# Externally Led Patient-focused Drug Development Meeting On Membranous Nephropathy

# MEETING TRANSCRIPT

**Public Meeting: August 27, 2021**
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James Valentine, JD, MHS (00:12:11):

Good morning, my name is James Valentine. And welcome to the Externally Led Patient-Focused Drug Development Meeting on membranous nephropathy. I'm here with my appropriately socially distanced co-host David Feldman from the National Kidney Foundation. We're coming to you live from the Washington, DC metropolitan area, actually not too far from where the US Food and Drug Administration headquarters are located. To open today's meeting, it is my honor to introduce David, who is a Medical Project Director at the National Kidney Foundation, and he will be providing some welcoming remarks. David.

David Feldman, PhD (00:12:46):

Thank you, James. Hello everyone. Thank you for joining us in this EL-PFDD meeting on membranous nephropathy. I'm happy to say that 134 people registered for this meeting including patients, care partners, FDA staff, pharmaceutical company representatives, nephrologists, researchers, and others. And we're delighted to have representation from 28 states, and from Europe, the Middle East, Asia and Australia. We at the National Kidney Foundation are proud to partner for the second time with NephCure Kidney International in hosting an EL-PFDD meeting. And I just want to say how much of a pleasure it's been to work again with Kelly Helm at NephCure. We wished this meeting could have been in person, but for obvious reasons, we chose a virtual format because this was the safest and quickest way to bring your voices to the FDA now. At today's meeting, the patients and care partners that you are will have the unusual chance to speak directly to the two most important groups that will determine what treatments become available to you: the FDA and pharma companies that are developing medicines for MN.

David Feldman, PhD (00:14:04):

And believe me, they want to hear from you because they know you are the experts in living with membranous nephropathy. And so, during today's meeting, you can advise the FDA and pharma by telling them what they want to know, which is mainly what it's like to live with MN, what you're hoping for in new treatments, and what trade-offs you'd be willing to accept in a new therapy. In other words, your input today can actually help influence drug development for MN, and therefore help make drugs that matter to you become available. Today, we're asking you to open your lives up to us. Please don't be bashful, make your voices heard today.

If you want to see today's agenda, just scroll down on your screen and click on the meeting agenda link.

And now for a few thank yous. First to our patients and one parent care partner who will provide testimonies today. Thank you for your dedication and your courage in preparing your talks. It's really been an honor to work with you.

David Feldman, PhD (00:15:10):

And thank you to our discussion panelists, who will add even more insights into today's conversations. A special thank you goes to our meeting co-chairs, Doctors Laurence Beck and Ashley Jefferson, whose talks will prepare us for today's discussions.

This is the National Kidney Foundation's fifth EL-PFDD meeting. And once again, we're happy to thank the FDA for their involvement. And I especially want to thank Shannon Cole for her support in planning this meeting, and Dr. Aliza Thompson for her contribution today and for her continued and strong support of EL-PFDD meetings on kidney disease. And of course, we're very grateful to our sponsors, Alexion, BioCryst, ChemoCentryx, Mallinckrodt and Novartis for their generous support.

And now, I want to talk specifically to the patients and the care partners. We know from previous EL-PFDD meetings that seeking hope is paramount in your lives.

David Feldman, PhD (00:16:11):

I think today's meeting actually gives reason for that hope. And here's why I think that. First, over the last several years, there have been major advances in the understanding of the causes of MN. And secondly, partly because of this new knowledge, several pharmaceutical companies are now interested in MN. In fact, as I mentioned before, five pharmaceutical companies are supporting this meeting. So, think about that. This means that the scientists and the executives in these companies understand the importance of finding drugs for membranous nephropathy, and believe that it's worth investing efforts and resources into it. And so our wish is that you can take hope from knowing that there are research efforts around the world seeking treatments for MN.

David Feldman, PhD (00:17:03):

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

Aliza Thompson, MD (00:17:40):

Good morning. Good afternoon, I guess. Good evening. Thank you so much, David, for that introduction. And thank you all for joining us today. As David mentioned, I'm the Deputy Director of the Division of Cardiology and Nephrology at the FDA. And I'm very excited to be here today with all of you, as is the team of people from FDA who are joining in this meeting. And very much, we all look forward to learning from you today and to listening to you. I think as David noted, this is an incredibly exciting time for drug development for membranous nephropathy. Because of important advances in the science, because of your efforts, pharmaceutical companies are interested in developing therapy for you. And so this meeting is truly critical. It's critical that we, both FDA as well as our partners in industry, hear from you today and learn from you in terms of what you need and how we should proceed moving forward.

Aliza Thompson, MD (00:18:46):

It goes without saying that patients should be at the center of the drug development process, but some would argue that we've lost track of that along the way. Fortunately, there are a lot of efforts that are ongoing to rectify that to make sure we do a better job moving forward. Next slide, please. Thank you. Some of you may already be familiar with some of our efforts in this space. But for those of you who are not, I'm going to go over them, at least at a high level on this slide and the next. If you think about our efforts, you can really bin them into two larger categories. One category is focused on listening to patients and learning from patients, what matters to them, how they view risk versus benefit of the therapy and the trade-off.

Aliza Thompson, MD (00:19:42):

A separate aspect is what I'll call the scientific aspect. And that's really focuses on the science around ensuring that we rigorously and systematically incorporate the patient voice in drug development. And so, as you'll see, based on some of these descriptions of our initiative, some are focused on that science piece, and I will speak to those, but others are focusing on really what we're doing here today, which is listening to you about what matters to you and learning from you. Another important aspect of this program and of these meetings is also understanding from you about how you want your clinical trials to be done, bearing in mind that the clinical trials are how we establish the safety and efficacy of new therapies for diseases, and understanding how you consider the trade-off between the benefits and risks of those therapies, or what constitutes an acceptable trade-off between benefit and risk. Next slide, please.

Aliza Thompson, MD (00:20:52):

And so you see some of that summarized here, though it will not be the focus of today's meeting. Other parts of this initiative at FDA also focus on how we best as an agency and our labels and other communication can communicate information to you about the drug benefits and risks so that you can make more informed decisions about what is right for you. Next slide, please.

Often when I'm asked to speak at these meetings, I'm asked to share how they have impacted us. And by these meetings, I mean, patient-focused drug development meetings. I suspect that in the years to come, there will be scientists both from within the agency, within FDA and also outside FDA that will conduct rigorous scientific research and evaluate how these meetings have impacted us. But I can really only speak to this issue from a personal level. And in doing so, I really want to speak to it in terms of what I would say are the immediate impacts of these meetings, as well as some longer-term impacts.

Aliza Thompson, MD (00:22:03):

In terms of the immediate impacts, I think it's fair to say that the stories that we'll hear today, your stories are powerful. Although many of you see us as regulators, we are people, we are parents, we are children. We have many people we love. And some of these people and some of us have been patients. Some of us have been caregivers. And I think fundamentally we connect with the stories that we hear. When we see you, we see the ones we love and we very much want to help. I think your stories, the stories that we'll hear today also remind us of the urgency with which we must act to really overcome the obstacles to drug development in this space. And certainly, they inspire us to do better than we have done before. I also think that the stories we hear today speak to why many of us who work at the FDA decided to pursue careers ultimately in medicine and why we decided to come to the FDA. Simply put, it's not enough to be able to tell someone that they have a disease. We need to be able to treat it.

Aliza Thompson, MD (00:23:23):

And so with that, again, I want to thank you for your willingness to come today and share what are going to be very personal stories. So thank you for that.

On the slide, you'll see we have been fortunate, and as David alluded to, to have a number of PFDD meetings. And I would say the stories that I heard, the individual stories that I heard stay very much with me. But even beyond that, and I spoke also to the fact that these have a longer-term impact, these meetings, I wanted to address that. As David may have mentioned or will be mentioned later on in this meeting, one output of this meeting is a report. The report that summarizes what you all share today. And that report will serve as a roadmap, a roadmap for us at the FDA when we provide guidance to

sponsors, and also a roadmap to industry when they design their trials. And that will help us do a better job moving forward and making sure that we develop and find safe and effective treatment for membranous nephropathy. Next slide, please.

Aliza Thompson, MD (00:24:34):

So in closing, I just want to say that successful drug development takes a village and that you all, the people living with the disease, need to be at the center of this process. As I previously noted, these meetings, the meetings we're having today, this meeting is critical. It's critical for us at FDA. But I just want to highlight that this is really just one step in a much larger and longer process, because to truly accelerate drug development for membranous, we need all of you who are participating today to remain actively involved, and essentially to drive this process and to inspire and encourage those who aren't on the call with us today to be involved. Next slide, please.

Aliza Thompson, MD (00:25:21):

All right. But before I close, I do want to make one final comment. Earlier, I noted that we need to be able to do more than tell someone that they have a disease. I said we also needed to be able to treat it, but I left something out. People who are diagnosed with the disease also need to know what will likely happen to them so that they can make decisions about treatments and they can make plans for their future. For example, people living with membranous nephropathy need to know whether or not they're likely to undergo a spontaneous remission. And they also need to know what it means if their proteinuria improves, but doesn't completely go away.

Aliza Thompson, MD (00:26:11):

We also need to understand these same issues when we design clinical trials. We need to know this to design these trials efficiently in effective way. But really the only way we can answer these questions is with data. And so moving forward, I hope you'll all actively participate in discussions about data sharing and the use of your data to answer questions such as these.

With that, I will stop. From the team at FDA, we thank you very much for sharing your experiences and stories. We are eager to hear from you and to learn from you. And we very much look forward to working with you in the years to come. Back to you, David.

David Feldman, PhD (00:26:59):

Thank you, Dr. Thompson. You perfectly put today's meeting into context. Now I'm very happy to introduce our first topic speaker, Dr. Ashley Jefferson. Dr. Jefferson is a nephrologist and clinical researcher at the University of Washington School of Medicine, where he's a Professor of Medicine and Director of the Glomerular Disease Clinic. Dr. Jefferson is an expert in membranous nephropathy and will present an overview of the natural history of membranous nephropathy and its treatment. Welcome, Dr. Jefferson.

Ashley Jefferson, MD (00:27:36):

Well, thank you for the introduction and it's a pleasure to be here. And I'm going to give you some background information on membranous nephropathy and its current treatment. So first of all, what is membranous nephropathy? So, as I think we all know membranous nephropathy is a kidney disease and really primarily affects the kidneys. It's an autoimmune or an immunological kidney disease. And what I mean by that is that the body forms antibodies and these antibodies are directed at cells in the kidney

called the podocytes. And these cells are actually in the filters of the kidney. So, the filters in the kidney are called glomeruli. And of interest, the condition is called membranous nephropathy because of the thickening of the glomerular basement membrane that we see on a kidney biopsy.

Ashley Jefferson, MD (00:28:27):

So, I mentioned the filters of the kidney. This is the glomerulus. And we can see on the left-hand side that the glomerulus is really a ball of blood vessels or a ball of capillaries. And filtration happens across this capillary wall. And on the right-hand side, we can see a filter. And what we want to happen is that fluid or water and small molecules will be filtered across this filter, but the filter when it's intact will stop things like blood cells and protein from going across. Now in conditions like membranous nephropathy, we have damage to these filters and this allows blood cells and protein to cross into the urine. And this is the big clue when we see persons who have glomerular disease, that we see protein in the urine.

Ashley Jefferson, MD (00:29:23):

So how do we make a diagnosis of membranous nephropathy? So typically, we do a kidney biopsy. So many of you may have had this done, where you lie on your front. We put a needle into the kidney and we take three little pieces of the kidney away. And on the right-hand side, you can actually see these pieces. And sometimes with the native eye, you can actually see these little red dots that are the glomeruli. But obviously, we look at these under a microscope. And this is the sort of pattern that we see. We can actually see the thickening of these capillary loops. And using a different technique called immunofluorescence, we can actually see the antibody that gets deposited along these capillary walls. And on the right-hand side under EM, we can see these little dark areas, which are called immune complexes. And this is actually the antibody that's being deposited underneath the podocyte, leading to some of the damage in membranous nephropathy. I'll come back to this with a summary slide in a little bit. So many of you are familiar with the clinical features of membranous nephropathy. So we have a condition we call nephrotic syndrome. And this is a condition where we get a lot of protein in the urine, greater than 3.5 grams in a 24-hour period, associated with swelling of the ankles. So sometimes membranous nephropathy is just picked up on blood tests. We see protein in the urine or low protein levels in the blood. Other times, patients present with symptoms. We often see fatigue or weakness in patients who have membranous nephropathy. I suppose the cardinal feature is the swelling that we see. Now, swelling goes where gravity takes it. So typically, the swelling is found in the ankles. And often it gets worse throughout the day and maybe improves a little bit at night when people are in bed. And over time, this can lead to kidney damage. We're also concerned about some of the complications of membranous nephropathy. Patients are at risk of blood clots, also at risk of infection. And over the long-term, partly due to the high cholesterol levels that we see, patients are at risk of cardiovascular disease.

Ashley Jefferson, MD (00:31:43):

So when we're thinking about treatments, we want to try and understand the mechanism of membranous nephropathy. So I mentioned that this is an autoimmune disease caused by antibodies. So antibodies come from B cells or more accurately plasma cells. And a lot of our therapies are directed at these B cells and plasma cells that make the antibodies. I mentioned the antibodies that attack the podocytes or get deposited in the filters. These black dots again are the immune complexes. And then there's a variety of pathways that injure the filtration barrier. And some of the treatments are directed against these pathways. And once the filtration barrier gets damaged, we get protein leaking into the urine, proteinuria and then eventually kidney damage. So a big question for many years was what are the antibodies or what is the antibody that causes membranous nephropathy? And this was identified

by my co-chair, Dr. Beck in July 2009. And this was really a landmark paper in the field of nephrology. And he and his group identified the M-type phospholipase A2 receptor as the target of the antibodies in the commonest form of membranous nephropathy. And we find these antibodies either in the blood or we can see them in the kidney as well in 70 to 80% of patients with primary membranous nephropathy. And clinically, as I'll describe, we actually use this to try and guide therapy.

Ashley Jefferson, MD (00:33:25):

Now, it's important to recognize that there are many different types of membranous nephropathy. These are broadly categorized as primary membranous nephropathy when they're not associated with other clinical diseases, or secondary membranous nephropathy. And whenever we find a patient who has membranous nephropathy, we're always careful to look out for secondary causes, such as cancer particularly in older patients, lupus particularly in young women, infection such as hepatitis B, and certain medications that have been associated with this disorder. The majority of cases are actually primary and we do not have a secondary cause. And most of the clinical trials that we will be discussing will be with primary membranous nephropathy.

