or two more on a drug, but as the panelists were discussing, it really comes down to the specifics of the treatment like certain treatments I've tried. If they were a trial treatment, I could totally hang on for a year or two and do this extended arm. But other treatments have been so debilitating and side effects are not helping me. So I have edema and proteinuria that's severe that I couldn't do it. So it's almost like that question is one I can't make a decision on. It would be unknown for me just because the specifics are so important.

James Valentine (03:44:19):

Sure. So let me see if I understand that because I think that what you just said is really important. For you, you'd be willing to join this type of study and your decision of whether or not to stay depends on your personal outcomes. If you were doing well, you would stay but if your proteinuria was getting worse, if the edema was getting worse or maybe just continuing to not get better, that would make you want to look for other options. Is that what I heard?

Nicki (03:44:54):

Yes, that's correct. And I'm sure a lot of other patients, it's probably the standard, right? If it's working for you like any other – even the treatments they use now – you're going to stay on that treatment. But if it's not working, you're going to move on to something else. So it's scary to be stuck in a treatment for a few years without knowing, is this going to really cause GFR to drop or give me side effects that keep me in bed all day? So I think, really quality of life and at least stabilizing, even if it doesn't help you get better is key.

James Valentine (03:45:24):

Sure. No, that's incredibly helpful. And I saw many nodding heads on the panel. So I think as you guessed, that is seemingly a common perspective. So thank you so much Nicki. I want to bring Amanda from Chicago into this discussion. She also had some thoughts about what would allow her to decide to stay in the extension arm or the extension phase-

Amanda (03:45:49):

I wanted to say that I think...

James Valentine (03:45:52):

Sorry, welcome Amanda.

Amanda (03:45:55):

Hi. I do want to say that because I have a transplant, I haven't been able to participate in a clinical trial. I do think the question can be difficult to answer for a lot of patients. However, I think that if the treatment has a chance to reduce my urine protein levels or edema that, that would motivate me to stay in an extended trial. Because again, that was my worst symptom. I would have up to 30 pounds of edema in a span of a few days and I'd have that for a week. And I'd be in extreme pain and not able to do anything. So I would be motivated just for the fact that I could potentially maybe feel better or improve my quality of life and perhaps even slow the progression of the disease and live a more comfortable life.

And of course I'd have to evaluate if the drug was helping me or not causing me harm or other debilitating symptoms. My treatment did not work for me. So taking a treatment where we're not really sure that's working or not would kind of have been the same thing to me. I do want to say though that the example of prednisone in the question, I think, when we're educating patients, I think that would potentially scare a lot of people away because I think that there's a lot of agreement that prednisone is probably one of the worst medications they've taken.

James Valentine (03:47:17):

Sure. So, if you were able to be enrolled in the study, you were able to stay on your standard of care even once the drug was approved, as long as your outcomes were continuing to be stable, you would continue even though there's still a chance you are on standard of care, you wouldn't know that. But what you're saying is that you would be willing to, based off of your specific outcomes at the time of that extension phase?

Amanda (03:47:47):

Yeah, absolutely.

James Valentine (03:47:49):

Great. Well, that's so valuable to hear and I love the richness of your specific tradeoffs in thinking about this. So really appreciate your input on this. I want to check in with David, see if we're getting any comments here on the web to add to this dialogue.

David Feldman, PhD (03:48:07):

Yes, James. Amanda from Chicago writes, she would be motivated to join a trial by the chance to "help others and to help me feel better." Ken from Maryland, "I would be willing to stay in my assigned treatment arm during the post-marketing stage mainly due to my age – I'm in my early forties – and how beneficial the treatment can potentially be." Lisa from Massachusetts writes, "I would like to see case studies using this drug before beginning the trial." Again, looking for evidence.

James Valentine (03:48:44):

Sure. No, that's great and very helpful. I'll just remind everyone, if you want to call in and contribute to this, you can call on at +1 703-844-3231. And you can also continue to write in using that comment box under the live stream. I want to go back to our Zoom panel here and see if there's any considerations that maybe we haven't talked about yet or maybe a unique take on one of these perspectives. I'd like to go to Valerie to see what your thoughts are about what would motivate you to participate in this type of trial. Valerie, you're on mute.

Valerie (03:49:27):

It will depend on my stage, the stage of my disease. I wish I had done this years ago. I had a transplant two years ago with my son and it failed. So I'm back on peritoneal, I do it at home. But I would look at the stages of dialysis. If I was on stage three and my GFR was within a certain range of 30. And I would say, I would consider it because I'm all for prevention. And if it is something that's going to prevent it, I'm all for it. I'm on the same path as my nephrologist, I will want to see what my nephrologist says also and how often the labs are going to be checked. So those are the type of motivators that I would have. I wish I had this. I'll get a transplant soon. I'm back on the transplant list so I'm praying that I will get one soon. But if these things had been in place before and knowing my nephrologist, knowing my labs, knowing they – just the stage of my illness – and if it's going to prevent it from getting on dialysis quick, I would go with it.

James Valentine (03:50:43):

Oh. Well, that's wonderful Valerie. And we wish you the best of luck. We're hoping for you to get to the top of that transplant list soon. I know Janice, you have had experience in at least one clinical trial before. I wonder how that might inform your perspective around answering this question. What would motivate you to participate in this type of trial? Oh, and in Janice you're on mute. There we go.

Janice (03:51:24):

Something that hasn't been brought up yet was logistics and how far do you have to travel to participate in the trial. And in my case, it was a bit of a challenge driving to a larger city than where I live and traffic jams. It was a challenge and actually stressful at times. And that would be a consideration too, how far would I have to go? Would I have to fly there or drive there? And how comfortable are you going to be at the location you're going to? Sometimes I would stay a day and necessarily wasn't compensated for an overnight stay if I chose not to drive all the way home. So, those things are a consideration for me as well. As well as checking with my nephrologist. So, yeah.

James Valentine (03:52:34):

Yeah. So that's a really important and also interesting because I think as we're talking about this case study where there's the main first trial phase where that's where the drug's being studied, based of proteinuria, to get the drug approved under accelerated approval. And then we entered the second phase, the drug gets approved, and so it's available on the market, but that the clinical trial's continuing.

So you're still in the study, you're still participating. And so those burdens might be even more important during those next couple of years because you have the option of getting the drug outside of the trial, if those burdens are too great. So does that sound right to you, Janice?

Janice (03:53:22):

Yeah, it does, yeah.

James Valentine (03:53:26):

Great. It looks like Diane has something to add. So, Diane why don't you turn on-

Diane (03:53:29):

I just want to add a real simple thing, which is how many 24 hour proteins are required and at what periodicity. It sounds crazy if you haven't gone through it. But I was in Manhattan when I did my trial. I did a year-long trial, was very glad I did, I had a great experience, but do you know what it's like schlepping through Manhattan carrying 24 hour's worth of urine? And that's what's called for. It meant taking public transportation, holding a bag of my pee. Now my friends lightened me up and said, Diane, you're not the only person today in Manhattan doing this, but nonetheless, it's not easy. And I obviously did it and figured out ways, but I started a second trial and had to drop out because I relapsed, but that was even more onerous.

And there was no way that I would have been able to do their protocol even to get into the study had I not had great flexibility in my employment and the ability to meet their time schedule, much less their demand for 24-hour urine collection. So these little things really matter. It's the distance driving. It's how we're taking care of overnight, but it's also the frequency. And you just got to think through, what's it like to do a 24-hour protein test even if you're staying in a hotel. I know it's just-

James Valentine (03:54:55):

Diane, would that impact how long-

Diane (03:54:57):

[inaudible 03:54:57] but it's real. And it really will inform my second decision making. So if my doctors say, yeah, go great for it. The second is, is this actually feasible? Is the tradeoff worth it?

James Valentine (03:55:09):

Yeah. And does that impact your thinking that around how long you'd be willing to stay in?

Diane (03:55:14):

Completely. Because if it's just been crazy like that, then why not just go get off and get on the market? I would love to be able to support the science, but at the same time, the design of the study needs to incorporate the fact that we are fully active, engaged people and want to stay that way.

James Valentine (03:55:35):

Absolutely. Thank you so much Diane. So we have a caller, Marlene from New York who is a caregiver of a pediatric patient with FSGS who wants to share her thoughts about motivation to participate in this type of trial. Marlene, are you with us?

Marlene (03:55:53):

I am. How are you?

James Valentine (03:55:55):

I'm great, welcome.

Marlene (03:55:59):

Thank you so much. As a caregiver of a pediatric patient, I found that – and my daughter has been in two drug trials – I found that the level of care that was received was superior. The fact that we were in a lot more and gotten a lot more testing than the average if we had not been in a drug trial. I also think that the infusions made her feel better, even if it didn't put her into remission, her quality of life was better. My understanding of the disease was better because I could see the labs. The doctor was very good with sharing all of the information and it was super valuable to have all of those things. Especially as a mom, who's worried about our daughter. It was well worth it and I would – she's in her second drug trial currently – and if there was a third, we would be signing up for that because we need to make sure that she's getting the absolute best state of the art care that we can get her.