Ashley Jefferson, MD (00:34:14):

As I mentioned, 70 to 80% of these are associated with the anti-PLA2R antibody. But over the last few years, another 5, 6, 7 or 8 antibodies have actually been identified. And tests for most of these are not yet clinically available, but we certainly hope in the future, we will be able to clinically assess this panel of antibodies to get a better idea of the underlying etiology for the individual patient.

Now, I mentioned that we use these anti-PLA2R antibodies clinically. So, one way we use this is when we're thinking about starting immunosuppression therapy. So, we know that the patients who, when we measure their anti-PLA2R titer in the blood, when we see them usually around the time of biopsy,

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

Ashley Jefferson, MD (00:35:03):

those patients who have low level antibodies or declining antibodies actually have quite a good chance of going into a spontaneous remission. In other words, their kidney disease will get better without therapy. By contrast those who have high titers or particularly titers that are increasing, their chance of going into a spontaneous remission is much less. And then secondly, we can actually use these antibodies when we're treating patients to see how well our treatment is going. And there's really two things that I want to show you in this slide.

So one is, if you look at this blue line, this is the proteinuria response to treatment. We can see that when we start, it actually takes quite a long time for the proteinuria level to fall. So, on the axis here you can see that we're getting up to about 24 months before the proteinuria has resolved. So membranous is kind of a slow disease that takes a long time to improve, but notably you can see the antibody and this level falls much more quickly. And so this won't give us a good idea if at an early stage, an earlier stage, if our treatment is improving. So, if we see a fall in the antibody, but not a big change yet in the proteinuria, we're still happy that our therapy is actually doing what we want it to do.

So in summary, we can follow anti-PLA2R levels at early on when we're deciding whether to start therapy or not. If we have low levels or falling levels, we might watch and observe the patient to see if they go into a spontaneous remission. Whereas if we see high levels or climate levels at the beginning,

we're more likely to start immunosuppression at an earlier stage. And then secondly, during treatment, if we see falling levels, this is a marker of effective therapy and actually tends to precede the improvement in proteinuria and other measures that we have.

Ashley Jefferson, MD (00:37:14):

And then finally, just the treatment of membranous nephropathy. So, membranous nephropathy the treatment is broadly divided into these two categories: supportive therapy and immunosuppression. So, supportive therapy is therapy to protect the kidneys and try and reduce the protein in the urine. And this is something that we do for a wide range of glomerular diseases. We're not treating the root cause of membranous nephropathy at this stage but we're treating many of the symptoms. So these are things like diets that are required for membranous nephropathy, particularly a low sodium diet and moderate protein diet. We want to achieve good blood pressure control typically less than 120 over 75 or somewhere in this range. We want to control the edema. We do this with diuretics. The ACE inhibitors or angiotensin receptor blockers that we use for blood pressure also are to help reduce the proteinuria. We may consider vitamin D supplementation. And we also want to prevent some of the complications of nephrotic syndrome, such as cardiovascular protection with statins to lower cholesterol. And some patients are at higher risk of clots. We may consider anticoagulation for those patients.

Ashley Jefferson, MD (00:38:34):

The other arm is actually getting to the underlying cause of the membranous nephropathy. We want to actually decrease and get rid of the antibodies that are causing this disease. And so some patients we will treat with immunosuppression and we tend to target the treatment to those who are at higher risk of either progression of the kidney disease or of complications from the nephrotic syndrome. So those who have severe edema, very low serum albumin levels or high clotting risk, patients who have disease that does not seem to be responding to other therapies and possibly getting worse with persistent proteinuria, patients who were starting to see kidney function decline. And we measure this with the serum creatinine and then also those who have high or climbing titers of the antibody levels as they are less likely to go into a spontaneous remission.

Then my last slide is just summarizing sort of three of the common treatments that we use in membranous nephropathy. So, we use calcineurin inhibitors such as tacrolimus or cyclosporine. We also use rituximab, which is an IV infusion, and cyclophosphamide, which is an alkylating agent. This is usually used in the combination with steroids and depending on the severity of the disease and the clinical course, we'll choose typically one of these treatments or occasionally a combination of them.

There's also a wide range of other treatments that have been investigated in this disease. But it's important to remember that this is a difficult disease for many patients. Often, they do not respond to these standard therapies.

So there's a great need to look for new therapies of membranous nephropathy and hopefully this will be the discussion at this meeting.

So, thank you for your time and we will head back to the studio.

David Feldman, PhD (00:40:35):

Thank you Dr. Jefferson for that very clear, wonderful presentation and for setting the stage so well for our upcoming discussions. And now, we are at the core of the meeting, hearing from you. And to lead us through the rest of the meeting, I'm happy to introduce our moderator, James Valentine. James has worked for the last 13 years as a champion for The Patient Voice. He previously worked at the FDA

where he was a patient liaison, helping to incorporate The Patient Voice into review of medical products. There, he helped to develop and launch the patient focused drug development initiative, which became the Externally Led Patient-focused Drug Development Program that we're a part of today. James moderated all four of the National Kidney Foundation's previous EL PFDD meetings on kidney disease and has moderated 34 of the 48 EL PFDD meetings for other diseases that have been conducted so far. That's about 70%. So, we are in the best of hands today. And it's a pleasure to now turn the meeting over to James.

James Valentine, JD, MHS (00:41:48):

Thank you David and it's such a pleasure to get to be a partner with National Kidney Foundation and work with your partners, NephCure in planning this meeting today. And now it's so great to move us into this core of the meeting and start to hear from patients and caregivers.

So, now that we've heard that clinical overview from a disease expert and we're moving to the core of today's meeting, which is again to hear from you, individuals living with membranous nephropathy, as well as direct care partners and caregivers about the experiences of persons living with MN, we're excited to do that. And I'm going to explain what that looks like. But you've heard, and to set the stage, that PFDD is a more systematic way of gathering patient perspectives on their condition and on available treatments.

James Valentine, JD, MHS (00:42:38):

As you also heard from FDA's Dr. Elisa Thompson, your input can help inform the agency's understanding of MN to inform drug development and review. Today marks, as you saw from David's comments, the 49th externally led patient focused drug development meeting and due to the ongoing COVID- 19 pandemic, today is actually the 16th, fully virtual EL PFDD meeting of its kind. And so I have to say with over 7,000 known rare conditions, this is such a unique and important opportunity for this rare disease community to be heard. Today's meeting is interactive. So let me tell you a little bit more about what we'll be asking of you and how today's meeting will be organized.

First, we'll be, in the morning, exploring the patient and caregiver experience living with membranous nephropathy and the impacts that this condition have on your daily lives. In our second session which will be in the afternoon, we'll bring everyone back together to explore the various approaches to treatment, including experiences in clinical trials.

James Valentine, JD, MHS (00:43:46):

We will also be asking about your preferences for future treatments. So, how in those two discussions, will we be working with you? What will that look?

Well, we will be primarily using three methods for hearing from you. First, we're going to start off with panels of individuals with membranous nephropathy and their care partners. These individuals will be providing some of their journeys and experiences to set a good foundation for the discussion. These individuals have been selected to reflect a range of experiences with living with MN and treatments for MN. However, we know that it's impossible to fully describe the range of experiences, which is why it's then so important.

And the second thing we'll be doing is moving into a facilitated audience discussion. We'll be welcoming and joining all of you who are tuned in today, patients and caregivers, to help build on what the panel has described.

James Valentine, JD, MHS (00:44:44):

I'll be posing discussion questions and inviting you to comment. This can be done with one of two ways: we'll be asking for you to dial in by phone throughout the day, I'll be sharing that number as we go along, as well as by contributing written comments. You'll actually see if you look below the live stream on the webpage today, there's a place for you to provide written comments so you can put those in at any time and we'll be reading those throughout the program today.

You'll also see that we'll have a Zoom panel of patients and caregivers also providing and contributing to the conversation.

The third and final way that we'll be bringing your voices into the meeting today is through use of polling questions. We'll be asking that patients and caregivers only use your phone to respond. You'll be able to open a browser on your phone.

James Valentine, JD, MHS (00:45:34):

If you're on a computer today, you could also open a new tab on your web browser on your computer. And in fact, you can actually go ahead and do this now. No harm in getting into the system because we'll be getting to put some polling questions in just a minute.

Once you're on the page it will be able to stay there throughout the day.

So, at this point, you can go ahead and pull out your phone. Again, open that tab, go to PollEV.com/PFDD. Again, feel free to go there now. That's P-O-L-L-E-V.com/PFDD. And we'll get to polling very soon. These questions will allow us to get a sense of our audience and the different experiences that they bring to the table, as well as bring those to broaden and bring in those topics into our live discussion.

James Valentine, JD, MHS (00:46:28):

I want to mention that we're going to try to hear from as many voices today as possible, but if you leave the meeting and feel that there was something else you wanted to contribute, maybe you were thinking about the issues discussed today and something comes to mind, or maybe you're watching this meeting on demand. We will be collecting written comments on the same webpage for an additional 30 days after the meeting. And all of the input from today, live and written, will be summarized in a Voice of the Patient Report. Dr. Thompson mentioned this, this is the summary report that will be provided to FDA as well as be made available to the public and researchers and drug developers.

So, one last thing before we get to our first set of polling questions, are a few ground rules I'd like to go through. First, I want to encourage individuals living with MN as well as their caregivers and care partners to contribute to the dialogue through those polling questions, calling in by phone, submitting written comments. The discussion today is limited to individuals with MN and their family members and other caregivers.

Our guests from the FDA, drug developers, and clinicians, we welcome you and they are here to listen and learn from all of you who live with MN.

The views expressed today are inherently personal and the discussion may get emotional at times. So it's important to mention this because respect for one another is paramount. And to that end, I ask that you try to be focused and concise in your comments so that we can hear from as many voices as possible.

So, let's get to it. We're going to get warmed up with our demographic polling questions.

James Valentine, JD, MHS (00:48:15):

So if at this point you can again pull out your phone, open that browser and go to PollEV.com/PFDD, where there are a set of demographic polling questions. This is to give us a sense of who we have in the audience today. You'll be able to see that URL link should be displayed right now, but it will remain at the top of the page as we start to actually see the polling questions themselves.

So in our first question for you today, again, these polling questions are for our patients living with MN, as well as their direct caregivers. We'd like to hear from you.

Are you A, a person living with MN or are you B, a caregiver? A spouse, a parent, maybe a child, a sibling of someone living with MN. Go ahead.

And we're going to give you a few moments while this may be the simplest question that we're going to ask you today, give you a few moments to get into the polling system. So that way we can make sure to know who we have represented today.

So we'll give you a few more moments here to get into the system, answer this first question.

We see some of the percentages shifting around, but as it stands it looks like the majority of our – the vast majority of our participants today are individuals living with MN. For the minority of you that are caregivers, we want to hear from you as well. So when we get not only to these polling questions, but when we are asking for callers, when we get to the point where we're asking for written comments, please contribute as well. We know that often you have important insights and observations about what it is to live with MN.

James Valentine, JD, MHS (00:50:15):

All right. So at this point we'll move to our second polling question. So here we want to know where do you or your loved one live. And from this point on, we're going to be asking you to provide – answer questions on behalf of the person that's living with MN. So for our caregivers, from this point on, like for example, here we want to know where your loved one with MN lives. That most likely is the same place as you, but valuable to know moving forward sometimes the questions will be more directed to the person living with MN. The options here are, A the US East Coast, B the US Midwest, C the US West, D the US West Coast, E Canada, F Mexico and the Caribbean Islands or G outside of north America, of course including Europe, South America and any other region outside of North America.

James Valentine, JD, MHS (00:51:19):

So we're actually seeing some good representation from across the United States. Not only are we getting those on the East Coast but we actually have representation across all of our US regions. We don't yet have anyone on from Canada or Mexico but we do have some representation from outside of North America. Today's meeting, we want to encourage anyone, not only within the United States to call in and write in, but no matter where you live or your loved one lives, we want to hear voices from around the world.

James Valentine, JD, MHS (00:51:54):

If we can move to our third polling question. So here we want to know, if you're a person living with MN or a caregiver, what is the age of your loved one who is living with MN? And the options here are A younger than 18, B 18 to 29, C 30 to 39, D 40 to 49, E 50 to 59, F 60 to 69 or G age 70 or greater. And this is the current age of the person that you're representing today living with MN, for most of you that's yourself, for our caregivers that's the person for whom you care for.

James Valentine, JD, MHS (00:52:37):

So we'll give you a few more moments here to get in your responses.

I see that we're getting responses still trickling in here. We're seeing some pretty good representation across age ranges from the youngest age ranges through the oldest age ranges. It's looking like about half of our patients that are represented today are age 50 to 59. We do not currently have anyone representing ages 40 to 49 or 60 to 69. However, although as we see, as the data trickles in, that can change at any second. All right. If we can move to our fourth polling question.

James Valentine, JD, MHS (00:53:35):

So here we want to know what does the person who has MN identify as, whether that's you or your loved one. Are they A male, B female, C non-binary or non-gender conforming, or D if you prefer not to say. I promise you as we advance through the program, these questions will get both more interesting as well as more difficult. Here, we're just really trying to understand who we have represented in the audience before we embark on some of the more – the deeper conversations about what it is to live with MN.

James Valentine, JD, MHS (00:54:22):

So as it stands, it looks like we see a greater proportion of our audience of those living with MN are female, about two to one to those who are male. And no one has reported not that they or their loved one is non-binary or non-gender conforming or prefers not to say. All right, if we can move to our fifth polling question. Here we want to know is, is your or is your loved one's race or ethnicity any of the following: A Caucasian, B African-American, C Native American, D Latinx, E Asian, or F some other race or ethnicity not listed here on this slide. Give you a few more moments here to get in your responses to this question on what is your or your loved one's race or ethnicity.

James Valentine, JD, MHS (00:55:47):

As it stands, the vast majority of our participants living with MN are Caucasian. However, we do have representation from those who are Latinx or Asian.

If we can move to our sixth polling question. Here we want to know what is the length of time since you or your loved one's diagnosis of membranous nephropathy? So, was the diagnosis A less than one year ago, B one to two years ago, C three to five years ago, D six to 10 years ago, E more than 10 years ago, or F if you're not quite sure how long ago it was that you or your loved one was diagnosed with membranous.

James Valentine, JD, MHS (00:56:47):

And regardless of the length of time that you've been living with a diagnosis of MN we know sometimes symptoms come before diagnosis, but we would love to hear during the audience discussion when we get to that point how your experience with living with MN might have changed over time. Many of you here – about half have lived with MN for three to five years, about a quarter more than 10 years, pretty staggering, a little over 10% six to 10 years. And also some of you with a more recent diagnosis of one to two years, whether it's been one or two years or more than 10 years, we would really like to hear how your kidney disease, how your symptoms and other health effects have changed over time over these years that you've been living with MN. So, thank you for answering this question.

And we've one final demographic polling question for you.

James Valentine, JD, MHS (00:57:50):

So here we want to get a little bit of a sense of where you are in your MN journey. So here we want to know, 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 that's in remission, D a kidney transplant recipient that has recurrent MN or E a kidney transplant recipient and is currently on dialysis for example from a failed transplant. So please select that response which most closely reflects your experience and your kidney disease.

James Valentine, JD, MHS (00:58:45):

All right. So it's looking like at least at this point in our day our audience participants are in the camp of not currently being on dialysis and have never received a kidney transplant. That certainly does not mean that you have not experienced a lot in terms of your disease or in terms of the treatment approaches to your disease which we'll be exploring.

So we want to very much hear from all of you throughout today's program.

So with that, I want to thank you for participating in these polling questions. You can keep that browser or that tab open. We'll be coming back to these polling questions throughout the day.

Now we move into our first topic that I had previewed for you. We really want to hear from you about what it is to live with MN. What are the symptoms and health effects that you experience, the impacts on your daily life.

James Valentine, JD, MHS (00:59:36):

If we could display our discussion questions, these will be the topics we'll be exploring through this first panel. We want to know, not only just what are all of the different symptoms that you experience, but which are the top ones that have the most significant impact on your life. We want to know not only what those symptoms are, but how they impact your life. So, of specific activities that are important to you, which ones you cannot do either at all or as fully because of your MN. As I mentioned, we want to hear about your condition and its symptoms and how that's changed over time. Both in terms of the symptoms and impacts on your life. Those changes, whether there – this might be a change from day to day, week to week, month to month, or of course, over the course of years.

James Valentine, JD, MHS (01:00:25):

And finally knowing that you will be continuing to live with MN, we want to know what your worries are about living with MN for you or your loved one, thinking towards the future.

So to get us started on this topic, it's my pleasure to welcome our first panel of today. These are your peers in the MN community, Marge, Taylor, Alma, Dean and Safa, who will be sharing their experiences of living with MN. So Marge, why don't you take it away?

Marge (01:01:01):

Hi, my name is Marge. My membranous nephropathy story begins in Little Rock, Arkansas three years ago. I was preparing for the annual Arkansas Women Can Run 5K race and I was eager to start training as I was gaining weight like crazy. And my feet and knees were so small and I could hardly walk. I thought it was because I had been sick with the flu the past six months and not been exercising during.

The first training session, I knew that something was extremely wrong. While walking a short distance I became exhausted and was gasping for breath. I saw a PCP and then a nephrologist who ordered a

kidney biopsy. Then diagnosis was MN with a GFR of 21, stage four CKD. I was in shock. I left her office very unsure of my future and very scared.

I was prescribed three rituximab infusions. After two infusions, I was a little better but was no longer able to function as a program manager for five surgeons and had to retire from my job and move to Houston to be near my son and daughter-in-law. It wasn't that I needed their help as much as I felt my life was slipping away and I wanted to have family close by in case of emergency or to help me with the day-to-day chores such as grocery shopping, vacuuming doctor appointments and even preparing meals.

My lack of concentration continued along with severe fatigue and dizziness. Once after walking the dog, I lay down on a neighbor's lawn. I was so dizzy, exhausted and couldn't make it home. It was only a matter - it was not only a matter of resting or catching my breath until I felt better, I had to lay down.

Driving my car would require a pullover and a nap.

Marge (01:02:58):

The heat in Houston affected me greatly. If I became overheated, I would pass out wherever I was followed by throwing up and defecating. This happened numerous times when I was walking, grocery shopping or riding my bike. An ambulance was called for me twice in Kroger's grocery because I fainted and fell to the floor. Those were certainly the most embarrassing times of my life.

I was disappointed that I was no longer able to walk or hike, but the biggest disappointment in having MN was having to give up my passion for pet therapy work with children in Arkansas Children's Hospital. There's nothing that compares to watching a young cancer patient smile with joy when the dog enters a room for long cuddles and silly tricks that make the child and the family laugh during dire circumstances. I was now wearing a mask long before COVID and I was immunocompromised.

Marge (01:04:03):

I could no longer work with kids or with developing other pet partner teams or testing new teams for licensing. The third rituximab infusion was scheduled for January, 2019. The ritux was working, although slowly. I was feeling stronger. I wasn't as dizzy. I learned to recognize when I was about to pass out so I could go grocery shopping now using the store's motorized handicap cart.

I was hopeful that my third infusion would help me get back to being me, but I was unable to get the third ritux infusion. I was now retired and on Medicare and that they would – and Medicare would not cover ritux because it's off label for MN.

I have a medical scooter so I can walk my dog on the days when I'm not feeling well, I'm still plagued by spasms and muscle cramps when I'm dehydrated. I'm now able to recognize when I need to sit down.

Marge (01:05:05):

On my best days, I have more energy, I can dance, chase the grants and swim. But I have to crash and sleep the day after. I'm now walking the dog a half mile twice a day. I live in a senior community now and I'm enjoying the socialization with my new neighbors.

My worst days, I sleep all day and have no energy or stamina. My time with family is limited to just a few hours at a time. The grands know when grammy must lie down, they see it on my face and bring me ice water and sit beside me and read and tell me stories until I recover.

My meals are pre-packaged and microwaveable to preserve my energy as I can't stand long enough to cook or clean up afterwards.

My biggest fear in life is that the MN will come back and destroy the rest of my kidney function. How will I treat it if rituximab is not an option? Will I need dialysis? Will I need a kidney transplant? Will I be a burden instead of a helper to my family?

I saw my new nephrologist this morning and the lab work was well below my expectations. I'm now waiting for that dreaded message from my nephrologist that I have been so fearful might becoming telling me my kidney function has declined and that the MN is returning. I am terrified.

Taylor (01:06:36):

Hello. My name is Taylor. I'm a 23-year-old registered nurse from Parkersburg, West Virginia. I live with my husband and one-year-old Labradoodle. In September of 2017, I had just started nursing school. I was more than exhausted. For the first few weeks of the semester I had pretty much doubled my schoolwork load and was also working a part-time job. So I thought nothing of my newly onset fatigue.

On my first day of clinicals, I noticed swelling in my lower extremities. I took a photo and send it to my mom who is also a registered nurse and we both chalked the swelling up to having been on my feet for 12 hours on concrete flooring and not being used to that. I ordered some compression socks and went about my normal life. The next several days, I noticed swelling in my feet when I did almost anything other than lie on the couch or in my bed.

Taylor (01:07:27):

I made an appointment with my primary care doctor who ran some labs and referred me to a local nephrologist who then ordered a kidney biopsy and confirmed my diagnosis of membranous nephropathy. I was 19 years old and scared about how this disease was going to affect me. I had just started a rigorous nursing program that required my full dedication and attention. My doctors were hopeful that since I was young, my disease would be easier to control. They were wrong.

We started treatment. I went through every treatment for the disease, none of which worked. Finally, we resorted to cyclophosphamide and other medications, such as diuretics and blood pressure medication to manage my symptoms.

My symptoms through nursing school were severe. I felt worthless. I was constantly exhausted, having difficulty concentrating and the swelling was so severe my skin was cracking and seeping fluid.

Taylor (01:08:21):

My face would swell and I worried if my patients would question my ability to care for them. I was – it was obvious that I was sick myself. How could I possibly care for someone else?

These symptoms made my daily life next to impossible. And every morning I looked forward to going to bed, even though I would wake up in wet sheets due to the weeping of my skin. I was in a tremendous amount of pain daily, mostly from feeling like my skin was going to burst open from swelling and the pressure that the swelling was putting on my joints.

I was so fatigued and not getting good sleep due to my inability to feel comfortable. I had difficulty sitting still for long periods of time and concentrating, which was necessary since I was in college and sitting for two-to-three-hour lectures. The majority of the time, I felt like I was in a fog and was going about my daily routine only because I had no other choice.

Taylor (01:09:17):

At one point, I was taking up to 20 different medications per day. I felt tied down to my medication regimen.

As an average college student, my life was severely affected by this disease. I was too exhausted to go out with friends in the evenings, too swollen to fit into any of my clothes and felt it was impossible to eat out while also trying to stick to my low sodium diet.

There were many activities I could not do that I used to enjoy. I had previously taken these things for granted. I enjoyed walking in the fall when it wasn't too hot, but with membranous, I cannot walk more than a few blocks without feeling completely wiped out or I couldn't walk at all because I was too swollen that day and it hurts so badly to take a step.

One of my favorite places on earth is Disney World. In July of 2018, my family and I took a trip to Disney World. By the end of the trip, I was miserable. Between the 16-hour drive, the Florida heat mid-July, and my disease, I couldn't walk by the third day and was being pushed around the parks in a wheelchair. Many people were confused when they saw me in a wheelchair, because those who had not seen me prior to the onset of my disease would often think I looked normal.

Prior to my diagnosis, I had easily put on 30 pounds of weight. I thought this was the freshman 15 as many called it, only much more severe. I even had people reaching out to me about weight loss plans and fitness classes when they noticed my weight gain. Also very humiliating.

Taylor (01:10:49):

Currently my disease is in remission. I have been free of symptoms since October, 2019, but just because I remain in remission does not mean I can live my life as anyone without the disease. I still take medications, weigh myself daily and have periods of exhaustion. I think about how the disease has affected me and how it will affect me in the future. I live fearful about if or when my disease will relapse. I worry about my ability to have children in the future, and if my children will have the disease too.

Taylor (01:11:21):

I think about my loved ones who will have to care for me if I need dialysis or a transplant if I progress to the end stages of my disease and the financial burden that it could cause. Since this disease has no treatment or cure, these are the things I think about daily.

Thank you for letting me share my story and for listening.

Alma (01:11:45):

Hi, my name is Alma Sandoval and I am the mother of four children. And my oldest daughter, Lauren was diagnosed with membranous nephropathy in August of 2018. Lauren was 12 years old at the time. She was a healthy thriving child who only suffered from seasonal allergies and ear infections. Lauren went to sleepover camp in June of 2018. During her fourth week at camp, the camp nurse called asking for permission to take her to urgent care. She mentioned that Lauren's eyes were swollen shut when she woke up that morning and mentioned how in the previous week, Lauren had begun to swell. Lauren was hospitalized and her dad and I were in shock. We spent four days at the St. Louis children's hospital getting her stabilized so she could return home to Texas. There were still so many unknowns and the possibility of a kidney biopsy was mentioned.

Alma (01:12:39):

My head was spinning. Looking back, I believe Lauren's symptoms started about seven or eight months prior to her hospitalization. I had noticed that she was gaining weight and her legs were getting larger. It

was very gradual, but still noticeable. At times you could see deep clothing marks her legs. I also noticed that she was tired more often, but I thought it was the weight gain. I also remember she had mild swelling around her eyes, but we attributed that to her allergies. When we left the hospital, Lauren was placed on a strict liquid intake and dietary restrictions. She would cry some days saying that she was thirsty, but had already had her limit of liquid for the day. We also had to do a daily log of her urine protein. She would get irritated when I reminded her about checking her morning urine. She had to learn to take pills, something she had never done before.

Alma (01:13:42):

She had frequent urine and blood tests and on multiple occasions, she would cry from the pain and frustration of being poked multiple times to get blood from her swollen arms. Lauren complained about having to book doctor appointments during school because she didn't want the attention or people asking her where she was going. After Lauren's kidney biopsy, she could not do physical education class for three weeks. She was frustrated because her friends and classmates asked her why she was not participating. Lauren did not want her friends to know anything about her diagnosis.

Lauren is a very friendly and social person, but her medical condition was not something she wanted to share, because she didn't want to be treated differently. Lauren also resisted scheduling 24-hour urine tests because they were awkward and disruptive to her schedule. When she had strict dietary restrictions and was invited to a friend's house for pizza and movie night, it made her feel uncomfortable that she couldn't eat.

Alma (01:14:52):

As a parent, the diagnosis brought on feelings of guilt. What did I miss? What could I have done differently? I immediately began searching online for information and support, feeling helpless, with absolutely no knowledge of this disease. It was frightening. Finally, NephCure connected me with parents whose kids had membranous nephropathy. Having the support and a chance to ask questions from parents' experience with MN was informative and encouraging.

Currently Lauren's condition is stable. While on her medication, her urine protein and kidney functions have been normal. We have discussed with her nephrologist about stopping the medication and we're working through that process to see if she can come off the medication with no significant impact to her kidney function.

Alma (01:15:46):

Every day I wake up hoping today won't be the day that Lauren's condition takes a turn for the worse. I constantly look at her eyes, touch her legs and wrists for signs of swelling. I look for clothing marks that may mean she has swelling. I asked her to check her urine for foamy pee. She told me this morning, "mom, my urine was foamy." I secretly start to freak out but tell her we need to check your protein in the morning.

Mornings like this make my mind start to wonder, how much damage is this disease causing her kidneys? What are some of the long-term side effects of this medication and how will a change in her condition impact her future?

As my sweet daughter will say, mom, we have to focus on today and hope everything will be okay. Thank you for listening.

Dean (01:16:45):

Hello. My name is Dean and I live in Boland Springs, South Carolina with my wife and children. I was diagnosed with MN at the Naval hospital in San Diego, California, when I was 16 years old. I most likely exhibited symptoms of MN as early as 14 years of age but didn't realize it. Some of those early symptoms were extreme pain in my back around my kidneys. This caused me to miss school many times. Other earliest symptoms were moderate swelling that extended from my lower calves to my ankles, and urinary tract infection that required a hospital stay. I also experienced times when I was bedridden due to back pain and I could not participate in physical sports and missed time with family and friends. Eventually I was admitted to the hospital due to extreme swelling in my face and pitting in my legs. The span of 24 hours, I had gained 24 pounds of water weight.