James Valentine (03:57:10):

And is there anything that would change your willingness to stay in a study for those extra additional years into that extension phase? Is there anything that would-

Marlene (03:57:25):

I think if her levels were not stable, I think if it was causing harm to her or her native kidneys, I think if she was not feeling well, if the edema was not being controlled, all the things that make – and as such an insidious disease – if that was still happening while she was on the drug trial, then we would have a serious conversation with her nephrologist with the study and have a discussion about whether or not we would continue. But we haven't had that experience, we've only had a good experience.

James Valentine (03:58:04):

Oh, well, thank you so much for sharing that, Marlene. I want to give for our Zoom panel, Kent, the last word here. What do you have to say, Kent that maybe we haven't heard yet or your personal take on something?

Kent (03:58:19):

Well, this is hypothetical, but we all know that very little has changed in the way of getting new drugs in the system and new treatment plans. I've been on prednisone for 45 years. I've also was transplanted for 33 years, and I've been on immunosuppression for that entire time. In that particular time, if I start seeing any protein in my urine, it's going to indicate most likely that the FSG[S] is attacking my kidney. That's my brother's kidney, and I'm going to do everything I can to protect it. So consequently, if this was available, I would certainly want to dig into it and I'd want to drive it hard. I'd want to make sure that I was able to do all of the study if I was going to get in. The only thing that would be troublesome to me would be the biopsies, but at that stage, if I start throwing protein at my age, I'm going to look at protection. So that's just a different take.

James Valentine (03:59:27):

Sure, and a very important one. So I really want to thank our Zoom panel for participating in this discussion today. I want to give another chance for us to hear from all of our participants who have been writing in. So David, if you can share with maybe some of the top comments that you've seen.

David Feldman, PhD (03:59:45):

Sure. So many of these responses are about enrolling in a trial. Debra from Georgia writes that what's important to her is to "understand the number of pokes, visits and how medicines would be administered, and she wants to understand what pain is involved."

Bernadine from Washington DC would like to know, she wants to make sure "if I was sure it would not negatively affect my transplant." That's very common response. Pamela from Connecticut writes, "My daughter would not participate in a trial were it to affect her fertility and negatively affect her other organs."

James Valentine (04:00:40):

Great. Well, thank you David, for sharing those and thank you to everyone that wrote in. We've gotten tremendously valuable input both from this and the previous discussion on your preferences around clinical trials, and what would make you more likely to enroll in studies as well as stay in those studies, which of course, as we heard from Dr. Udani, very critical that we overcome some of these challenges so we can get safe and effective drugs out to patients.

TOPIC 4

James Valentine (04:01:14):

So now we're moving into the fourth and final part of our discussion today, where we're now going to transition into talking about current challenges to treating FSGS. So we've talked about the symptoms and burdens and daily life of the condition. We've talked about clinical trials. Now we want to understand what it is that you're currently doing to try to help treat your condition.

When we talk about treatments here, we're not talking just about medications, but it might be medical procedures, certainly transplants. It might be other things that you do. Other types of therapy, more holistic approaches, diet, exercise, even modifications that you need to make in your life to help make living with FSGS just a little bit easier. As we explore what you are doing, we want to understand how well those treatments are helping with those symptoms that you educated us about earlier in the day. We want to know also, knowing that no treatment comes without some kind of trade-offs, what are the most significant downsides of your current treatments? How do those downsides, whether it's a side effect or the amount of time it takes to get a treatment, how does that affect your daily life?

Then we're going to conclude this next session, looking towards the future. While we all would want a cure for FSGS, what we want to do is think about what that next treatment might be coming down the pipeline. We're going to want to hear from you, what specific things would you look for from that next treatment that would be meaningful to you in your life?

So to get us started off on these important questions, we have a panel of members from your community who are going to be sharing some of their stories. We have Becky, Taylor, Nikki and Melissa. So Becky take it away.

Becky (04:03:06):

Hi, my name is Becky. I'm a 40-year-old mother of an eight year old boy and a six year old girl. I live 30 minutes outside of Boston. My OB GYN discovered protein in my urine during the first visit, when I was pregnant with my daughter. Four months postpartum, I was diagnosed with FSGS via biopsy. I was spilling around nine grams of protein.

I started taking a cocktail of prednisone, omeprazole to combat the stomach side effects of the steroids, calcium and vitamin D also for the steroid side effects. Lisinopril, levothyroxine, Lipitor and folic acid. I was on prednisone for eight horrible months. I felt a hundred percent fine until I started the steroid treatment, and during the eight months I experienced extreme steroid rage. It was like an out-of-body experience. I felt like I was sitting on my own shoulder, watching myself be completely irrational and telling myself to stop, but I couldn't.

I had a two-year-old, a newborn and a husband who all took the brunt of my extreme mood swings and anger. I've also never been that hungry in my life. I completely lost the ability to feel full. I gained 30 pounds and got the dreaded steroid moon face. The steroids also give you so much energy. I would wake up every morning at 1:00 AM, feeling like I could run a marathon.

Just when you think it can't get any worse after a chronic disease diagnosis, you get fat and crazy. Every time I got my lab results, I cried because the protein numbers were not going down, which meant I wasn't getting better. It's so defeating to be on this devil drug and see zero changes in the proteinuria.

We finally gave up on steroids and switched to Prograf. This is all part of the normal throwing-spaghetti-against-the-wall-to-see-what-sticks way of treating FSGS. We did Prograf for four months and the hardest part about that was, in the shower it felt like my feet were going to burn off. I had severe restless leg syndrome and started losing my hair. Like steroids, Prograf had no effect on my protein.

After that, we decided to try rituximab infusions. I did four rituximab infusions across a one-month period. The first one was the hardest. I felt nauseous and it took about six hours. They got easier after that, but still were about four hours in the cancer treatment clinic. Because of the Benadryl they give you to combat any allergic reactions you may have, I was also tired during infusion days and had to have someone drive me to and from the appointments. Unfortunately, this poison did not work to reduce my protein either.

At this point, I was able to qualify for an upcoming clinical trial of Abatacept. The clinical trial was one year and required weekly or biweekly visits to Boston for infusions of the drug or the placebo. The drug itself caused few side effects. The drug also was ineffective for me as well.

Four years later, and still spilling five grams of protein a day, we felt like the treatments were worse than the disease for me and decided to take a break. In 2018, we did a second biopsy to reconfirm what stage I was and to see if we could uncover any additional information. The pathologist was able to see what he believes to be a recessive genetic mutation of my kidney filters. They confirmed that the mutation was there in my first biopsy as well, we just missed it.

With the genetic form of FSGS, it is rare any of these traditional drugs to actually work. So everything I went through, the steroids, the trips to Boston for infusions, the clinical trial for a year could have all been skipped, and I would be in the exact same spot that I'm in today.

The good news from the biopsy is I'm still stage one, which still leaves us time to find a care. Today I'm on lisinopril, Inspra, levothyroxine, calcium, vitamin D, and Allegra. My only constant symptom of the disease is foam in my urine and swelling in warm weather, or when I eat salty foods. I'm out of options for treatments, and just hoping for some new clinical trials to come to bring my protein down. I need a treatment that's going to focus on curing the actual disease, not creating more side effects that make our lives harder than they already are.

Taylor (04:07:13):

Hello from the sunny state of Florida. My name is Taylor Faulkner. I'm 24 years old and I currently work as a personal banker. A few weeks before my freshman year of college, I started to notice swelling in my legs. I went to my primary care doctor who sent me to have a urinalysis and to have blood drawn. A few days later, she told me she was referring me to a nephrologist. When I asked her why, she told me the normal amount of protein in one's urine should be about 12 milligrams. At the time I was spilling 9,000 milligrams.

A few weeks later, I was diagnosed with focal segmental glomerulosclerosis. My ultimate fear was of irreparable kidney damage, but the only tangible evidence of my kidney disease were the symptoms which hindered my everyday life. So as with most patients, I was prescribed a diuretic to treat the edema, and 60 milligrams of prednisone in the hopes that my body would stabilize and stop spilling protein.

My body reacted positively to the steroid treatment and my nephrologist was able to wean me down to 20 milligrams of prednisone. However, we quickly realized that anything below that dose would result in proteinuria and edema again, thus indicating a relapse. My doctor believed the best course of action to be increasing my steroid usage back to 60 milligrams, and to start over again.

After several relapses, I began to realize my body could not tolerate high steroid usage for much longer. I know the medication was meant to help me, but my life was severely restricted by it. Prednisone alone, caused multiple panic attacks that affected my ability to attend my classes. I experienced weight gain of over 30 pounds, which caused me to lose my confidence. I withdrew from friends and eventually had to set everything aside to move home with my parents so that I could focus on my health. I felt hopeless.

The trial and error of searching for alternatives to prednisone was exhausting and limiting. When I would try a new medication, it would cause another issue that needed to be treated with a different medication. For example, I needed to be on a diuretic to treat my edema and keep it down. The diuretics I tried caused me to lose potassium, which resulted in me adding a new medication to combat that side effect.