Dean (01:17:41):

I was put on a low sodium diet, spent a week in the hospital for further testing. That included a kidney biopsy that diagnosed my MN. Looking back at my medical charts recently, I was shocked as to how sick I actually was during those early years.

My symptoms were consistent with my disease and included swelling, migraines, and periods of back pain.

After high school graduation, I was in a period of denial as far as my condition goes and neglected care for a few years. At age 19, my blood pressure got out of control and the swelling in my legs returned. I will get flushed at times and my pulse will be very fast. My protein spillage had gone back up and I had gained some weight. While all these symptoms were not as severe as when I was first diagnosed, I decided to start seeing a nephrologist again because I was concerned about my kidneys and how they would impact my overall health.

Dean (01:18:39):

I had recently attempted to enlist in the U.S. Army. Even though I had a letter from my nephrologist, endorsing the enlistment, the army turned me down, due to my kidney disease and high protein in my urine.

In my twenties and thirties, I had hypertension related migraine headaches. The headaches will be so severe that it made it impossible to work or spend time with family. One of those times was my and my wife's wedding practice. I had to leave early due to a migraine headache, but I showed up for the wedding the next day, and now we've been married 29 years.

The only relief I could really get from a migraine was being in a dark room, had to be quiet, and plenty of Tylenol. My doctor eventually prescribed a blood pressure medicine that brought my blood pressure under control. And then because of that, my migraines got under control.

Dean (01:19:36):

And my blood pressure was all related to my disease. Since my first diagnosis until 2019, I had gone into remission several times. Now my doctors attribute that to my strict adherence to his protocol recommendations, following his directions, basically. Some of the remissions were spontaneous and some were induced by treatments that I had received. During remission my symptoms would go away and my life was pretty normal with no symptoms that MN, I would think for a brief moment, I'd beaten the disease, but MN would creep back in.

In my thirties, I developed a new symptom: gout. And it would show up in my big toes and my knees, most of the time. The pain was so severe it just felt like needles poking you. You didn't even want a

sheet touching them, it's so painful. Eventually I was able to take some medicine that brought that under control.

Dean (01:20:39):

I had discussed dialysis and a kidney transplant with my doctor over the years, but that always just seemed so far away. I tried not to dwell on what the future would hold and just take it one day at a time. But in February of 2020, right before the pandemic, my doctor and I, and my wife, and my family decided upon his recommendation to start dialysis. He said that the scarring had gotten so severe that it impacted my kidneys to the point to where they just couldn't filter properly anymore. I started peritoneal dialysis at home, and I'm still doing that therapy today.

Dean (01:21:21):

I still have symptoms of MN that will never go away. The swelling still persists today in my lower legs. Dialysis is a burden; it does not fully replace the function of your kidneys. I have to take phosphorus blocking medicines, and I have to have different types of shots to help regulate my iron. I have monthly lab visits and doctor's visits that I didn't have before. And I just think there should be a better alternative that would be effective treatment of this disease and help the symptoms, possibly leading to a cure. Thank you for your time.

Safa (01:22:04):

Hi, my name is Safa. I'm 18 and live in California with my parents and four siblings. I graduated high school this summer and I'm starting community college in the fall. I was diagnosed with nephrotic syndrome in February of sixth grade, then membranous nephropathy around May. At first, we didn't know something was wrong. I'd been noticing for a couple of weeks that my legs were hurting, but it didn't seem concerning. Growing up, I always had growth pains and that's what we shrugged this off as. This went on for weeks until my dad noticed that my nose looked extra big. When he saw that my legs were also swollen, I went in to see my doctor. My pediatrician referred me to a nephrologist. It took over a month to be seen.

That month felt extremely long. We were beyond stressed with my parents continuously researching nephrotic syndrome. Between the referral and starting treatment I noticed more things that were different. The edema caused my face and ankles to become puffy too.

The first couple of years with MN I wasn't myself. My dad says I was the loudest, most outspoken and happy kid in the family. But after my diagnosis, I withdrew from everyone. I became depressed spending most of my time alone or crying and being comforted by my dad at least once a week because of depression, I wasn't able to get out of bed and missed school. I would sit with my dad as he just hugged me, because nothing else made me feel better. I didn't know what was going to happen. How long I'd have MN or what it would mean in the future. I was just so scared of having to live with MN for the rest of my life. On most days that I did go to school, I didn't participate in PE because the edema in my legs and pain in my ankles made it too difficult.

Safa (01:23:43):

My close friends knew about my diagnosis and while they were supportive, others would make hurtful comments implying I was lying about my pain to get out of class. Because of my pain, my family had to cut down on our outings. We couldn't go out on hikes, visit downtown San Francisco, or tour lighthouses.

Whenever I felt down, I wrote letters. Sitting in our home office, I filled pages with my fears, explaining why I felt the way I did. I wrote about how I was scared my kidneys would fail, that I would never be myself again, and that I would always be sad and angry. I would leave the letters for my dad to read so he could begin to understand what I was going through. I needed someone to understand because all these fears were eating away at me. I was angry at everyone for saying I'd get better because there just was no guarantee. I even began seeing a therapist to talk about my fears and the negative ways MN was affecting my life.

Even years later, every time I felt depressed, I would pull out those letters and reread them. But a couple years ago, I destroyed every single one because they brought back such bad memories. Taking me back to a time in my life when I felt hopeless and alone.

Because of MN, I couldn't do things I found joy in. Before my diagnosis, I always slept over at my cousin's house. We'd stay up all night watching Lord of the rings and eating Doritos, then make pancakes for everyone in the morning. After my diagnosis, these sleepovers became scarce because as an 11-year-old, I wasn't able to dip my urine alone. My parents didn't trust me to take my meds on time and I'd eat too much sodium – easily triple my allowed amount.

Safa (01:25:14):

And so I was usually always home where my parents could keep an eye on me. This chipped at the close relationship I had with my cousin, and we began to grow apart. My diagnosis impacted my entire family. Everyone kept an eye on the sodium entering our house and the food I ate. We stopped dining out because we couldn't calculate the sodium in dishes. I couldn't even eat store-bought naans, since each had nearly 500 milligrams of sodium. My mom had made everything she cooked from scratch, including naans, ketchup, and yogurt.

At the mall one day there was a seasoned fries stall, meaning they'd be delicious, but full of sodium. My family bought tubs, but I wasn't allowed to taste even one and felt angry at being left out.

This consciousness of sodium is so instilled in us that even now when grabbing anything, even though my protein levels are much lower and I no longer need to watch my sodium, the first thing we do is check the sodium.

Safa (01:26:07):

One of the biggest changes from MN relates to Ramadan. Since seven years old, I've looked forward to fasting each year. I was devastated when I was told it was out of the question with all my meds. Now, the years that I can fast, I worry about my labs and if my meds will need to be increased after.

MN doesn’t just dictate whether or not I can fast. It robs me of the joy of Ramadan. Even if I can fast, I can’t pray Taraweeh at night because I can’t stand on my feet for long. For an entire month, I feel separated from my family because instead of focusing on what Ramadan symbolizes, I’m preoccupied with concerns.

Today, I have the same fears as six years ago. I'm scared of being on meds forever, of never being in full remission, and that my kidneys will fail to the point of needing dialysis every so often these thoughts plague my mind and I am fearful of what my life could become.

END OF TOPIC 1 TESTIMONIES

James Valentine, JD, MHS (01:27:09):

Wow. I want to thank you Safa and to all of our panelists for being brave and really kicking off this discussion of sharing your personal experiences of living with MN and what this has really looked like and meant for you and your lives. I know it's not always easy to share this aspect of living with the condition, but so important for us to have heard it. So, thank you.

Now is our first opportunity today, to broaden the discussion and hear from all of you who are in our live audience, our individuals living with MN, their direct caregivers and care partners. If you'd like to contribute to this conversation about the symptoms and health effects of MN and the impacts they've been having in your lives, this is a good opportunity for you to call in. The number you can dial is 1-703-844-3231.

James Valentine, JD, MHS (01:28:03):

Again, that is 1-703-844-3231. If you call, you can let us know the topic you want to talk about and we'll get you in our queue so we can hear from you and welcome you into the conversation.

But to get us started in thinking about this topic as a group, we're going to go back to a few polling questions to get us started off. So please pull out that phone, go to that browser go to, if you're following along on your computer, if you had a tab opened up, go back to PollEV.com/PFDD.

This is for all of our patients and caregivers in the audience. It's okay if you were not able to participate in the earlier questions, we'd still love to have you participate in this set. So at this point, our first polling question for you is we'd like to know if you've experienced any of the following MN-related difficulties.

James Valentine, JD, MHS (01:28:58):

And here we want you to select all that apply. So the options are A, muscle and joint aches and pains including gout. B, bone and teeth problems. C, issues with eyes. D, high blood pressure. E, high blood sugar or diabetes. F, anxiety and or depression. G, brain fog. You might think of this as forgetfulness, poor concentration, losing track of time. H, being tired or exhausted. I, gastrointestinal problems. J, recurrent infections. K, swelling including in the ankles or in the face. L, some other symptom or health effect related to your MN that's not displayed on this slide. Or M, if you do not have any symptoms related to your MN. And again, select all that apply.

One thing that I will say is for this question, any polling question where our respondents are able to select more than one option as is the case here, you're seeing a percentage of responses. So this is not the percentage of people who have selected each response, but the percentage of total responses that have come in. So the best way to think about this is look at those bars, that's kind of a ranking. So that's just a way to look at the data as it comes in.

So we'll give you a few more moments here to let us know what are all of the different MN-related difficulties you or your loved one has experienced.

As it stands, it looks like the most common experiences of our audience today are swelling, followed closely by being tired or exhausted, and having anxiety and or depression. We're also seeing large proportions of responses, reflecting brain fog, and high blood pressure, as well as muscle and joint aches and pains, including gout. Although what we're really seeing is across the board, there's a wide range of different difficulties related to MN that this audience, our audience today has experienced, including some other symptoms that aren't reflected on this slide.

James Valentine, JD, MHS (01:31:18):

So, as you're thinking about each of these different difficulties, we'd like to hear from you and how have these things impacted your lives. I should note that no one has reported that they have no symptoms related to their MN.

We go to our second polling question. So you'll see, notice that the response options here are the same, so I promised that these would get more difficult as the day went on.

Now, we want you to prioritize and think about which of the up to three of the following symptoms are, or other aspects of your MN have most negatively impacted your life. So you can only select up to three responses and the response options are the same. A, muscle and joint aches and pains. B, bone and teeth problems. C, Issues with eyes. D, high blood pressure. E, high blood sugar diabetes. F, anxiety and or depression. G, brain fog. H, being tired or exhausted. I, GI problems. J, recurrent infections. K, skin problems. L, swelling. M, some other symptom or health effect that's not listed here. Or N, again, if you don't have any symptoms.

David Feldman, PhD (01:32:35):

So this polling question and the previous one emphasize the importance of tending to the psychosocial and the cognitive effects of kidney disease. And here membranous nephropathy is very interesting. I think that this is very common across kidney disease and I think also across many chronic inflammatory states.

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

Absolutely. And it would be so important to hear the specifics around these. So for those psychosocial issues people may be experiencing, when did you experience that? Was there something, or some series of events that, that you think led to those feelings? What underlying symptoms were you having at that time?

So important for us to hear, although I'll just report as it stands, it looks like our top of the top three symptoms that are reported as being most impacting daily life. We're seeing the tiredness and exhaustion being perhaps number one, followed by, as we were just talking about, anxiety and or depression, as well as the swelling.

So we want to hear about how these things have impacted your life. What I think also stands out to me is that there's a wide range of things.

James Valentine, JD, MHS (01:33:56):

We saw in the previous polling question, there's a lot of different symptoms that are experienced, but it's not like that meant that only a few were people's top three most bothersome symptoms. We're actually seeing a lot of these being in people's top three, most bothersome impacts. So we want to hear from you and that diversity of what you picked and why it was picked in your top three.

So one final polling question before we go into our audience discussion is how much does your MN impact daily life in general? And so here thinking about all of those things that we just showed on the previous slides, the other things that you identified, we want your general assessment. Does this impact you A, not at all. B, minimally. C, moderately. Or D, a significant amount in your daily life, again in general. And what will be important is to hear why you rated this the way that you did.

So what we're seeing right now is that about three quarters of our audience is reporting that MN has had a moderate impact on daily life, generally speaking. 20% have said it's been minimal. About a little over 10% have said it's been impacted a significant amount, and nobody is reporting that it is not

impacting their life at all. So again, we're going to want to hear about that and to start us off on hearing about that, I would like to welcome our zoom panel.

START ZOOM PANEL 1

James Valentine, JD, MHS (01:35:41):

So these are some of your peers in the MN community who are going to be joining us throughout the session this morning, sharing some of their inputs, in addition to all of you who are calling in.

Before we go to the zoom panel here, remind you that you can call in at 1-703-844-3231.

So, as you were thinking through those polling questions, what were you thinking? Give us a call, but maybe to get us started on this topic, we can go to Alma.

Alma, when you were looking at those polling questions, what aspects of living with MN stood out to you as being most bothersome?

Alma (01:36:25):

Good morning, everyone, or afternoon, wherever you are in the world. My name is Alma and I am in Texas. And my teenage daughter is the one who is the membranous nephropathy patient. As far as symptoms for us, I would say minimal today, because the things that we have to do is, as a teenager, I have to remind her, take your medicine. As a teenager, she doesn't like to take her medicine. But I think some of the other things that I put, like anxiety and problems with her eyes, for me as a caregiver and as a parent, it sits in the back of my mind constantly. When are things going to develop. Is the shoe going to drop? Is she going to get worse, her condition? And what does that mean?

James Valentine, JD, MHS (01:37:21):

Sure. And do you have those worries because those particular symptoms have been getting worse already, or when you're talking about waiting for the shoe to drop, maybe can you put that in a little bit more perspective for us?

Alma (01:37:36):

Well, I think initially, because she's only been diagnosed for a few years now, it was all symptoms at once, and progressively they've gotten milder and milder, and now she doesn't have much, as far as symptoms, we see a little bit of swelling every now and then. And so it's just, what will happen in her body that might cause this to kind of full-blown symptoms?

James Valentine, JD, MHS (01:38:12):

Right. And is there a particular - I know you were saying it was kind of everything was almost being experienced at first and over time they've become milder. Maybe some of them have resolved, but you just were kind of expressing that you're worried that they'll come back or is there a specific one that when it was present had the greatest impact in daily life? Can you give me an example maybe of what that looked like for your daughter?

Alma (01:38:47):

The swelling was definitely the one. Again, when she started, she was in camp for a whole month prior, so those symptoms she was developing and we weren't there. So it's that fear of what do I have to look

for? What am I looking for to see that she's swelling? Is it going to go down? Do we need to call the nephrologist? What steps do we need to take?

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

Sure. Thank you so much, Alma. I want to bring Eric into the conversation. Eric, as you were thinking about those same, very long list of impacts of MN, which stood out to you as being one that has impacted you most in your daily life?

Eric (01:39:37):

This is Eric, I'm in Alabama. So one that comes to mind is actually one that one of the presenters mentioned, which was gout. That's something that I've been diagnosed for about 20 years now. And it started up a few years after I was diagnosed for the first time. And it just knocks you out. Even with medications you can't do literally anything for three or four days at a time because you're just completely immobile.

James Valentine, JD, MHS (01:40:05):

Sure. So Eric, can you maybe tell us when did you first experience gout and was it since the first day you had it, has it been pretty much as bad as you just described or did it build up to that?

Eric (01:40:20):

So the first gout attack was probably a good 10 years after I was diagnosed. I was actually graduating from college and I had a gout attack walking across the stage... Or not walking across the stage, but I had to have crutches and all of that, going across the stage. And then more recently, just in the last couple of years, I actually had a bout of shingles and gout at the same time and it was quite miserable.

James Valentine, JD, MHS (01:40:48):

And maybe just to put this terrible experience of having to deal with gout into perspective, how often do you have this type of gout attack or flare up? Is this something that's weekly, monthly, every, every few months? What does this look like for you?

Eric (01:41:06):

For a long time it was just once per year, on average, about three or four years, probably about two or three years ago I would say, there was actually probably a three-month period where I did have that shingles infection as well, that it became much more frequent, like maybe once every month. And I started taking some medication and did some diet adjustment, and that's helped a lot for sure.

James Valentine, JD, MHS (01:41:30):

That's great to hear. Thank you so much, Eric. I see, we actually have a caller who wants to share some of her experiences of symptoms related to her. And then we have Amy from Collinsville, Illinois. Want to welcome Amy to the show, are you with us?

Amy (01:41:50):

Yes, I'm here. Thank you.

James Valentine, JD, MHS (01:41:51):

Welcome, I would love to hear what you were calling in to share about.

Amy (01:41:58):

Well, I discovered my MN after my second pregnancy, I had the proteinuria and no swelling, so they just chalked it up to preeclampsia. I gave birth and the swelling initially went away and it came back. So the swelling for me was the number one issue before I was diagnosed and then it eventually went up into my face and that's when I knew something more was going on.

James Valentine, JD, MHS (01:42:35):

And Amy, was that over a period of days or when did it kind of advance to not just being in your feet but to your face?

Amy (01:42:46):

Well, I didn't discover I had MN in until two months after I delivered. So between that time period, the swelling from the pregnancy and all the medication from that died down. And then I would say, another month it went back up into my feet and then just overnight it went up into my face and around my eyes.

James Valentine, JD, MHS (01:43:14):

And is this something that is still bothering you? Is it still something you're living with on a daily basis?

Amy (01:43:22):

I reached remission pretty quickly, about six months after, and I've been in remission, but the treatment that I was – they decided to do the advanced treatment, because I was so young and the amount of protein and the amount of swelling I had, they didn't want to risk the time waiting for the less aggressive treatment. That really caused a lot of mental and physical drain on me in such a short amount of time. I think the main thing – I'm glad that I'm in remission, but I think, quality of life is something that you have to think about too. And I wish that there were other treatments available that weren't as severe as far as side effects to those medications.

James Valentine, JD, MHS (01:44:25):

When you say it's really taken it out of you, you just mean it makes you feel fatigued, maybe makes you feel drained of energy, or is it something different than that?

Amy (01:44:38):

So some of the side effects I was on just throughout this period of time, cyclophosphamide first with the prednisone and then to tacrolimus after, because it had a side effect to the cyclophosphamide that I had to get off of it, but I lost my hair. The moon face, the swelling from the prednisone.

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

Amy (01:45:04):

Temperament, like I had anger issues because of prednisone. Sweating, just, you know, any time of day. Things like that, I had to seek psychological help, because it started to have an effect on my family and I just had a baby. So, you know, it was supposed to be one of those times where it's happy and you're

supposed to be connecting with your family and your new newborn. And it was just kind of, me just trying to keep up and keep going for my family.

James Valentine, JD, MHS (01:45:43):

Yeah. Well, Amy, thank you so much for calling in and sharing this. I think we'll be spending some more time this afternoon going into details of side effects, but so important to know your journey and of course, you know, symptoms and treatments go hand in hand. So I want to really thank you.

I want to encourage others to call in just as Amy did to share their stories, again, you can call in at +1 703-844-3231. Again, that's +1 703-844-3231.

James Valentine, JD, MHS (01:46:18):

But I see that we have actually, I also had some individuals writing in with comments on this topic. So I want to check in with David, what are you seeing from the web?

David Feldman, PhD (01:46:26):

Yeah, right. So Eileen from Norwood, Pennsylvania writes, "while symptomatic, every day was a struggle to get through. There was extreme fatigue, nausea, itching that was relentless, and just a foggy feeling". So there we have that cognitive aspect again.

David Feldman, PhD (01:46:44):

Charles from Greenville, North Carolina writes, "I experience intermittent aches and pains, which come and go without warning, including severe muscle cramps".

James Valentine, JD, MHS (01:46:55):

Sure.

David Feldman, PhD (01:46:56):

And Barbara from Merritt island, Florida writes, "with COVID, my life is stressful and anxiety ridden". So again, that sort of triad of psychosocial, cognitive and physical aspects.

James Valentine, JD, MHS (01:47:08):

Yeah, absolutely. I want to thank those of you who have been writing in, continue to do so that as well, we have that comment box under the live stream on the webpage today. So you can continue to send those in, we'll be sharing those throughout the program as well.

James Valentine, JD, MHS (01:47:24):

I now want to kind of broaden the discussion. We're still on the topic of symptoms and health effects that are impacting you in your daily life. We want to maybe understand, what are some of those activities that have been impacted.

So to help us begin to explore this topic, we have another polling question for you. So you can go ahead and pull out those phones, go to that tab in your browser. You know, we want to hear from you and get you thinking about what are the impacts in daily life.

James Valentine, JD, MHS (01:47:54):

So here, that question is, which of the following statements is true for you, as related to living with MN. And again, this is one where you can select all of the different impacts that apply to you or your loved one living with MN.

James Valentine, JD, MHS (01:48:08):

The options are A, your general daily function is limited. B, you miss work or school more than you're comfortable with. C, family stress is common in your life. D, others don't know what it's like to live with MN. E, you cannot participate in sports or other physical activities that you enjoy. F, you cannot participate in other types of hobbies that you enjoy. G, you feel socially isolated. Or H, none of the above statements are true for you as it relates to your living with MN.

James Valentine, JD, MHS (01:48:43):

So again, we're seeing percentages of responses, not percentages of people selecting each response since our respondents can select more than one option.

So one thing we're seeing here, I know results are coming in, and I want to encourage you to keep submitting those, but want to point out that right now, it looks like one of the top statements that's true here, is that others don't know what it's like to live with MN.

So I want to invite you to call in, write in, letting us know what that actually looks like in your life, how has that impacted your life? You know, what does that really mean specifically for you?

But what we're also seeing, is that a wide range of these impacts from work and school, to family stress, social isolation, and limited hobbies, whether that's physical or otherwise have been impacted for many of you. And so we want to hear what those specifically are for you.

James Valentine, JD, MHS (01:49:48):

So to help us understand some of these impacts on activities in life, we're going to come back to our Zoom panel here. Seferiana, I want to maybe start with you. As you're looking at that list, and relating that back to what we were talking about earlier, in terms of symptoms, what have been the biggest impacts in your daily life?

Seferiana (01:50:09):

Hi, thank you for having me today. I'm Seferiana, up in Seattle, good morning. For this one, I chose the "others don't know what it's like to live with MN". And actually really, I was very impacted by that first question, because mine also, my most kind of common effects now, are around mental health. Anxiety, depression. Cause I was diagnosed back in 2016 and my worst physical symptoms came on, like the swelling came on very quickly. I gained about 30 pounds that eventually came off, I believe it was a lot of water weight. But those physical impacts were really felt in the beginning. And since my – I've never gone into remission, but since my physical symptoms have kind of subsided, I really can feel those, the impacts of just the uncertainty and the not really being able to share what it means.

Seferiana (01:51:06):

And I've also had a lot of brain fog and kind of lack of – it's hard to concentrate and things like that. And so just the fact that others don't know, and how do you explain when it's not visible, as others have spoken about through the videos. That it's not, you can't really see it, and so how do you talk about it?

James Valentine, JD, MHS (01:51:25):

Right. And so how, when has this transition happened for you, where it kind of went from visible symptoms, like the swelling, to it more being now this invisible disease, that's hard to bring up or explain to others?

Seferiana (01:51:44):

Yeah, I would say probably in the last couple of years. I've been on sort of a minimal treatment over the last couple of years. And at first I was running like half marathons, I was very physically active, and then all of a sudden I wasn't able to do that. The other option I chose was that I couldn't participate in activities that I was really into before. And so I could gradually kind of increase my physical activity.

Seferiana (01:52:11):

And so there's just sort of the feeling of not being able to share that I feel anxious about the future, and that I kind of keep it to myself.

James Valentine, JD, MHS (01:52:23):

And has that feeling, you have to keep it to yourself, impacted any particular relationships in your life? Any family, relationships, friendships, or other social contacts?

Seferiana (01:52:36):

I mean, I would say that it just means I kind of keep it. I mean, keeping it to myself, it just means that I'm not fully being honest with my loved ones. And really, I was actually texting my partner saying, "I feel seen here". I feel like there is more to talking about this illness, and just how it's impacting our daily, like mental health. That's so important.

James Valentine, JD, MHS (01:53:00):

Absolutely. Thank you so much. I want to bring Daniel into the conversation here. Same question, as you're thinking about the range of impacts in your daily life, what stands out to you as an area that maybe has been most affected by MN?

Daniel (01:53:16):

Hey, David, James, thanks for having me. Daniel Holmes, I'm in Palm Bay, Florida in Berberine County. I moved to Florida three years ago because of wanting to be by the beach and do those outdoor activities from up north, right? Now that I've been diagnosed a little over a year and a half with MN, it's hard. It's hard to find the energy to get up, to get out to the beach, to manage the swelling, the sun. I've been on a regimen of Cyclosporine, which says you can't really be in the sun very long. That kind of stuff really affects your daily activities and what you want to do. I work in the outdoor environment, so it really impacts what I can do at work.

Daniel (01:54:09):

Some of my biggest symptoms are the retention of water, right? The water retention. Staying hydrated outside when it's 95 degrees out with a hundred percent humidity, having to pound water, but yet limit the amount of water you can drink because the amount of water you store, it's this vicious cycle of water pills, and trying to stay hydrated while the water pills are dehydrating you at the same time.

Daniel (01:54:34):

It's difficult. It is just that difficult. And like Eric brought up, I just found out I have gout, three days ago. So I'm dealing with the pain of that severe flare up, that I've never experienced before a day in my life. And it's not fun. So last Sunday, before going out to the beach, I ended up having to go to the urgent care, so I can get some kind of treatment for the gout. But, you know ...

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

Yeah. I mean, there's a range of things, it sounds like, that are impacting your ability to work on your feet outside. How often does this affect – I mean, are you having to take sick days or, I don't know if in your career, there's, maybe a light duty option that maybe your work, you've been able to do for some days when the symptoms are worse? Can you maybe give us a little bit of color around how this really has impacted your work?

Daniel (01:55:36):

So I've been on FMLA because of this disease. They pull from all of your vacation time first. So I basically don't get any vacation, they pull from that. My physical constraints of the job, I get so fatigued, on doctor's orders, I have to leave work by three o'clock in the afternoon. Where they would like me to stay till about six o'clock. So every day I'm charged three hours of vacation just to leave work early, so I can have the energy to carry on everything else that I have to do. Which is hard to explain to the people that you work with, because they look at you and you look fine and you sound fine, and you know, "oh, you're just trying to leave work early" type of thing.

And they just don't get it. They don't understand, you know, they don't understand the water pills that you have to take just to get to work, and the 10 pounds you gained last night while you drank all that water yesterday, like they just don't get any of that.

Daniel (01:56:41):

So it is a significant impact on your daily work life, and trying to find a balance. I can only imagine if I was trying to find a job right now, how I would explain that to a new employer, as a condition of employment that I need to be able to leave work at a certain amount of time because my energy level expires.

James Valentine, JD, MHS (01:57:04):

Right. Wow. Well, Daniel, thank you so much for sharing that, it's really profound impacts on your ability to work, such a vital part, of course, of life.

James Valentine, JD, MHS (01:57:15):

I do see that we have some written comments that have been coming in. Before we go to David, I'll remind you that if you want to call in and share your input with us live today, you can do so at +1 703-844-3231. Again, that's +1 703-844-3231. But now let's go to David.

James Valentine, JD, MHS (01:57:36):

David, what are you seeing in terms of impacts on life?

David Feldman, PhD (01:57:39):

James, I'm going to have to punt back to you, for just a minute.

James Valentine, JD, MHS (01:57:43):

Okay. We'll come back and hear some of those statements that I do see trickling in. So I want to make sure that you know we are seeing your comments, but we'll be right back to you with that.

James Valentine, JD, MHS (01:57:54):

Maybe let's bring in Kim, we haven't heard from you yet on this topic of impacts on daily life, the symptoms that are most bothersome. What has stood out to you as part of this discussion and what your personal experiences have been?

Kim (01:58:09):

Well, good morning. I'm Kim and I live in Northeast Ohio. I was diagnosed a couple of years ago with this, and I can echo several things in here. I was diagnosed after – it was my blood pressure. I had just finished a half marathon and it just went sky high, out of nowhere. Perfectly healthy up to that point in my life.

Kim (01:58:35):

I can relate with Daniel and being so exhausted by a certain point in the day, that if my coworkers knew I was sitting there thinking about sleep, and that was literally all I could think about was, "I just want to go home and go to sleep". And I can even recall times where I've been so exhausted making myself get through that workday, that I can hardly remember walking through the door to lay down, to go to sleep and just being gone. You know, you hit that certain point. So fatigue definitely, definitely is one of my major things and it does impact my life. Anything from canceling out with friends, because I literally don't have it left in me to do things.