At one point I was taking five different medications, totaling to 11 pills every day. I have tried fluctuating amounts of prednisone, lisinopril, Prograf, Pravachol, three different diuretics, multiple vitamin supplements, and even dietary changes. Finding the right cocktail of medications took a few years. Eventually the right mix turned out to be six milligrams of Prograf, five milligrams of prednisone, 40 milligrams of lisinopril, five milligrams of amiloride, and 20 mEq of potassium. This mix supplemented my potassium loss, controlled my blood pressure and limited my proteinuria long enough for me to heal without harsh side effects.

Unfortunately, the effects of prednisone will follow me for the rest of my life. I was diagnosed with osteopenia last year, due to the five and a half years of extensive steroid treatment. While I understand that there's no perfect medication out there for my disease, I'm hopeful that one will exist soon.

I've thought about what my ideal medication would look like. My idea is so different from what my actual regimen was. I would like to take one pill, one pill once a day. The side effects would not hinder my quality of life and they would not feel worse than the disease itself. It would not ruin my plans of starting a family one day. It would not cause vitamin deficiencies, it would not be steroids. It would however cater specifically to my disease. Instead of piecing together multiple medications for other illnesses that just so happened to work for me, it would be for FSGS.

The thought of relapsing again gives me a feeling of hopelessness. FSGS quickly robbed me of my dreams and aspirations of living a normal life. It might seem like a tall order, but it is my dream to have a medication that lets me regain control of my life and confidence in my future health.

Nicki (04:11:36):

Hi, I'm Nikki and I'm 23 years old. I grew up in Chicago and graduated last summer from Northwestern University. I currently reside in the Detroit suburbs and work in product management.

I was diagnosed with nephrotic syndrome, February of 2019. My first treatment, a high dose of prednisone was great for a few weeks. I had a lot of energy, a sense of euphoria and my disease symptoms subsided. I was spilling just above two grams of protein, but soon enough, I chowed Tums like candy to ward off heartburn. I ate like a rabbit and developed large pockets of fat. I gently bumped another person and I bruised black and blue. I was never able to sleep deep enough or long enough. My vision was blurred, but my eyes weren't getting any worse. I never knew when or for how long I was getting my period. I snapped at my loved ones constantly when all they did was support me. I shaved my face and my back for my college graduation. 2019 was a year without memories because I hid my moon face from photos and spent most days on the couch.

At this point, the prednisone side effects were way worse than the disease, so I tapered off as fast as I could. During tapering, I lost half of my hair. I vacuumed my apartment and car daily because it fell out faster than I could keep up with. My knees felt like they were completely busted. I couldn't even bend down two inches without forcing back tears. My joints were in so much pain that I could hardly complete simple tasks like grabbing a water glass from the cupboard. It was like I woke up one day and instead of 22, I was now 90.

I began my second treatment, tacrolimus, while I was tapering prednisone. It gave me debilitating migraines and brain fog leaving me in bed every other afternoon for two months. It also did not help my nephrotic syndrome. My protein spill had shot back up to six or seven grams a day. Again, the treatment was worse than the disease.

My third treatment, CellCept, correlated with a bad case of angular cheilitis, a highly visible, itchy and burning rash of the lips. The only thing that cured it was going off the drug and CellCept also didn't help my disease. My legs were swollen, like hot air balloons, 24/7. I attended a wedding and spent the whole event alone at the table. I had my legs hidden beneath the tablecloth and held a cold glass of water to my burning lips.

My fourth treatment, Rituxan, sounded like my dream come true. A couple of infusions and a drug free remission with no side effects, but after an eight-month long insurance battle for approval, it took just 10 minutes into the infusion for me to break out into full body hives with unbearably itchy ears and a throat threatening to close. I was drowning in tears as the nurses deemed it unsafe to continue the treatment and unhooked me from the IV. I was only 22 and I felt like I was out of options.

I began my fifth treatment, Cyclosporine, alongside a three-week burst of prednisone. This time the steroids gave me around-the-clock anxiety, a tight chest, difficulty breathing and panic attacks. But after nearly eight months, I finally saw my ankles again. Fast forward, and on cyclosporine alone, I have been able to maintain a daily protein spillage of just above two grams. In an ideal world, there would be no side effects, but they are more manageable, mildly puffy and bleeding gums, a little extra facial and arm hair and tingling in my hands and feet when I touch something too hot or cold. Bottom line, I can finally live my life again and feel comfortable in my own skin, but I still live in fear. If I miss a dose of cyclosporine, I swell up.

I do not believe I can achieve a drug-free remission on it. And what's going to happen when I have to go off of it to get pregnant? Or what if it just stops working? It is too scary and painful to comprehend a future that includes dialysis or a kidney transplant. I believe those last resort options are a band aid to a disease that begins with the immune system.

Right now, there are no other good treatment options for me to explore. I am relying on new drugs to come to market and allow me another shot at achieving remission. The ideal treatment would both prevent kidney failure and not force me to sacrifice the quality of my life. Otherwise, what's the point of a cure? Thank you.

Melissa (04:15:51):

Hello. My name is Melissa, mother, a 14-year old Alyse. Alyse's journey began in May of 2017. While waiting to see our pediatrician for well checks, I noticed Alyse's legs were edematous. He sent us to the hospital for labs, which revealed protein and blood in her urine. We were then sent to a pediatric nephrologist in New Orleans, Louisiana, three hours from home, and Alyse was diagnosed with nephrotic syndrome and immediately started on oral prednisone.

After only a month and a half of trying prednisone, we decided to seek a second opinion with one of the top nephrologists in another state. She was put on more high-dose prednisone, cyclosporines Neoral and Sandimmune, Prograf and CellCept. Without seeing any decrease in the protein spillage and a continual rise in the creatinine, Alyse had now progressed to FSGS. Medical treatment for our chronic kidney kid is not just limited to medications for the FSGS. With chronic kidney disease also comes Zofran, Pepcid, Prilosec, lisinopril, Norvasc, Synthroid, Crestor, and the list goes on.

Currently Alyse takes 23 timed daily oral medications with an infusion and an injection every week. Alyse's kidney functions still continued to decline despite all medications, and in March of 2018, she began peritoneal dialysis. PD was not easy on Alyse as it was a rough 10 hours every night with pain. Things like baths and swimming and sports became more difficult each day.

After 10 months on dialysis, we began preparing for transplant. It was determined that I was a perfect match, and on December 27th of 2018, I donated my kidney to Alyse. It took some immunosuppressive medication adjustments, but after 11 days in the hospital, Alyse and I were home. Unfortunately, Alyse's FSGS reoccurred about a month after transplant, even though her FSGS was not to reoccur as it was genetic.

Despite the addition of more steroids, rituximab, plasma, blood, IV Ig, Cytoxan, and a total of 62 plasmapheresis treatments, things began to take a toll on her body, psyche and our family. Four months after transplant, despite all efforts of trying to stop the reoccurrence of the FSGS, Alyse and I moved to Wilmington, Delaware to participate in a clinical trial for liposorber, lipid apheresis. Although the lipid apheresis was easier on Alyse as only the lipids were being removed, mentally and physically living on the East Coast with our family in South Louisiana was difficult.

Unfortunately, this treatment too was unsuccessful at putting the FSGS and its side effects into remission. We returned to children's hospital in New Orleans to begin Acthar injections. Alyse had a 50-50 chance of fact Acthar working, but at this point we were willing to take the risk. Due to the adrenal surges, there were so many days she was so uncomfortable she couldn't walk or go to school because of the swelling and soon began albumin diuretic infusions. But with the rising creatinine levels yet again, and a decrease in hemoglobin, Acthar was discontinued after six months and it was determined that Alyse was allergic to Prograf and her sister, Rapamune. She was quickly taken off of both.

After more medication changes, a kidney biopsy and a bone marrow aspiration, the diagnosis of TMA or atypical HUS was confirmed, yet another thing to deal with, and they were both medication-driven. She

has since received additional steroid infusions, increased doses of diuretics, and currently she is on Solaris infusions once a week in an attempt to halt the effects of TMA, aHUS. And we're praying that the kidney will fix itself and give Alyse many more years of use.

Alyse has had a very rough three years for any child, and despite having to deal with so many multiple comorbidities, we're still struggling to find a treatment that will halt the progression of her FSGS and the need for another kidney transplant for her and many kids like her.

Alyse (04:19:58):

Although this journey has been a rough one, it has strengthened me mentally and physically into one strong person. I know this journey is not done yet, but we will find better treatments for other kids like me.

James Valentine (04:20:15):

Wow. Another incredibly impactful panel, really showing that there's so much more to living with FSGS than just the disease itself, but really everything that comes along with the treatments and which is exactly what we want to focus on in this next discussion.

So to get us started thinking about these topics, we want to start to understand from all of you that are following along today, participating live about the medications that you use and how they're working for you. So we're going to start with a couple of polling questions again, for those of you who have been following along, pull your phone back out, go back to that tab.

If you've just joined us – you weren't able to make some of the earlier sessions – you can go open up a web browser and go to pollev.com/PFDD. We want to have you – or if you're a patient, or if you're the caregiver of a person with FSGS – to select the medications that they use, select all that apply. Your options are A) ACE, or beta blockers, or diuretics sometimes known as a water pill or any other drug that you use for blood pressure, B) allopurinol for gout or high uric acid, C) statins or other drugs for cholesterol, D) Veltassa or other drugs for high potassium, E) Sevelamer or other drug for high phosphate, F) antidepressants or antianxiety drugs, G) drugs affecting the immune system like anti-inflammatories or immunosuppressants, H) other drugs, including non-prescription remedies that aren't listed here on this slide. Or I) if you do not currently take any medications for your FSGS. So please select all that apply to you in terms of what medications you or your loved one use.