James Valentine, JD, MHS (01:59:23):

And how predictable is this? You know, obviously what you just said really struck me, that you're making plans, so you're hopeful that you'll be able to. Is that because some days are better than others? Are you able to predict when you're going to have a good day versus a bad day?

Kim (01:59:43):

No. Honestly, for me personally, it's like a rollercoaster. Including like, everything that goes with this disease, from symptoms to the amount of protein I spill. And I think that contributes to the anxiety and the feelings that you struggle with internally, because I can go and have really good labs today, and I can go next month and they'll be just like all over the place. There's no predictability and that's very hard.

Kim (02:00:15):

So you can't make plans. While you know, "I'm going to have a good day today", or you just don't know, sometimes it comes out of nowhere, and with my family, you know, I've come – and getting people, and they do look at you, you look normal, you look fine, there's nothing wrong, you know? Well, no. So with my family, I've tried to explain it to them. Every day I'm tired, but it's days of, "today, I feel like I've been hit by a car", or "I've been hit by a bus". And when it's really bad, it's a "freight train" day, I need to sleep.

James Valentine, JD, MHS (02:00:50):

And just to kind of really help us understand this, how often are those "freight train" days, as you put it? Is that, you know, once a week, more, or less?

Kim (02:01:02):

It depends. It depends on where I'm at with the spill. You know, at least twice a month, the "freight train" days come. Most days, I would say are at least "car" days, you're dragging, dragging. And, you know, especially by the end of the day, I can't think. After three o'clock in the afternoon comes, I can't think. It's over.

James Valentine, JD, MHS (02:01:27):

Yeah, sure. Well, thank you so much, Kim, for helping us understand that. And I just really appreciate your input and comments. I want to check back in with David, see if we are able to share the written comments we've been seeing.

David Feldman, PhD (02:01:44):

Yes. Thanks James. So Charles from Greenville, North Carolina, writes, "before I got sick, I biked 10 miles a day, kayaked, as well as doing a bit of running and a lot of yoga. Now, most of that is not possible. Holding down my job is hard, given my fatigue levels and my anxiety levels have been rather high".

David Feldman, PhD (02:02:06):

Jamie from Sanford, Maine writes, "MN causes me to swell so greatly that I cannot walk. I also cannot write, cook, play with my child, or do anything that requires dexterity. I have a four-year-old child and because of my MN, I'm only able to fully take care of her two or three days per week".

David Feldman, PhD (02:02:32):

And Nina from Richmond, Texas writes, "we look fine, but we hurt mentally and physically. Secluded socially because of COVID and drugs that I take. Very lonely".

David Feldman, PhD (02:02:46):

Very, very devastating affects.

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

Absolutely. Yeah. I can see the range of things that you were wading through there, David, and it's a lot, but we want to really encourage people to keep sending in those comments. It really helps us understand.

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

I see we have a caller who wants to share maybe something a little different than what we've heard so far in terms of symptoms. We have Andrea from California, who wants to share some of her experience, some of her thoughts. So Andrea, are you with us?

Andrea (02:03:18):

Hi yeah, this is Andrea.

James Valentine, JD, MHS (02:03:21):

Andrea, welcome to welcome to the program.

Andrea (02:03:26):

Yeah. Thank you for giving me the platform to speak to this.

James Valentine, JD, MHS (02:03:30):

Sure, go ahead.

Andrea (02:03:32):

So I just wanted to touch base on the nausea that I experience, I don't think that's been mentioned yet. So I wanted to make note that, you know, when I was first getting diagnosed, I guess the level of toxicity in my blood was high enough that it was caused, causing me to feel nauseous a lot. So that was a symptom that wasn't highlighted previously, just I didn't notice that.

Andrea (02:03:54):

Something else that I wanted to touch base on and how it's impacting my daily life, is the heat exposure that people have mentioned. You know, I find myself struggling to do things that a 25-year-old would have done in normal circumstances, like going to outdoor concerts, going on these like hikes that were out in Hawaii, couldn't go on hikes with friends because it was going to be too hot for me and it wouldn't be able to keep up with everybody, things like that.

Andrea (02:04:18):

So that's been something that was limiting for me. And in regards to like, daily impacts, taking time off of work, to seek treatment for IV therapy, and having to take time off. And it was never like, a couple hours, it was like a day. And then I had to come in late because I get labs done in the mornings or, you know, it was accommodating for doctor appointments, lab draws, treatment sessions. It's just very taxing on your day to day time constraints, and the work-life balance there. It's really hard to work there with a nine to five job.

James Valentine, JD, MHS (02:04:51):

No, absolutely. So I want to unpack some of these things that you've shared, because it's so valuable to have the opportunity to hear your experience. Maybe we can start with the nausea, was this something that was kind of like, a feeling that you'd have chronically throughout the day? Or is this like, sharp kind of nausea, maybe like kind of spells maybe? Can you give us a little bit more of a color of what this nausea kind of looked like for you?

Andrea (02:05:21):

Yeah. So it would just come and go. It was just really sporadic, but it was constant throughout the day. So it wasn't any time of day that it happened more than others, it was just constantly like, it would just be like, "oh, I got to stop. Got to take a breather, cause I'm feeling a little sick right now". So it was just constant nausea.

James Valentine, JD, MHS (02:05:38):

Wow. And even though it was kind of pretty persistent when it was there, how did it look in terms of like, week to week, month to month? Was it pretty persistent over longer periods of time? Or would you have periods of time maybe with no nausea?

Andrea (02:05:57):

It was pretty consistent for the first couple months that I was diagnosed, and then once I started treatment, it was hard to tell if it was the actual disease that made me nauseous, or the drugs that made me nauseous. So I was pretty much nauseous for a full year.

James Valentine, JD, MHS (02:06:14):

Wow. Okay. No, that's really important to know and thank you for sharing that.

James Valentine, JD, MHS (02:06:22):

Then on the heat exposure, you talked about lots of different things that you enjoy and are maybe important to you, outdoor concerts, hiking. You mentioned that if it got too hot, I'm just kind of curious, is there a certain temperature or heat index, that when you see it in the morning, you're like, "Nope, there's no way I can go out and enjoy the outdoors" that day? What does that look like?

Andrea (02:06:49):

Definitely. I feel like, you know, once it gets past 85, maybe 90, it's an indoor day for me. Just being out in the heat will drain me much quicker than I think the average person. And, you know, I also get nauseous with the heat exposure too, and just really need to take it easy.

James Valentine, JD, MHS (02:07:05):

I see. Well, thank you, Andrea, so much for calling in and sharing. I think it's so important to hear the range of different impacts. And so want to commend you and thank you for that.

James Valentine, JD, MHS (02:07:20):

And our final time as we're on this topic of what it is to live with MN, I want to, again, broaden it one more time, to not only focus on the things that you have already experienced, but also what are your worries and fears for the future about these symptoms, maybe that you've already had, maybe something that you haven't experienced yet? And not only just the direct symptoms, but also your worries and concerns about your kidney disease kind of overall.

James Valentine, JD, MHS (02:07:48):

Maybe if I come to our Zoom panel, is there anyone on our Zoom panel, quick show of hands, that might want to weigh in on worries or concerns for the future? Any takers? Yes, Daniel.

Daniel (02:08:04):

I have a 14-year-old son who's now involved in high school sports. And my biggest thing, I help coach the football team at his high school. And it's difficult to be able to muster the energy to continue that. As much as I try, as much as I will fight to keep that stuff continued, there's always that worry of like, at what point, maybe one day I won't be able to do this. Will I have to coach from a wheelchair? Will I have to use a walker in order to get there? There's always that in the back of my head.

Daniel (02:08:43):

I fight pretty hard to try and maintain my own personal health, but, you know, this is something that we're all fighting against, you know?

James Valentine, JD, MHS (02:08:53):

Right. And those are pretty near-term worries, Daniel, are you worried also that your kidney disease will progress in that time period and cause that? Or is this just even within kind of the realm of where you are with your kidney disease, you're worried that these symptoms will get worse?

Daniel (02:09:14):

It will. I mean, things are looking up for me personally. My kidney disease seems to be getting a little better. I've reduced the amount of medication that I'm required to take, but it's a roller coaster. I'm a year and a half into this thing, there's no end in sight until there's a cure, right? So it's just a matter of getting on the roller coaster and attacking the hurdles that present themselves. I try not live my life in fear daily, and I just try to attack what comes my way. You know, you wake up one morning, you got gout. Who would have known, you know? You just got to tackle that hurdle first and get to the next one, you know?

James Valentine, JD, MHS (02:09:52):

Absolutely. Thank you so much, Daniel. Alma, I saw you shaking your head there at points, want to check in with you. Do you share some of the same worries? Is there anything different that you're thinking?

Alma (02:10:05):

Oh, absolutely. I mean, my daughter's 15 today and you know, she has a whole life ahead of her, and what is that going to look like? You know, will she be able to go to college? Will she be able to have kids? You know, will her condition progress, that she has to go into dialysis? Will she have to have, you know, a transplant? And at what stage in her life could that happen, and how that will affect just her quality of life in general? Yeah, absolutely.

Alma (02:10:38):

And as a mother, I worry. You know, the constant worrying about what if, and trying to balance all of that, is very tough.

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

Yeah. And has she ever expressed any of her own, in her own words, any worries to you?

Alma (02:10:57):

She does. She really tries to be optimistic, and again, as a child, she doesn't understand what the future could look like. As much as I've tried to explain in terms that won't scare her, right? You know, teenagers think they're invincible and that nothing that happens will affect them, but that's not the reality. And I, as a parent, know that. And trying to, you know, get that message across to her is tough.

James Valentine, JD, MHS (02:11:38):

Sure. And Eric, I'll give you the final word on the Zoom panel. Your thoughts about the future, any specific concerns or worries that you have?

Eric (02:11:52):

I mean, I think I probably share a lot of the same concerns that all of us do about the progression of the disease and stuff like that. I think something that's been kind of drilled into my head, probably a lot of our heads the last year, is just how out of control all of this is. We can take our medicine, we can take the treatments, and then a pandemic happens. And, you know, as some people have talked about the isolation we have too, because I have to take extra precautions that a lot of folks that I know, don't. Maybe they should, but they don't necessarily, maybe it's just not as important to them because I've been on immunosuppressive therapy, so it brings all kinds of risks.

Eric (02:12:27):

And so, you know, I think that's something I've never been concerned about, but assuming we get out of this COVID thing at some point, in the back of my mind, it's like, "well, what if I'm around somewhere, then a new one is born", and it's just one more thing to add to the future worries, I guess.

James Valentine, JD, MHS (02:12:49):

Yeah. No, and I'm glad that you raised that, because it's probably been in the back of everybody's minds, but we haven't said it yet. Just with the additional complexity of navigating COVID and you know, the extra burden that that puts on all of you.

James Valentine, JD, MHS (02:13:08):

So I do see that we've had written comments coming in on this topic as well. So as the final word on this overarching topic on what it is to live with MN, I'm going to check in with David to share those commons.

David Feldman, PhD (02:13:21):

Right. So with worries for the future, Mark from Massachusetts writes, "I feel stressed. A stress of potential relapse". Eric writes, "I'm worried I won't recognize the symptoms before the MN gets out of hand".

David Feldman, PhD (02:13:36):

And Betty writes, "hearing the words, membranous nephropathy was devastating and frightening".

James Valentine, JD, MHS (02:13:43):

Yeah. So a lot of fears, it seems, have been echoed by all of you. So I want to thank all of you so much. Our Zoom panel, our callers, all of you that have written in, and of course our panelists from earlier, for sharing what it is to live with MN, impacts on your life and worries for the future.

James Valentine, JD, MHS (02:14:03):

At this point in the agenda, we're going to take a bit of a lunch break, although I'll encourage you, it's 30 minutes if you need longer, that's okay. We're going to be coming back to a presentation, but we'll be, after that presentation, inviting all of you back to be sharing your experiences with current approaches to treatments. So we'll look forward to continuing the discussion in the afternoon.

James Valentine, JD, MHS (02:14:27):

So for now we're going to take a 30 minute break. We will resume at 12:35 Eastern Time. So look forward to seeing you then.

James Valentine, JD, MHS (02:23:48):

Good afternoon, and welcome back to the Externally Led Patient-Focused Drug Development Meeting on membranous nephropathy. Again, my name is James Valentine. I'm here with David Feldman, your co-host for this program.

James Valentine, JD, MHS (02:52:04):

We had a wonderful discussion this morning, where we heard about what it is to live with MN. And now we're, this afternoon, going to be building on that discussion to learn about the different treatment approaches that you all have tried as well as your preferences for future treatments.

James Valentine, JD, MHS (02:52:22):

To get us though started on this topic, and to give us some background on how we even get to treatments for MN, we have a presentation talking about the challenges and opportunities in designing clinical trials to help study drugs that will ultimately treat this condition.

James Valentine, JD, MHS (02:52:40):

So, to do that, please welcome me in joining Dr. Larry Beck, who is a nephrologist at the Boston Medical Center and Associate Professor of Nephrology at the Boston University School of Medicine.

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

Dr. Beck, thanks for joining us.

Laurence Beck, MD (02:52:58):

Thank you for that introduction. Again, I'm Larry Beck from Boston University. And I'm going to be talking about challenges in clinical trial design in membranous nephropathy.

Laurence Beck, MD (02:53:07):

So why should we discuss clinical trials and the challenges for membranous nephropathy?

Laurence Beck, MD (02:53:13):

Well, randomized trials represent the best path forward for finding new treatments in membranous. But the planning, the conduct, the analysis of these trials, all takes a long time. We want to make sure that we and the industry sponsors get it right from the outset. And your participation in this and your discussion will help inform a better clinical trial going forward. We want to make sure the outcome measures provide a clear answer to the question being asked. And the trials need to be designed to maximize acceptance, both from you, the potential participants, but also from referring healthcare providers who want to enter you into the trial.

Laurence Beck, MD (02:53:55):

So when I think about the ideal clinical trial, you'd want to have a large number of participants that are both diverse but also representative of who gets this disease. You want to make sure they have the same disease. And ideally, that all patients are in the active phase of disease.