Again, as a reminder, this is the first question in this set of questions we're seeing that allow our respondents to select more than one option. So you're seeing a percentage of the responses, not a percentage of the people who have responded. So you can think of the bars as a ranking and as it stands, it looks like the class of drugs that are used by this group today are those that are used for blood pressure, including ACE, ARBs, beta, blockers, and diuretics. After that, it looks like the greatest experience is with drugs effecting the immune system like anti-inflammatories and immunosuppressants. Third, we have other things, so we definitely want to hear from you about not only the things we have listed, but anything that was not able to be included on this slide and your experiences with those medications.

Then I would say just behind that, and maybe the fourth highest used medication being statins or other drugs for cholesterol. However, we do have good experience across each of these and a few people reporting that they do not use any medications at this time.

If we can go to our second polling question here. So now that we know what treatments it is that you use, we want to know how well do your current treatments reduce the most significant symptoms of your disease? So you told us this morning what the most significant symptoms of your disease are. How

well would you rate your current treatments at reducing those? A) very well, B) moderately well, C) somewhat, D) not at all, or E) again, if you do not take any medications. We'll give you a few more moments here to get in your responses.

You are letting us know how well your current treatments reduce the most significant symptoms of your disease. All right, while the final responses come in, it looks like we've had a pretty close ranking of those that are reporting that current treatments work very well, moderately well and somewhat well. It looks like we're starting to see a little bit of a staggering between those. We do see after that a little over 15% of people reporting that their treatments do not help at all, and about 8% of our participants today not taking any treatments.

Can we go to our third polling question? So now that we understand kind of generally how well your treatments are working, we'd like for you to describe for us or pick for us, which of the symptoms or health effects that you have that are not addressed fully by your current treatments? So your options are A) muscle and joint aches and pains, including gout, B) bone or teeth problems, C) issues with eyes, D) high blood pressure, E) high blood sugar and diabetes, F) anxiety and or depression, G) brain fog, including things like forgetfulness, poor concentration and losing track of time. H) being tired or exhausted. I) gastrointestinal problems, J) recurrent infections, K) swelling of ankles and the face as examples, L) other symptoms and health effects that you have that are not addressed fully by your current treatments, or you can choose M) if you do not currently have any symptoms.

So we want you to select all of those symptoms and health effects that you would say are not being fully addressed by your current treatments, selecting all that apply. All right. So it sounds like from what we're seeing, the highest symptom that's not being fully addressed, that's got the greatest number of you reporting that is being tired or exhausted. Following that, we are hearing brain fog and anxiety and or depression being not fully addressed. After that, it's looking like muscle and joint aches and pains followed by swelling and gastrointestinal problems. However, everything except for high blood sugar and diabetes is being reported as not being fully addressed. And a few people are saying that they do not currently have symptoms.

So, what we want to do now is understand from all of you, kind of get some understanding of what is working well, where things are addressing your underlying condition, where things are addressing some of these symptoms. We're going to explore, build on that a little bit later in this session looking at some of the trade-offs, but we want to start with what is working. So if you have thoughts about that, I would encourage you to call in. That number is +1 703-844-3231. Then alternatively, you can write in, and we have that comment box still open below the live stream on the webpage. So in this discussion of what has worked and maybe how did you notice that it was working, I'd like to start with our Zoom panel here that's joined us and maybe we can start with Fred and Christina.

Fred (04:28:17):

Hi, thanks for having us. Right now, in terms of our daughter, she's actually not on any medication. She was diagnosed just over 13 months and we've been lucky that she's been in remission of late. So mostly our focus right now is on her diet, in particular, maintaining a low sodium diet. So, knock on wood, she's been maintaining that for now, but it's certainly something that we're continually mindful of.

James Valentine (04:28:45):

Sure. That's perfect because when we, as I mentioned at the beginning, we really do, when we're thinking of treatments, don't want to only think about drugs or medical procedures, but really the entirety of what you might be using or doing to try to help. So it sounds like with some of the diet

modifications that you're talking about, that seems to be helping in terms of perhaps at least supporting the lack of progression.

While we're on that topic, how hard is it for her to comply with those kinds of modifications? Is that something that's been pretty easy to implement, or-

Cristina (04:29:32):

It gets harder the older she gets and she sees what, you know, she's six so as she sees what other children are able to eat, it gets harder. But for her, it will always be what she remembers. Her earliest memories will always having been of having to adhere to the low sodium diets, so that helps. But yes, it does get a little bit more challenging the older they get.

James Valentine (04:29:56):

Sure, sure. Well, thank you for sharing that, Fred and Christina. I'd like to go to Kimberly and hear from you on anything that you view broadly in terms of treatments that might have helped you in managing your FSGS.

Kimberly (04:30:12):

For me, I've tried a lot and it's taken about five years for me to see any kind of remission. I do plasmapheresis and Acthar gel, and then my normal transplant meds. Acthar gel, and plasmapheresis are about the only thing that's given me any kind of lower numbers and that's a lot.

James Valentine (04:30:39):

Is there anything that you feel – when your numbers lowered – did that translate to anything to you in your life? Or is it just the knowing that your numbers are lower makes you feel better?

Kimberly (04:30:52):

Definitely knowing the numbers are lower makes me feel better, but as they kind of creep up higher, I'm always like, [inaudible 04:30:58] I start feeling like, but I'm like, "Wait, I think my numbers are creeping up. I can't wait to see what my labs are, just to see it." What I feel corresponds to my labs, and usually I'm right. So just knowing that they can be lower and that the plasmapheresis helps, that helps me a lot just to feel better too.

James Valentine (04:31:17):

Sure. You said that usually you can tell when your numbers are doing better or worse, what is it that you feel that kind of gives you that instinct or that heads up that your numbers might be changing?

Kimberly (04:31:31):

Just overall exhaustion. I mean, I'm pretty exhausted most days as is, but just when it comes to normal things, such as just cleaning around the house, when that becomes extremely difficult and it's lasting more than a day or two, that's when I know something's up, that something's not right.

James Valentine (04:31:48):

Sure. Thank you so much for sharing that – very insightful and good to understand that link between your numbers and then what you feel. But I'm glad that there is something that is able to help you. I'm

going to keep going around the panel here a little bit, maybe ask Jenn, if there's anything that you've noticed that has helped.

Jenn (04:32:12):

Well, I kind of feel less like an FSGS patient rather than more a dialysis patient now. I had a transplant five years ago, and my FSGS came back two days after my surgery. The kidney only lasted 14 months. They did the plasmapheresis. Like Kimberly, I have tried every drug there is, I think – except for a cytoxin – is the only drug that I haven't tried.

So now what I do, I do my therapy to just kind of get through this until my next transplant is, I exercise a lot when I'm able to. Dialysis presents its own challenges. I'm kind of severely anemic. So the rollercoaster of anemia has been a struggle when it comes to trying to stay physically and mentally fit for all of this.

Prior to my transplant, I think the thing that probably helped me the most outside of – there weren't really any medications that helped me – but I had a blog. And that was my place where I just ranted about all the injustices of this disease, how frustrated I was, how crazy I felt and that didn't change my situation, but I guess, just having an outlet for it helped.

I did notice that after my transplant, when everything was falling apart, I think I felt like when I was going to get my transplant, I never thought that I would have to deal with recurrence. It didn't even occur to me. It wasn't something we really talked about a lot, and I thought that I had suffered enough, that I was going to get away with it. That obviously didn't help. And I stopped blogging and I haven't really – I've been trying to pick it up again, but it's harder this time around because it's a little bit less hope. But I still am working toward trying to do that still, as to have some kind of an outlet for all the things that we have to deal with.

James Valentine (04:33:57):

I really appreciate you sharing that. We'll put it in the more holistic types of treatment approaches. But I mean, we heard so much this morning about the psychosocial aspect of living with FSGS. And so, having those outlets, it sounds like – or having that outlet for you – was really important and valuable, and so I appreciate you sharing that.

James Valentine (04:34:21):

If we can go to Elizabeth, do you have a something that worked or helped you in some way?

Elizabeth (04:34:30):

Well, for me, well, with all the panels you guys have been, I feel like I'm the oldest in the group. I've had FSGS for over 15 years now, so granted, when I first was diagnosed, for me at least, I felt there was really no treatments out there. I treated it aggressively, taking 120 milligrams of prednisone straight out, because I chose not to give in, to go straight into dialysis. And so, although it did help me go into remission and I've been in remission since then, I did have to pay the price of gaining, over a hundred pounds of weight. I did have to endure the swelling in all of these things that come with the price of having to do that.

Now with that said, in today's world and in current, the things that I do question is, what now, because even though I am in remission, I have other health issues that are coming up. For example, currently, the only medicine that I take right now is the one for the blood pressure and the water retention. And even

though the blood pressure is technically for your kidneys, it is tanking my current blood pressure. And so my blood pressure is constantly too low on that aspect.

So yesterday I was at the doctor's and now they're changing my blood pressure medicine again, because they're trying to figure out how to balance all this madness. But, now I find out that my gallbladder is not functioning, so does it have to do with any of this that's going on?

James Valentine (04:36:34):

Right.

Elizabeth (04:36:35):

So, it's kind of crazy. Did what do 15 years ago, to put me in this space, have any effect to what's going on now? So those are the things that I kind of think about.

James Valentine (04:36:51):

It's kind of this two-sided coin that I think we're going to be talking about this whole session of, "What has Worked." It seems like a lot of things do have trade-offs. And so, really valuable to hear that you were able to kind of go into remission, but also very important to hear, what might be these long term consequences of the drugs that helped you get there. So thank you so much for that, Elizabeth.

James Valentine (04:37:18):

I want to give Erich our last comment on this question of, what maybe has helped and how did you notice that? So take it away.

Erich (04:37:29):

Sure. I'm sorry. Similar to Jenn, but a little different. I lost my kidney 50%, in high school. Didn't know what the cause was. I did have gout, so everything went swimmingly until I was 35. And then all of a sudden for months I spilled protein, but the kidneys were too hard for biopsy, so I went into emergency dialysis. But I was also – my wife had tested – and so I was really looking forward for the couple of months, on dialysis, I mean.

Actually dialysis made me feel better, but I was looking forward to her kidney. So I got her kidney and it stopped working basically after the operation. And we thought it was rejecting it, because this is back in 2000, we thought it was rejecting. We did that first. And then, and then we'd plasmapheresed. Eventually there was no urine. And then we pheresed for about three months. Later, it got infected, we removed it. And we sent a sample. We did get a sample of that kidney to Dr. Saban's lab in Milwaukee. And it was identified as FSGS back then. They didn't even know if it was a protein, we call it a factor.

So one of the things that helps me get through this is, we've learned a lot. My doctor had said, "You've got horrible disease, we know nothing about," which many of you have probably heard. But we have learned a lot more in the last 20 years. So that helps me to look forward. It was until three more years later that I did get that second kidney from a deceased donor, and basically the same thing happened. Pheresed for about three weeks while I was in UW Madison, and eventually that too later on got infected and was removed.

So for me, this is going to sound odd, the way I best treated FSGS is to be on dialysis. Now, three times a week dialysis, is really difficult, it was difficult for me. And many of you who have been on three times a week dialysis know exactly what I'm talking about. Others, I know fear dialysis, they think, "Anything but dialysis. I don't want to live with a machine," but what I've learned over the basically, 20 years I've been

on dialysis – the transplants were in between and I'm still waiting for science to catch up – so that if I get a deceased donor, I can either be treated before and after and then have a better outcome. And I look forward to that.

But what I've learned is how to do home hemodialysis and peritoneal dialysis. The more I take into my own control of taking care of sticking my own needles, which was another story onto its own, but I learned how to do that. But the more I take control of my future, by doing home hemodialysis – I do it for eight hours a night, three nights on, one night off. We were able to adopt our daughter at birth while I was on PD. My son was one, when I lost it. She's 21, she's 16. It's a terrible roller coaster ride that you've all been on. But if you can find some solace and some consistency, it gives you a breath before your next big hill.

So for me, it has been dialysis, but I am eagerly looking for treatment, so I could have a transplant. I'm 55. There's a lot more to give. So anyways, I'll stop at that, but that's what's been helping.

And I guess the one last thing, especially when we deal with low blood counts, like Jenn was talking about, it took me a while, but I've learned that on the days I don't do anything. I don't do anything. At first, it was tons of frustration, because I was letting my family down, I wasn't able to go to work, but then what you realize is, the days you can't do anything about it, you got to let it go. Some people may be disappointed, but if they love you dearly, they'll learn that those days come and there'll be supportive. They might be angry, and bit frustrated because you're not cooking dinner, but you're going to be on to the next day and chances are, you're going to be starting to feel better.

James Valentine (04:41:30):

Sure. Well, thank you for sharing that experience. And I do want to say, when you were mentioning that information is kind of power – intriguing – everybody else was nodding their head on the panel, so that was definitely a shared experience.

Now I want to move us and build on this discussion. I'm still talking about, treatments that you're either currently using or have tried, but we want to understand now, knowing that we're talking about this two-sided coin of not only what has worked, but maybe what hasn't worked so well, or maybe what are the downsides of these things, whether or not they're working. I think as part of this, we'd really like to know: is it something that caused you to stop using a particular treatment, or is it something that you continue to use and you just live with and bear those burdens in daily life? And if so, what that looks like.

James Valentine (04:42:25):

I want to go to maybe our written comments first on this, to see what have we heard about treatment burdens. David?

David Feldman, PhD (04:42:32):

All right, James. I have Randy from San Antonio writes about his young son who has been on high dose steroids. "Physical and emotional pain is real from prednisolone, which is very similar to prednisone. His bones hurt. The swelling causes pain in his skin, where anything that touches him causes extreme sensory pain. When he is on high dose steroids, his body changes so dramatically that his friends and even his teachers do not even recognize him. This causes such severe depression in him."

And Ashley from Medina, Ohio, writes about her daughter who is on tacrolimus. "She has had burning in her fingers and toes as a side effect of the tacrolimus."

Allen from Australia writes, "After five months of steroid treatment and no positive responses, he's also been on cyclosporine which was nephrotoxic, damaged to his kidneys. CellCept, and now he's thinking about going on rituximab. He says, "I am finding this disease, and the associated medication, debilitating. It has been difficult to continue taking medication that makes me feel ill without any evidence of improvement with the disease. The try-and-see-approach to medicating this illness is frustrating. And I have virtually lost hope that immunosuppressive therapy will help me. I'm preparing myself for a retirement life with FSGS."

Randy from Arkansas writes about her son. "He's never been in remission. There was nothing that would work for him. Nothing. This disease stole so much of childhood from him. He was in the hospital for years."

And Vicky from the UK rights, "Prednisolone has made me feel depressed, have suicidal thoughts. Dizzy. My body is constantly vibrating and shaking. Muscle weakness, especially in the legs. Constantly feel like I'm going to fall over. Insomnia. Palpitations after eating, my hip has been affected. Brain zaps. My concentration and cognitive abilities have been affected and my hair is falling out. I feel like Prednisolone has affected my quality of life over my medication and should not be offered as a first line therapy."

James Valentine (04:44:58):

Wow. Some of these things are echoing what we heard from our panelists, but really starting to paint a picture here of a second set of burdens that patients really have to live with beyond the disease itself. So thank you so much.

I want to encourage you to keep writing in with comments. Again, if you want to call in, we encourage you to do so. The phone number is +1 703-844-3231. We do have a couple of callers that want to add to this conversation about challenges with treatment. The first we have is Madeline from North Carolina, who is the mother of a pediatric patient.

So Madeline, are you with us?

Madaline (04:45:44):

Yes, I am.

James Valentine (04:45:45):

Welcome.

Madaline (04:45:48):

Thank you for having me.

James Valentine (04:45:51):

Great. So if you want to share some of those treatment challenges, we would love to hear them.

Madaline (04:45:58):

So, yes. So my daughter was diagnosed about four years ago with FSGS, she's 10 now and has been unresponsive to everything we've tried. We've tried prednisone, tacrolimus, CellCept, rituximab. We tried lisinopril, anafranil, losartan. We've tried mixing it. Mixing the ACE inhibitors and the ARBs with the immune suppressants. We've tried again, like I said, we tried infusions of rituximab. Her most recent

infusion was Obinutuzumab. I hope I pronounced that right. And still nothing has changed, literally no reduction of her protein.

Her hemoglobin is still going down and now she's starting to swell and that's always been something that we never really had to deal with, because we were always dealing with high lipids. We even tried two different types or two different rounds of apheresis. First time was in 2017. And then she did even a longer time of doing apheresis last year, where it was nine months long and that was still unresponsive. And sadly, now she's progressing and we're just trying to maintain her. And even like over counter supplements of vitamin D and iron are just not doing it. It's just trying to put it back into her body since she's losing it.

James Valentine (04:47:26):

Sure. No, I mean really appreciate you sharing that treatment journey that, I'm sorry to hear, has not been successful. In terms of the things now, given the current situation, is there anything that you've found maybe outside of the medications and some of the supplementation that makes living in this stage, a little bit easier? Is there any, even lifestyle modifications, that might be helping to some degree?

Madaline (04:48:12):

She's been in therapy, and now she's on an antianxiety medication that helps her. She has so much anxiety from all of the numerous hospitalizations and medical procedures. And we've had to have her doctor increase the antianxiety meds because, it's just an overwhelming amount of anxiety that she's dealing with. So we've increased it and she's doing the therapy, one-on-one with a therapist. And that's the only thing that seems to just kind of help. Other than that, everything else is really, sadly not working.

James Valentine (04:48:44):

Sure. Well, I appreciate you sharing that very much Madeline and thank you for calling in to tell that important story about your daughter.

Madaline (04:48:55):

Thank you.

James Valentine (04:48:56):

Yeah, thank you. So we have another caller, Lexie from Washington, Pennsylvania, who has some treatment experiences to share as well. Lexie, are you with us?