Laurence Beck, MD (02:54:13):

And you can consider two potential designs. One, you could have your new and improved treatment being compared to the standard of care. Or you could have a new treatment that maybe has a new mechanism of action in membranous nephropathy, that is added onto the standard of care and then is compared to standard of care plus a placebo or sugar pill.

Laurence Beck, MD (02:54:35):

And in terms of the outcomes, you want to have well-defined, easily measurable outcomes. You want those responses or outcomes to occur within a reasonable amount of time. And the trial needs to provide a clear answer, if this new therapy is indeed better.

Laurence Beck, MD (02:54:51):

So why is this such a difficult task in membranous nephropathy? So what are the challenges?

Laurence Beck, MD (02:54:59):

When you think of the phases, you think of the enrollment and the screening for the participants, you think of the conduct of the trial itself, and you think of the conclusions. Is all this effort and time that's put into this, is this going to give an answer that tells us if, is this treatment something that we should be using or shouldn't be using for all patients with membranous or maybe just a few?

Another problem is that these trials and the designs take place over years, and in that time period, we may have new understandings of the disease. There are ongoing trials that may come to an end and have new treatment recommendations, and the general patterns of treatment may be changing.

Laurence Beck, MD (02:55:42):

So, in terms of enrollment, we know that membranous nephropathy is an ultra-rare disease. So, finding enough participants with active disease can be challenging especially when multiple clinical trials are going on at the same time. As I mentioned, health care providers need to be convinced that seeing if their patient would be interested in a trial would be worth it before they refer any patients and the patients themselves, the participants need to weigh having a pretty good treatment that already exists against the hope for either a more effective or a quicker or a safer therapy.

Laurence Beck, MD (02:56:21):

So, another problem is that there's more than one type of membranous nephropathy. There's primary, also known as idiopathic, which is the autoimmune disease that targets only the kidney, versus secondary forms that may be secondary to cancers or certain medication use or infections. There's the type that occurs in adults, which is most of membranous nephropathy, but there's also pediatric forms. There's the target antigen that can be used to define types of membranous.

So, PLA2R is the major target antigen in the kidney that gets attacked by the immune system, but there are also non-PLA2R types of disease. Of those, there may be some that we know what the antigen, the

target protein is, and there may be others that we still haven't discovered what the target is. Another problem is that clinical outcomes in membranous nephropathy take a long time to develop and may be further removed from the actual treatment duration.

Laurence Beck, MD (02:57:24):

So, to recap what Dr. Jefferson had talked to you about earlier, antibodies are normally protective, but in autoimmune disease, they can attack proteins in the kidney. So, antibodies from the bloodstream attack kidney protein, forming deposits that cause injury to the glomerular filtration barrier, the kidney filters, and the injury in proteinuria that occur from these deposits, and I showed them down in these circles down here. These are the immune deposits in the kidney. The injury persists even after the antibodies disappear from the bloodstream.

Laurence Beck, MD (02:58:03):

So, this is how I think about membranous nephropathy occurring over the course of time. The gray shading represents the antibodies in the bloodstream, in this case, antibodies against PLA2R, and with either immunosuppressive treatment or about 30% of patients may go into a spontaneous remission, the antibodies can come down and disappear and decline. The immune deposits that are causing injury to the podocyte making the filter of the kidney, those will go away in time, but there's also a time period where the antibodies are coming down, but there's still deposits forming. There's still ongoing injury. This may be a new type of mechanism that a company could address in terms of treating the disease, but eventually, the protein will come down. The protein filter will go back to normal, and the disease will be over.

Laurence Beck, MD (02:58:59):

Many of the inclusion criteria, the criteria that the trials use to figure out who's going to come in are based on the diagnosis of the kidney biopsy showing membranous nephropathy and the amount of protein, typically, nephrotic range proteinuria over four grams a day. A nice study from China looking at almost 600 patients with membranous nephropathy with PLA2R antibodies in the blood has shown that 75% of them have active disease at the time of biopsy. These are the patients that would be expected to respond to immunosuppression. However, there was another 25% that were already showing signs of remission. They didn't have antibodies in the blood. They did have the antigen in the kidney, and these are the patients that may not need immunosuppression.

Laurence Beck, MD (02:59:51):

Other possible outcomes, we talked about the loss of antibodies. The blood albumin protein can come up. Most trials these days look for partial remissions or the complete disappearance, a complete remission of proteinuria. We could ask longer term outcomes, avoidance of dialysis, or the need for transplant, stability of kidney function, patient's symptoms like fatigue, swelling, side effects.

Laurence Beck, MD (03:00:17):

What we know though, is that the most concrete answers, avoidance of dialysis, these come years out, five, 10 years later. Trials don't have that time, but unfortunately, the earlier predictors aren't always well-established surrogates for the end point. So, we're sort of at an impasse about what we use as the clinical trial outcome.

Laurence Beck, MD (03:00:40):

Another issue and challenge for clinical trial design is that our standard of care, how we treat patients with membranous is evolving. So, the first glomerulonephritis guidelines that came out in 2012 recommended the time-tested treatment of alternating months of cyclophosphamide and corticosteroids as first-line for membranous nephropathy. Then there were some observational trials, some small, randomized trial that showed that cyclosporine or tacrolimus were another alternative first-line agent. Then, recent trials and other observational data has shown that therapies that attack B cells, the antibody-producing cells, are actually superior to cyclosporine and are now being the first-line recommended treatment in the upcoming 2021 guidelines, but we also know that many of them may have been treated with other agents, and other treatment approaches exist. So, how is a trial supposed to keep up with the standard of care that keeps changing?

Laurence Beck, MD (03:01:40):

So, knowing all this, how do we move forward with clinical trials? We want to make sure that participants get, at the least, the standard of care. We want to design the enrollment strategy to enrich patients who are immunologically active, especially those patients who have received a prior treatment months or years ago. We want to include all types of patients, especially anti-PLA2R seronegative, but we do want to make sure that those patients aren't already in remission, so we need to look at the biopsy to make sure they don't have PLA2R in the biopsy tissue.

New treatments, especially those that address new mechanisms, such as complement inhibitors should be added on top of standard therapy, not necessarily compared to standard therapy. Importantly, we need to educate referring providers, nephrologists, primary care doctors, and potential participants about the benefits of enrolling in clinical trials.

Laurence Beck, MD (03:02:40):

So, with this, I will end the formal presentation. Thank you for your attention, but I have been asked to introduce a topic, which you will be talking about in the upcoming audience discussion, and it has to do with the clinical outcome response to a treatment in a trial.

So, partial remission is defined typically as a drop from a baseline proteinuria at the start of the trial greater than 50% drop to a level less than 3.5. This is a partial remission. 3.5 grams of protein is chosen because anything above that is considered nephrotic range. Anything below it is sub-nephrotic.

Laurence Beck, MD (03:03:21):

Now, many patients, if they achieve a partial remission, will already have a decrease in leg edema, will have increases in the blood protein albumin. We know from studies that achievement of any remission and how long you're in a remission is correlated with a better kidney prognosis years later. One thing to consider is that a partial remission has a number of outcomes after that. Some patients will go on to a complete remission. That's the expected outcome. You can't get a complete remission without first going into a partial remission. Some patients will be left with some degree of proteinuria. So, they'll always be in a partial remission. Then, the more concerning thing is some patients may relapse, have a increase in their proteinuria after treatment is stopped.

Laurence Beck, MD (03:04:14):

So, if we think about a trial that might use partial remission as an endpoint, you can think of the simple study below, enrolling 120 patients with membranous nephropathy, equally randomizing them to

treatment A, let's say rituximab, and treatment B, some novel treatment. The treatment goes on for 12 months, and you ask how many patients achieved this primary outcome of partial remission.

Laurence Beck, MD (03:04:40):

In the first group, 50%, 30 of 60, and the treatment B, the new treatment, 75%. This should be a 60. So, 45 of 60 patients achieved the response. That may be a good partial remission. This is something you can discuss in the next – in the upcoming discussion, but I think any trial that looks at partial remission as a primary outcome needs to have an observation phase to say, how many of those patients went on in each group to achieve a complete remission, how many stayed in partial, and how many relapsed, because those are also important outcomes to know after the end of the trial. So, with this, I will leave you. Again, thank you for your attention.

James Valentine, JD, MHS (03:05:24):

Thank you so much, Dr. Beck, for that presentation, both giving us a kind of current state of affairs of the challenges, but also opportunities in designing clinical trials to evaluate treatments for membranous nephropathy as well as for highlighting at the end there that possible clinical outcome of partial remission, which as you'll see later in the discussion, we'd like to get your views of whether you would be interested in taking a drug that has only demonstrated an impact on partial remission, knowing that maybe further follow-up will confirm whether that translates to complete remission or maybe even relapse.

James Valentine, JD, MHS (03:06:08):

Before we get there, there's going to be a number of questions that we're going to be working through together to discuss current challenges to treating membranous nephropathy. So, if we can pull up our discussion questions for the afternoon, these are what we'll be exploring together and asking you all as people living with MN and their direct caregivers to help answer.

So, first, we want to get a assessment from you of what you're currently doing as well as things that maybe you've tried in the past to help treat your MN and its symptoms. When we talk about treatments, we're not limiting this to only medicines although, of course, we do want to hear about the different medications that you're using as well as medical procedures but also other types of treatment approaches. So, you might be trying more holistic medical approaches. We heard a little bit this morning about the diet, but of course, diet, exercise, maybe even lifestyle modifications that you've had to make.

Really, when we use the shorthand of treatments, we're talking about anything that you do or use to try to make living with your MN a little easier. So, we want to hear about, what are those things that you've done and that you've tried? We want your assessment of how well they help manage the most significant symptoms. All of those things that we learned about in the morning session. How well do these different treatments actually help with those things?

James Valentine, JD, MHS (03:07:36):

In addition to hearing about the treatment kind of effectiveness, we also want to know, knowing that most or no drug comes without some side effects, what are the significant downsides of your current treatments, whether that's a side effect of the drug, the burden of actually undergoing a treatment or what something else that you might view as a downside? Knowing that in a rare disease like MN, and as Dr. Beck mentioned, many of you will consider or maybe have considered clinical trials as a possible

option for you, and so we also want to know what factors would be most important to you if you were considering participation in a clinical trial for MN.

Maybe some of you who have been in trials already can talk about your decision-making and your choice to raise your hand to join and participate. Even if you've haven't, we want to hear maybe why you've chosen not to participate even if it's letting us know that for you, the current treatment options, you're still working through those and trying those.

James Valentine, JD, MHS (03:08:39):

Finally, we're going to end our afternoon session looking towards the future and thinking about all of these treatment options that you currently have. We want to know what your preferences are still for future treatments.

So, the way that we'll ask this and want you to think about this is assuming there's no complete cure for your MN, what specific things would you look for in an ideal treatment for your condition?

James Valentine, JD, MHS (03:09:03):

So, to help us start this discussion, like in the morning, we're going to start with a panel of individuals living with MN who will be sharing their perspectives. We have Mark, Eric, Seferiana, Nina, and Eric who will be sharing their experiences. Mark, why don't you take it away?

Mark (03:09:26):

Hello, my name is Mark Parisi. I'm 63 years old. I live a Newburyport, Massachusetts with my wife, Laura, and we are both retirees. We're physically fit and socially active. I was diagnosed with MN at age 43. I was experiencing fatigue, swelling in my ankles, blurred vision and muscle spasms for many months. A kidney biopsy confirmed that I had irreversible damage to my kidneys and had advanced MN. I realized how serious my diagnosis was when my doctor suggested that I attend a pre-dialysis class at a local clinic the following week.

Mark (03:10:05):

My MN treatment started immediately. I was instructed to stop the use of over-the-counter anti-inflammatories such as Advil, Aleve, and Motrin as they could cause further damage to my kidneys. Blood pressure and cholesterol medications were prescribed to help control the progression of the disease. My nephrologist explained there were no drugs developed specifically for MN, and that my treatment would consist of trying off-label drugs developed for other diseases such as cancers and organ transplant rejection. He said if one does not work, you typically move to the next. He confirmed that MN studies have shown that these off-label drugs can help control the disease but not cure it.

Mark (03:10:46):

I felt confused and stressed especially when I tried to explain my extremely limited choices to friends and family. For the next 12 years, I was prescribed and endured the existing standard of treatment for my MN. The treatments were prescribed for an eight to 12-month period with blood work monitored every other week. I remember being overwhelmed with fear and anxiety after researching each drug and their side effect profile. We started with Cytoxan, then tacrolimus and then cyclosporine. These were supplemented with prednisone and an antibiotic that would help my depleted immune system fight seasonal infection.

Mark (03:11:25):

During the 12 years of treatments, I suffered debilitating side effects such as severe headache, nausea, vomiting, extreme high blood pressure, muscle cramps, joint pain, episodes of painful gout and excessive weight gain. My overall mental and physical health had deteriorated to a point where my life had been so negatively affected that I could not travel, socialize with friends, or collaborate in person with work colleagues for fear of being exposed to common illnesses.

Mark (03:11:55):

In 2013, my local nephrologist referred me to a Boston hospital for an MN consult. I was sent to a renal dietician for the first time since my MN diagnosis and another nephrologist from Boston who enrolled me in his MN research study in which patients were treated with four rituximab infusions. The study also included the development of a diagnostic test to detect PLAR2 levels in patient's blood samples that provide a direct correlation to the overall level of disease activity in an MN patient.

In coordination with my scheduled rituximab treatments, I incorporated the lifestyle changes that the renal dietician recommended. I controlled my overall protein intake to 70 grams per day, controlled my salt and sugar intake, cut down the consumption of dairy products, control portion sizes, minimized the use of alcohol, eliminated soft drinks and fruit juices, and increased my hydration level with water. Some substitutions included regular milk to coconut or almond milk, white bread to whole wheat bread, white pasta to wheat pasta, regular salt products to low salt products, and low fiber to high fiber products.

Mark (03:13:11):

After four to six months of these dietary changes, my energy levels increased. I lost weight. The swelling in my ankles disappeared, and my muscle and joint pain subsided.

The rituximab infusions were easy to schedule and accessed through my local hospital. I had minimal side effects from the rituximab. There were temporary fatigue and minor headaches that subsided two to three days after the infusions. Three months after my first series of rituximab infusion, my PLA2R, urine protein and creatine were down significantly. At six months, my lab tests were close to the normal range, and at 12 months, my lab results stabilized, and my PLA2R was undetectable. After enduring 13 years of treatment using the existing standard of care for MN, my MN was officially declared in remission after only 12 months of the rituximab infusions.