Lexie (04:49:11):

Hi.

James Valentine (04:49:12):

Hi. Welcome. Love to hear your treatment experiences.

Lexie (04:49:19):

I was diagnosed with kidney disease when I was three and I had a transplant when I was six. My disease came back and I had to do plasmapheresis every week for over two years, and it kept me in partial remission. And did an experimental treatment lipopheresis, I was the first patient to try it, in Surgeon

Hospitals, Pittsburgh. I've been in remission since December of 2016. And I'm 12. All I have to do is take my pills and get blood work every month.

James Valentine (04:49:49):

Oh, well, thank you for sharing that Lexie. It sounds like, where you're at now, you're in a place where you're feeling better. How long has it been since you've been feeling better?

Lexie (04:50:10):

About four or three years.

James Valentine (04:50:12):

Oh, wow. Well, that's so great to hear. I really appreciate you calling in and sharing your diagnosis and treatment journey with us. I'm glad that you're in a better place now. So thank you so much, Lexie.

We'd like to see if any of our panelists by wave of hands has a treatment downside that hasn't come up yet, that they would like to share with us. Some burden or trade off related to treatment, to add to this discussion. Kimberly?

Kimberly (04:50:49):

Yes. When I first was diagnosed, there was prednisone right off the bat. And then when I had my transplant, it returned immediately and it was high levels of prednisone again. And prednisone never did anything. And so now I am 33 with the hip replacement from avascular necrosis, which I never knew that prednisone could do that, wasn't ever brought up, but it happened to me fairly quickly. And it's something that I'm still dealing with from being immune suppressed and having surgery and all of that.

It's a lot being 33 and dealing with that. And then with plasmapheresis, I've done over 400 treatments. I've done dialysis for two years and now I've done plasmapheresis for five years. So I'm basically living off of a machine; like it's helping me live and that's an hour away from me with no traffic in Atlanta. So that's a lot too, just the time constraints of everything.

James Valentine (04:51:47):

Sure. And that's actually really important. And we haven't talked a lot about that. What have those time constraints and needing to travel and take the time out of your day, has that impacted different parts of your life? Whether school or work or other activities that are important to you?

Kimberly (04:52:06):

So when I was diagnosed, I was a pre-K teacher and I ended up getting strapped. So kids were not a good thing for me and my low immune system, so I had to give up teaching. But when I was going with plasmapheresis, I was doing it sometimes three times a week, and I would leave my house at 7:00 and not return till 11:00 or 12:00. So the day's practically gone. It just depended on the week of how many doctor's appointments I've had, how many times I had to go to plasmapheresis. It's put a lot of things you have to really plan around that.

Luckily, my doctor allows me and gives me a lot of leeway with it now, which I'm only on it once every two weeks. So it's a little better, but it's still, once every two weeks, I have to take a whole day out of it, to go do that. And then sometimes my blood pressure drops, which the rest of the day is gone after that. So it's definitely a big time constraint of working everything around doctor's appointments, treatments, and everything.

James Valentine (04:53:01):

Sure. Thank you so much, Kimberly, was there another hand before I go to our next phone caller? Just want to double check. All right. We are two. All right, so we'll do a Jenn, Elizabeth, and then we're going to go to the phone. So we have Melanie from Pennsylvania who wants to talk about some of her treatment challenges.

Jenn (04:53:19):

I think this has been brought up a couple of times, but it is managing the other effects that happen to your body, that your nephrologist tells you are not related to your disease, but you've spoken to several people and you're convinced that it's related to your disease. And then there's also things that occur from other things. Like after my transplant, because of all the plasmapheresis I had been doing, my IgG levels were low, I became susceptible to bronchial infections, and now I have acquired a lung disease that I have to also deal with for the rest of my life. And that's just been a really frustrating thing.

I know a lot of people are going to be shaking their head and they're dealing with similar things. Kimberly with her hip issue, who knew? All of these things are related to this circulating factor in our blood that causes us to possibly lose our kidneys. But it also causes all of these other problems that are strange and seemingly unrelated like, I have neurological problems now too.

These are problems that aren't easily identified by a blood test. It's 500 doctors that you got to see and hoping that one finds some correlation or can tell you that, "Yes, your symptoms are valid. What you're going through is real," and being able to put a label on it for you. The unknown of what is happening in our bodies is so frustrating. And it's really not something that most people can grasp if they've never dealt with it, they just can't even grasp the concept of it. I've heard it's very isolating, I think for a lot of us.

James Valentine (04:54:49):

Sure. So one thing I hear from you is, either the unknowingness or the unpredictability of some of these side effects, even many years down the line. So thank you for sharing that. And Elizabeth?

Elizabeth (04:55:04):

See, for me, and I'll try to make it as short as possible. Kelly knows me and knows who I am. Guys, you want to take this and make it as possible as you can. Like I said, I've had this disease for over 15 years. I'm 57 now. And this is my list, from since I've gotten my kidney disease. I've had thyroid cancer. I have neuropathy. I now I have a frequent urination that I cannot control. I have huge muscle cramps in the evenings, that I'm lucky if I can sleep four hours a night. I now have to take my gallbladder out, in the next three weeks.

And yesterday, because I had to have a CT scan, as you can hear in my throat, how I'm speaking, I had to have a CT scan in my throat, they found a spot in my lungs. So, all these things come in, and they drive you crazy and nuts. But my attitude is, I am not going to let this defeat me or beat me. I am going to be positive about it, learn about it and defeat it, because if I sit down and cry and let it beat me, it's going to beat me. So I always want to be proactive about it.

James Valentine (04:56:41):

I appreciate-

Elizabeth (04:56:42):

But unfortunately, this is what FSGS can kind of do to us. I want to tell you guys stay proactive and be positive because we can beat this stuff.

James Valentine (04:56:55):

Well, thank you so much for that – not only experience, but perspective, Elizabeth. Want to go to now – we have some callers who want to talk to some other treatment experiences. First we have Melanie from Pennsylvania, that wants to talk about some of the challenges she's experienced. Melanie, are you with us?

Melanie (04:57:19):

Yes, I am. Hi.

James Valentine (04:57:21):

Hi, welcome.

Melanie (04:57:23):

Thank you. So I'll just quickly go over what I've experienced. I was diagnosed in 1995. I was seven, almost eight years old. In 1995, there was just very little information, I'm surprised that even my primary care doctor even knew to send me down to the [inaudible 04:57:46] hospital. But back then, there was just very little information, very few options, obviously, no specific treatment.

I heard somebody earlier used the word or used the phrase, "Throwing spaghetti at the wall." I tried prednisone and an immunosuppressant drug, and those were pretty much my only options. The challenge for me specifically was how quickly I went from being diagnosed to renal failure. I believe it was a little less than two years. I was on dialysis by age nine. I don't really remember, I guess I was so young. I don't ever remember feeling awful. I don't really remember being sick, but I also maybe just don't know any different. Maybe that's a challenge that I deal with now, just not knowing anything different, just this is my life and I've dealt with it for so long.

So then I was on dialysis and I had a transplant. My dad gave me a kidney, and again, the same thing happened. I reoccurred immediately. And I went through the same basically, treatment options. And again, I went from reoccurrence to renal failure within two years, and then they removed that kidney. And during that time, since we had been dealing with this for a few years now, my dad was actually in contact with another father and they started the NephCure Foundation in 2001, yeah, it was 2000.

So the goal, I think, since the beginning of NephCure is to fight these challenges that we've all been dealing with. And this being the 20th anniversary of NephCure, I certainly believe that we've come so far, but we're still facing the same exact challenges that we faced when I first was diagnosed.

I think hopefully one day, we won't have to have these challenges. Listening to all these stories, I can relate to everything that everyone is saying. And my heart goes out to everyone and that I hope that one day we don't have to deal with this. I don't know, that's all I have for right now. I just certainly just wanted to call in and give my support for this amazing event today.

James Valentine (05:00:28):

Yeah. Well, really appreciate that, Melanie. And you have a lot of your own personal history and challenges that you described for us. And I think this meeting today really is a landmark event as part of that journey of the organization, NephCure.

Melanie (05:00:45):

I absolutely agree. 2000, 2001, when NephCure was first started, I don't think that my dad and the three other fathers that started it, could ever imagine it being this today, being an international foundation that is helping thousands and thousands of families. And we're certainly on the road to finding a cure, and I think that's obviously dream for everyone that's been on this call today, to find the cure for this awful, awful disease.

And hopefully the people that are listening that are making the decisions as far as funding and research, realize how detrimental this disease is. It just doesn't affect your kidneys, it does just doesn't affect one piece of your life, it affects just everything. And people just thinking about the challenges, the long term effects of all these awful medications that don't even work most of the time. And then, now we're dealing with side effects and serious complication, many years down the road. I just hope that– the reason for this call today is more research, more funding, more information, more awareness. It's just very important and I'm very thankful that everyone was able to share their stories today.

James Valentine (05:02:10):

Yeah. Well, thank you so much, Melanie. That's really appreciated. And to that end route, I want to definitely keep that input coming. Every voice we hear is adding more information that can help those researchers and developers in making sure we get treatments that are meaningful for patients. I'd like to take one more call on this question, and then we're going to go to our final discussion question of the day. I'm going to ask for Ben, from Ontario, Canada, who is recently diagnosed to share some of his challenges with treatment.

Ben (05:02:49):

Hi, good afternoon. This is Ben from Ontario, Canada. First off, I want to thank you very much for holding this forum and getting, giving this opportunity to voice our concerns, and our hopes, our dreams. So thank you very much for this.

I was diagnosed with primary FGS, back in April, so not too, too long ago. Being 45 years old and very athletic, it came as a complete shock to me that this happened, though I really haven't questioned why. Anyhow, I've been on eight milligrams of prednisone, and it's actually taken its toll on my body, from my stomach to just everything. It's just made me completely feel ill. About my height in hospitalization I was over 20 grams of protein spillage in a 24-hour period. It's down to 10 or 11, but when the pathologist believed that I'm steroid resistant, so I've gone on to a new treatment of cyclosporine. So it's been two weeks that I've been on that. And I've been tapering off on my prednisone.

Anyhow, with just this [inaudible 05:04:08] medication and all of that, basically, my mornings would be, I would be sleeping all morning. And then in between that I would be on a toilet with my diuretic. So basically, I would be sleeping for about 12 to 16 hours a day, and then when I am up, I'm on the toilet for about two or three. So very difficult to maintain kind of a normal life.

It has been improving since I've been on cyclosporine, so I've been happy about that. Though being on his now has caused some other problems such as, headache, upset stomach and whatnot, but at least I don't have the nausea and dry heat that I was getting from the prednisone.

One of the ladies before me had mentioned about being upbeat and positive, I want to add a sense of humor to that as well. I think being positive, upbeat, having a sense of humor with all of this, I think it's actually key to helping to do something about this disease [inaudible 05:05:18]

James Valentine (05:05:17):

We'll add humor to the list – in addition to information we heard earlier – being upbeat, but also keeping that sense of humor. So I really want to thank you, Ben, for sharing so much.

We're going to now go to our final question for the day, which is, now that we've talked so much about the current treatments, we want to talk about now, what it is that you would like to see from that next treatment. And as I said, while we all would love that cure for FSGS, we want to kind of put our pragmatic hat on and say, "All right, with what drugs might be coming next down the pipeline, what is it that would be meaningful to you?"

So we have a couple of polling questions that are going to help us start this off. So pull out those phones. This is our last set of polling questions for the day. Open that tab in your browser, go to pollev.com/pfdd. Here, we want to know: if the side effects of a new drug were more severe than your current treatments, but clinical evidence indicated that the drug would significantly slow the progression of your disease and/or improve the quality of your life, how likely would you be to take this drug?

So, we've heard a lot about how burdensome, how impactful in daily life the disease is. We also heard though, all of the tradeoffs that existing treatments provide. So, in this scenario, where maybe the side effects are a little bit more severe than your current treatments, but the product might actually slow progression or improve quality of life, how likely would you be to take that drug? The options are, A, there's a high likelihood; B, moderate likelihood; C, slight likelihood; or D, you would not consider taking it.

I know this is a difficult question to consider, but please select the response that most closely resembles how likely you would be to take this hypothetical drug. All right. Well, it looks like results have mostly finished trickling in.

It looks like over half of you would say that there's a slight likelihood. I'm sure that like many of our conversations before it all depends on the details and what those side effects were, but we're seeing that between 50 and a little over 60 – actually now – percent saying slight likelihood. About a quarter of you saying that there'd be a moderate likelihood and just over 5% saying there'd be a high likelihood that you would take this. About 10% of our audience today saying that they would not consider taking a drug with this benefit risk profile.

If we go to our final polling question, still focusing on a future therapy, but now taking side-effects off the table. So without considering any side effects, which one of the following would be most important to you in a future therapy? The options are, A, reversing or halting the decline in kidney function, that is, halting the progression of the FSGS and delaying the need for dialysis; B, improving your quality of life and the symptoms or preventing future reduction in quality of life or worsening of symptoms; or C, prolonging your life. So please select the option of which one of the following would be most important to you in a future therapy, not considering anything about side effects.

All right. So as it stands, it's looking like we have about two thirds of our participants today that would prioritize reversing or halting the decline in kidney function. That is, halting the progression of the disease and delaying the need for dialysis. A little under a third saying that they would prioritize improving quality of life and symptoms or preventing a future reduction in quality of life or worsening of symptoms, and some smaller amount of you saying that you would want to prolong your life. That would be what would be most important to you of these options.

So, thank you for thinking hard about those. I know those were not easy options to consider and weigh, but now we want to use our remaining time today to ask you what specifically, if a future treatment could provide that for you, give you, how would that be meaningful for you in your daily life? So, trying to be as specific as possible, what is it that you're looking for and why would it be meaningful? For our

Zoom panel, I want to start with Fred and Christina and see what are your thoughts, what are your preferences for a future treatment?

Cristina (05:10:31):

So, I think having a child who has this disease, the things that we would be most concerned about or that would be most on our mind would be the frequency of blood draws, how invasive the check-ins have to be, how the medication is delivered, how frequently the child would need to go to the hospital. Those are all things that weigh heavily on our mind, because I mean, it's hard for an adult but it's really hard for a child to have to go through some of those things. So, those would be, I think, the things we would consider the most.

James Valentine (05:11:04):

Sure. So, a lot of those things being very relevant for treatments for this condition and being the supporting features of the drug, not necessarily the drug itself, but very important to know that that would be important for considering a future treatment. Final say from our Zoom panel would be from Eric. I want to hear any thoughts you have on what you would look for specifically from a future treatment.

Erich (05:11:30):

Sure. The one thing I guess we haven't really heard today is for those of us with recurrent FSGS that have shut down transplants, we are also dealing with desensitivity for a next transplant. There's not very much, many transplant centers are not offering desensitivity. So, I mean, not only do we need to see more progress on how to arrest the FSGS in a brand-new kidney, we also need to have the desensitivity in order to get to that next kidney. The last three items I just want to do quickly, and that is what I've been able to do and I found to help me when I'm feeling better is to get involved with organizations like NephCure and it's not ... Sorry, a little advertisement, and National Kidney Foundation. They give me a sense of confidence that I'm making a difference. They take me out of my reality. So, whether it's a local walk, whether it's writing a congress person, whether it's going to DC or participating in a panel like this, that helps.

The other thing that has really helped me is to deal with challenges is to get outside and breathe. I know, and this is very hard for care partners, especially if young people, this has gone both ways. It helps me as a patient to go out and breathe. I am always worried about my caregiver, who is my high school sweetheart, my wife. I know I need to give her breaks. I don't use her very often because I'm pretty self-sufficient, which I'm very blessed to be, but I know it's important to her. I know if my kids would be sick, it would be hard since our, we didn't really leave our kids much and they weren't that sick on other things, but it is important to take care of yourselves. It really is as difficult as that is.

The best way that I've learned, maybe similar to what Jenn has talked about, is to get outside in the woods, on the water, in the water, not just in your neighborhood. Anyways, I'll leave it with that, but those are ways that have helped me to feel more than I'm helping. And the last one would be getting involved in trials. I've been involved with an NIH trial since 2000 with Dr. Jeffrey Kopp and it's moved on now, but that makes me feel like I'm making the difference. It's a blood trial. It's not the same as having to experiment with drugs, but I would be willing to do that as well.

James Valentine (05:13:56):

Sure.

Erich (05:13:58):

Thank you so much for having this [inaudible 05:13:59].

James Valentine (05:13:58):

Thank you, Erich. We've added a number of things now to this nontraditional list and I love it. We're going to keep it going, participating, being active in the community and trials, getting out, getting some fresh air, all of these things, being helpful.

So really appreciate it and want to thank our Zoom panel for all of their contributions to the discussion today. I want to go and check in with David and see what have our online written comments been saying about what they want from future treatments.

David Feldman, PhD (05:14:28):

Well, we have one comment, James, from Kelly in Colorado Springs. "What we need in future treatments or those that are novel and developed specifically for FSGS designed to stop or lower proteinuria, extending the life of native kidneys, preventing dialysis while at the same time minimizing side effects and allowing patients a decent quality of life."

James Valentine (05:14:54):

Wow. Very on point and helpful comment. I think aligning with what we saw from some of those, that polling ranking of questions too, with that being slowing of the disease being the top-rated option of the three.

David Feldman, PhD (05:15:11):

Right.

James Valentine (05:15:12):

So, we have one final phone caller for the day. We have Kent from Texas. So, I want to ask Kent who I know just from your name and where you're from joined us earlier today. So, I want to have you, Kent, I'm going to give you the final word on this particular question of, assuming there's no complete cure for your condition, what specific things are you looking for, for an ideal treatment for your condition? So Kent, are you with us?

Kent (05:15:46):

I am.

James Valentine (05:15:47):

All right. Welcome, Kent.

Kent (05:15:48):

I would just like to ... Yes. Thank you. I just like to say after 33 years with the transplant and over 40 years with FSGS with the fear of it at some point in time that it could return and being at 70 years old and actually starting to think about end-of-life issues and getting prepared, my whole point is there's always hope. I really believe that hope springs eternal. And all the things that we do in kidney disease,

it's a matter of making sure that you get the right combination of hope and the belief that you can overcome it all. Don't give up hope.

Most of all, I would hope that the FDA looks at all of these medications that are coming down the pipe within the last five years. Nothing occurred for 40 to 50 years. In the last 5 to 10 years, we've had an explosion, and that explosion of medications and treatment options is a blessing. We need to, as a kidney community, go out and assist and hopefully the FDA will fast track everything. There's no need to be slow about this. We've waited for a long time. Here's our opportunity. So, thank you very much. Everybody out there, keep breathing.

James Valentine (05:17:16):

Yeah. Well, thank you so much Kent for that. I think a perfect place to conclude the part of our program where we're getting your input. It's been a long day, but I love ending on a message of hope, because that's really, if you remember where we started today, David mentioning that that's something that has been a common theme across the kidney patient communities, bigger picture communities. I can say confidently that I know that FDA, they were here, they were listening, they wanted this meeting and they wanted to participate in this meeting, so they could really put the experiences of patients in their mind, to set the context for decisions and really understand your preferences.

So I really, as your meeting moderator for the day and my job coming to a close, just want to thank all of you for just being so tremendously brave, really showing us, really, painting that real picture of what it looks like to live with FSGS. You did not hold back.

I think the entire field is going to benefit because of that, because you were willing to pull that curtain back and show us the not-so-great side of what it is to live with, but that's so important because that's what we need to know. We need to know the challenges so we can know how to target those challenges and overcome those challenges. So again, just thank you so much for everything.

We're now going to move into some closing remarks, some closing in summary remarks to wrap this meeting up. It's my pleasure to introduce our closing speakers, Lauren Lee, the Executive Vice President for Stakeholder Engagement and Josh Tarnoff, the CEO of NephCure Kidney International. Welcome, Lauren and Josh.

Lauren Lee (05:19:16):

Thank you, James. Thank you for your excellent moderation skills. Your experience in conducting these meetings speaks for itself. I too want to thank the hundreds of attendees who joined us today. As you can imagine, moving from an in person meeting to a virtual platform was not easy. It required flexibility and ongoing frequent communications to get it right. So, I thank Kelly and David for working closely together and getting it right. Having spent the day with all of you and based on the participation, it is obvious that nothing was lost in this transition, but instead so much gained. This format enabled us to open the walls of what would have been a meeting room with limited space to so many more of you, allowing more patient voices to be heard and amplified.

Whether you're a patient or family member of someone with FSGS, a clinician or researcher striving to improve care or outcomes of people with FSGS, a person representing a patient advocacy group, maybe you are from a pharmaceutical company currently working to develop new therapies for FSGS, or as we know several of you work in a regulatory capacity and make decisions every day about what drugs get approved, I thank you all for being here. Collectively, we have the power to make a difference in the lives of people and families impacted by this overwhelming and sometimes devastating disease.

Today, we learned FSGS rarely takes a break, whether it be the physical side effects such edema, exhaustion or joint pain, or the psychosocial effects such as anxiety, depression, and poor concentration, patients feel their disease every day. Although FSGS is rare, it's also significant that it is chronic and characterized by rollercoaster cycles of relapse and remission. FSGS makes it difficult to plan ahead, leaving families wondering if they will be able to take that vacation, attend a party or feel well enough to sign on to coach their child's football team.

Sometimes FSGS feels like a race against time and creates a ripple effect of other health issues. Patients also have a constant fear of it coming back. So, transplants are not a guarantee. FSGS requires flexibility. Some patients have been forced to change careers, moving to positions requiring less travel and with the option to work remotely, exercise routines modified and travel plans canceled. FSGS is invisible. How do you tell a teacher or your employer that you're sick when you don't look sick? Friends and families don't understand the seriousness of the disease because they can't see it.

FSGS patient families take key factors into consideration before joining trials, like the goal of the study, potential side effects, how might this affect their disease progression if they're forced to stop current medication or put on a placebo. The extras that are involved are all so important to patients. How many of their appointments, time off, and urine catches must I do? Ultimately, they want to check with their doctor to hear that this trial is right for them.

FSGS treatment options are inadequate and come with a host of side effects, both near term, hair loss, weight gain, and long term fertility problems, tremors.

Finally, FSGS patients are waiting for new and better treatment options designed to treat their disease, FSGS, as opposed to cocktails of meds designed to treat other conditions. These insights, perspectives, and realities carry with them the power to change the course of care for FSGS patients. What an amazing opportunity we've been given.

Before I turn this over to my colleague, Josh Tarnoff, I want to urge all of you to stay involved and to stay connected, advocate for yourself, ask questions and take comfort in knowing that you have many passionate and dedicated people cheering you on. With that, I will turn it over to Josh.

Joshua Tarnoff (05:23:32):

Thank you, Lauren. Thank you to our incredible moderators today, David and James, outstanding job. Really incredible day, long day and incredible presentation all the way through again. I think what we've heard today was a theme that was resonating throughout is that FSGS is really unique. As you said this morning, David, there's [inaudible 05:23:56] 37 of these types of forums that have happened so far, but this one is especially important. FSGS is very heterogeneous. We heard that this morning, if you remember back from Dr. Mariani, if you look at what this really is – if you look under a slide – you see fibrosis. In fact, you don't even see the fibrosis in the same spot every month. So, you may find it in this filter mechanism called the glomerulus in various places. You also heard following Dr. Mariani, Dr. Udani who said not only is it that, but it's also all these different pathways.

How do you deal with a disease like that? In fact, many of us in the healthcare community say that FSGS, we often say well it's a sub of nephrotic syndrome. The reality is FSGS itself is probably a syndrome. Meaning it's a collection of related disease, not even probably a disease in itself, which makes the challenge of finding a cure and treatments especially difficult. So your comments today, if you notice, they were varied. It's very much differing among the signs and symptoms of the disease, very much how people respond differently. So at the end of the day, it really tells us that this is a challenge.

The good news – and there's a lot of good news – as Dr. Thompson shared this morning, there are now over 30 clinical trials, that's human testing clinical trials going on. If you think about just three, four years

ago, that number, believe it or not, was three. So, we've come a long way. The beautiful thing about these trials is that they are very varied. They're not of the same pathway. In fact, if you can think about the eight or so prominent pathways, there's probably a trial going on right now addressing each of these different trials or each of these different pathways. So, hope is really a theme that I think should resonate with you because hope is really on the horizon. So, there's great cause for optimism.

So, what happens now? You've given some tremendous feedback over the day and now it's a matter of what do we do with this. So, you should know that the feedback that you've given, going to be written up, and David and Lauren and a whole bunch are just going to look at it then to your professional medical writer. That, in turn, goes to what's called a Voice of the Patient report, which gets turned over to the FDA.

That Voice of the Patient report will then be sent to sponsors and also put in the public domain. So at the end of all this, your voice today, your participation today, which was outstanding and we thank you sincerely, has a direct line of sight to changing and having a real impact on how these trials are conducted, how the FDA views for medications going forward and appreciating all the challenges that are unique again to FSGS.

So with that, I would like to say thank you to everyone, a tremendous thank you to the Cardio and Renal Division of the FDA, or we'd like to say, the Renal and Cardio division of the FDA. They are fabulous. We couldn't ask for a better partner. I mean this with all great sincerity. That we wouldn't be here today, without them, the spirit of the word collaboration is phenomenal. You'll see Dr. Stockbridge and Dr. Thompson and Dr. Kim at almost all the meetings and they really are at the forefront of bringing us into this. So, thank you to them.

I'd like to thank, again, the National Kidney Foundation and our moderators today. Of course, all the staff at NephCure Kidney International, speakers – fantastic, really very relevant – the panelists, but most of all, all of you for participating today. You were candid. It's incredibly heartfelt. We can feel that all the way through. So with that, a sincere and heartfelt thank you to everyone. We look forward to the changes and the evolution and the progress of disease that's happening there. So, all the best to you all. Thank you.

David Feldman, PhD (05:28:11):

Thank you, Josh, and thank you, Lauren. This has been a wonderful meeting. I have chills. James, it's been, as usual, a pleasure to work with you on an EL-PFDD meeting, and especially today. Thank you all for joining us today and staying with us during this long meeting.

We want to thank the patients and the care partners and our panelists for so vividly giving us an understanding of what it's like to live with FSGS. We hope that you know that the FDA and pharma have been listening very carefully to your input today, and we hope that you feel validated in your experience. We hope that you have hope.

In addition to all the people that I thanked at the beginning of the day, we're particularly grateful for the FDA staff who took the time to listen to today's proceedings. We especially thank Dr. Aliza Thompson and Kimberly Smith for their important and informative presentations.

Also, thank you to Shannon Cole and Meghana Chalasani at the FDA for their great support in planning the meeting. I want to personally thank my NKF colleague, Sarah Kim, for her tireless and expert work on this meeting. We thank crew here at Dudley Digital Works for their professionalism and expert and meticulous planning of today's broadcast – you guys were great.

Finally, I want to restate my deep appreciation for the seamless, fantastic collaboration with our NephCure partners.

So, thank you for tuning in today, and please watch for our voice of the patient report, which will be available in about six months. Stay safe, stay well and good afternoon.