Mark (03:14:08):

In 2018, after five years in remission, my lab test in PLA2R started to increase. After monitoring them for an additional three months, it was confirmed that my MN was re-emerging. It was recommended that I have a maintenance infusion of rituximab, two infusions for the study to help control my relapse. Then, three to four months of completing the prescribed maintenance infusions, my lab test results improved, and my PLA2R test was in the undetectable range again.

I'm happy to confirm that today, my MN is still in remission. I am hopeful that my experience will help industry leaders recognize the overwhelming need and opportunity for the development of new drug therapies for the increasing population of MN patients.

Eric (03:14:59):

Hello. My name is Eric. I'm a 52-year-old attorney, songwriter, husband, and father living in central New Jersey. In the spring of 2019, I noticed with my annual physical that my cholesterol had shot up. My internist put me on a statin, which I did not consider it to be a big deal. I figured that this was a changing

metabolism with middle age. Several months later, I was constantly bragging to my wife about how my new workout regimen was building up bulk in my calves, which were previously scrawny. I went for repeat blood work to see if the statin was working, and I found that it was working but that I had alarmingly low protein levels in my blood and alarmingly high protein levels in my urine. A couple of blood tests later and a biopsy confirmed that I had membranous nephropathy.

Eric (03:15:55):

I started taking a diuretic to deal with the swelling. That was not much of a big deal. I just had to get up a couple of times a night to go to the bathroom, had to cut down on coffee. As for the disease itself, I started the conventional approach of taking high amounts of high blood pressure medication and a blood thinner. I noticed that the combination or maybe just the high blood pressure medication made me dizzy.

As a performer, musically, I would normally stand up, and I'd found that after a couple of songs, I would need to have a seat because I would get very lightheaded. My harmonica playing, which I used to incorporate into live performance, was no longer possible, which actually is a good thing because I'm an atrocious harmonica player, but the conventional approach wasn't working, and my numbers were getting worse.

Eric (03:16:49):

So, a few months after we commenced the conventional approach, my nephrologist recommended Rituxan, otherwise known as rituximab. It's not approved for the treatment of MN. It is approved for several types of cancer and rheumatoid arthritis. For this reason, my doctor and I had to fight mightily with my insurance company to get approval for it. A lot of calls and letters and delays of my initial infusion ensued as a result of that. I finally got my first infusion on March 13th, 2020, a date that a lot of us remember because it was the first day of the great COVID shutdown across most of our nation. Second infusion was six weeks later.

Eric (03:17:36):

Unfortunately, the blood levels after those two infusions suggested that it might not be the drug for me. My 24-hour urine output went from eight grams to five grams, which is an improvement, but five grams is still unacceptably high, so we were a little worried we might have to go in a different direction, but a few months later, I had my third and fourth infusions. A few months after that, I'm happy to say that it brought my levels down to the point where I am now considered to be fully in remission.

Eric (03:18:12):

I continued to maintain by taking 40 milligrams daily of candesartan high blood pressure medication. I do my best to minimize sodium in my diet, staying away from cheeses and cured meats. My MN-related symptoms have pretty much been held at bay. I have occasional lightheadedness from the blood pressure meds and decreased endurance when I'm speaking for prolonged periods of time. This is a by-product of lower blood pressure and what is perhaps a good sign for my kidneys but a blow to my ego. My calves are now back to their pre-MN level of scrawniness.

Eric (03:18:51):

In terms of future treatment, I have a demanding job. I have two hormonal teenagers at home. I generally do not have a lot of time to worry about what's going to happen if I relapse. If and when I do

relapse, I would like to know that Rituxan is still a viable option, a safe option and an effective option. I read up on the Ponticelli method, which before were Rituxan, was the gold standard consisting of prednisone and cyclophosphamide for six months, I know that that carries some attendant risks that are not there with Rituxan.

Eric (03:19:27):

I've read about other modes of treatment. The common reality appears to be a lack of robust longitudinal data to support both efficacy and safety, which certainly I would like to see.

Any future treatment ideally would be oral medication instead of an infusion. I'd like to avoid life-changing changing side effects like incontinence, impotence, et cetera.

I really appreciate this opportunity to speak to you and to help my fellow MN patients and the medical community addressing this disease. Thank you very much.

Seferiana (03:20:09):

My name is Seferiana. I'm 35 years old and live in Seattle, Washington. I own and run a political consulting firm where my work is dynamic and fast-paced. I was diagnosed with membranous nephropathy in February 2016 at the age of 30. I remember waking up one morning to swelling in my ankles that I had never experienced before. This heaviness subsided throughout that first day only to return after a long day's work. I began a pattern of sleeping off this mystery swelling until it stopped going away on its own.

Seferiana (03:20:39):

I soon saw my doctor, and she ran a gamut of tests due to the high level of protein I was losing in my urine. She ordered a kidney biopsy, and I was diagnosed with primary membranous nephropathy and stage one chronic kidney disease. I was spilling 13 grams of protein in 24 hours. My treatment started right away with furosemide to ease the water retention, lisinopril and prednisone. Soon after beginning lisinopril, I came down with a persistent cough and face swelling that sent me to the emergency room. My doctor immediately ordered me off the lisinopril and switched me to the losartan. On the prescribed 75 milligrams per day, I experienced tingling in my arms and hands, so my dose was limited to 50 milligrams.

Seferiana (03:21:21):

The prednisone caused me to be hungry all the time and never full. I was moody at work, and my colleagues noticed that I was always on edge. At the time, I worked for the city council, and I found myself impatient and short with constituents calling in for help. Within six months of my diagnosis, I gained 30 pounds. I carried weight all over my body, and I didn't know if the weight was caused by water retention from the disease or the prednisone treatment.

Seferiana (03:21:46):

In the fall of 2016, I began cyclosporine, which caused a severe reaction of face swelling, wheezing, and fever. I went to the emergency room because the swelling in my face came on so suddenly. My doctor considered this a reaction to the dose of cyclosporine. My doses were lowered, and the acute side effects subsided. The cyclosporine diminished my immune system, and I was sick multiple times in the course of treatment. I caught every cold and bug that went around.

Seferiana (03:22:15):

This medication also caused my skin to bruise at the slightest contact. While on cyclosporine, I had to test for the PLA2R antibody, which came back positive. After seeing no real improvement from cyclosporine in my protein loss, my nephrologist ordered off-label rituximab treatments. I began one gram of four infusions over the course of one month, each lasting about four or five hours. The infusions left me physically exhausted, and I would have to take a full day off work to accommodate the treatments.

Seferiana (03:22:46):

The treatment itself is physically uncomfortable and anxiety producing, having an IV inserted each time and not knowing if my body would have an allergic reaction. Once, I made the mistake of looking at the infusion site and promptly fainted.

Three months after the rituximab treatment, my PLA2R level came down, and my swelling went down significantly. Even though the treatment reduced many of the visible signs of my disease, I still have symptoms that were not reduced by treatment. My proteinuria is still high, and a recent kidney biopsy showed permit scarring and a slight presence of the PLA2R antibody in the kidney.

Seferiana (03:23:23):

For the last two years, my treatment has consisted of 50 milligrams of losartan per day, Lipitor to lower my heightened cholesterol brought on by my MN, daily aspirin to lower the possibility of blood clots, calcium supplements, and 10,000 IUs of vitamin D. I haven't seen drastic improvements with this treatment, but I'm no longer spilling upwards of 10 grams of protein as I was a couple years ago.

Seferiana (03:23:48):

My nephrologist has called mine a tricky case, and at times, I felt like I'm in a dead end with no viable treatment or remission in sight. It is frustrating to feel like I've plateaued, and the lack of a viable option has made it impossible to plan for my life. My nephrologist has recommended Cytoxan as the next best treatment option, but among the side effects of this drug is early menopause, which would make it impossible for me to have children. I have declined this line of treatment twice, so he told that with my condition, I could have a risky pregnancy if I don't get my disease under control. So, where do I go from here?

Seferiana (03:24:24):

After consulting my case with fellow nephrologists, my doctor has proposed another round of rituximab, which would prolong getting pregnant by a year from the end of treatment. I will be 37 then. At this very moment, I'm weighing my options. I could do nothing, wait and see if my proteinuria continues to lower on losartan or move forward and prolong starting a family. As a 35-year-old woman, I feel like there's no viable treatment for me that does not risk my fertility.

I hope that a treatment can be found that centers on women's health, that acknowledges this disease can impact anyone at any age, and that this disease deserves a cure.

Nina (03:25:04):

Howdy. My name is Nina, and I live in Richmond, Texas, close to Houston, with my husband of 31 years. I have two grown boys who live close to us. I resigned from my dream job a few years ago as a preschool teacher because of my MN and the immunosuppressive drugs that I was on. I didn't want to leave, but I

had no energy to be the motor skills teacher every day. The principal thought it wouldn't be fair to the children if I had to keep taking time off. She made a very strong suggestion that I stay at home and take care of myself. I never did return.

Nina (03:25:38):

Since 2017, I take cyclosporine and prednisone and supplements twice a day. The nephrologist adjusts the dosages based on lab results and how I am feeling. Usually, within a year, this can occur four to six times, which includes increasing or decreasing the cyclosporine based on cyclosporine levels in my blood and protein spilling in my urine. Valsartan has to be adjusted at least twice a year because my blood vessels will burst in my eyes if my blood pressure gets too high. This feels like someone took a knife and stabbed me in the eyeball. Not very pretty for people to look at.

Nina (03:26:17):

My body is so tense and nervous the week before labs. Will the doctor have to increase the dosages, and will my body respond with worsening side effects? My pajamas and sheets soaked as well. Will the nerves in my fingers again be sensitive to hot water in the shower where I have to take a cold shower because my fingers tingle so much, I can't hold on to soap or wash my own hair? Or if he decreases my meds, will the disease rev up again?

Never a day that goes by that MN is not on my mind. I have to give myself a shot of Repatha in the leg every other week for high cholesterol caused by either MN or possibly the cyclosporine. The Alexa chiming to remind me to take the shot makes me nervous, and I get mad that because of MN, I have to do this. This shot is painful. It feels like a wasp sting. As I push the button to administer the drug into my leg, it brings tears to my eyes every time.

Nina (03:27:33):

I also have to take Prolia shots every six months in my stomach because of the osteoporosis caused by the long-term use of prednisone. All the weightlifting I do has not helped prevent bone loss, and that frustrates me tremendously. Prednisone also causes easy bruising, cuts, bleeding, scarring and contributes to the lengthy healing time of those cuts and bruises. I work very hard to keep my body in shape, and I'm proud of my legs, but because of the prednisone, if I bump up against something or seriously cut myself, the scarring is so bad and embarrassing. It makes me sad when I look at the scars, and I remember that this is my reality.

Nina (03:28:14):

After four years of taking prednisone and cyclosporine every day, my numbers for protein, creatinine ratio are in remission levels. My nephrologist wants me to stay on this protocol for another nine months, but I brought to his attention that, yes, this combo has helped my MN, but it's causing permanent damage to my bones.

I am nervous because I tried getting off prednisone and cyclosporine in 2019 after two years of being on them, but that only lasted five months when I noticed I was very tired, edema in my legs, Silly Putty, I call it, trembling and of course, bubbles in my urine.

Nina (03:28:51):

When we ran the blood work and of course, my protein creatinine ratio had gone up significantly, and I had a relapse. So, back on both drugs immediately. I can remember the feeling of victory weaning off these drugs in 2019, and I could remember the defeat I felt to jump right back into the protocol.

Why can't this disease just stay away? I don't want to be this disease. I've never taken this disease lying down. I've tried the paleo and Plant Paradox Diet, no alcohol, no protein, and none of these have seemed to help me. Working out helps keep me sane. I have been taking CBD oil, which has helped decrease the muscle cramps, tingly fingers and night sweats from happening three to four times a week to maybe one or two times a month. Very thankful for that.

Nina (03:29:39):

I just wish there was a treatment that would put those of us with MN in long-term remission quickly and not cause other diseases or serious side effects. Also, it's very important to have a treatment that has been tested specifically MN patients and was successful in its treatment, affordable, and one that can be done at home. To be able to get out of bed, have energy and be present in life is not something now that I take for granted. And yes, this combo of drugs has helped me to do this, but at a big price.

Thank you.

Eric (03:30:15):

Hi, my name is Eric. I live in Jasper, Alabama with my wife and four cats. I'm a data scientist working with healthcare claims data. I was diagnosed with membranous nephropathy when I was around 16 years old and I'm about to be 35. So, I'm approaching my 20th anniversary. When I first began treatment, I started with 250 milligrams of cyclosporine every 12 hours along with warfarin, a blood thinner, Atenolol and at least one other blood pressure medication to bring it under control.

The first month was terrible starting these medications. I had bouts of stomach pain and nausea very frequently that I never had before. I remember driving to school one morning and having to pull over because I felt like I was going to throw up or pass out. It was very scary. I also lost a lot of weight the first month because of the nausea. The blood pressure medications also cause numerous side effects.

Eric (03:31:06):

I passed out in Walmart one day and had to be taken to the ER. My nephrologist attributed it to a blood pressure drop. And even today I still become lightheaded from the blood pressure medicine if I happen to bend over and stand up too quickly. All of the issues I mentioned previously were worth it though, as within a year or so, my disease was under control, but not quite what we would call remission.

Perhaps interestingly, my first few nephrologists never attempted prednisone with cyclosporine, which is a commonly used treatment protocol for MN. The rationale was that due to being overweight, the prednisone could cause further weight gain.

When I was around 20 years old, we tried rituximab for about a week or two. I did not have many side effects that I could point to from this medication other than to say I was given high doses of Benadryl to try to ward off any allergic reaction.

Eric (03:31:54):

The Benadryl made me very tired and unfortunately, we didn't achieve our mission but we were able to reduce my cyclosporine from 250 milligrams every 12 hours to over 150.

I began a serious diet around 2011 and lost nearly a hundred pounds over a year or two by eating lots of vegetables and calorie counting. After losing about 60 pounds, my labs showed signs of remission. I didn't have insurance at the time so we couldn't consider doing a biopsy. My nephrologist speculated that there was a small chance that MN could have gone away and the proteinuria might have been weight related. I was weaned off cyclosporine but unfortunately, I relapsed about two months later.

Losartan controlled my blood pressure, but with my lowered weight and the increased vegetable intake, the losartan caused my potassium to spike. And as a result, I had to follow a low potassium diet, which was extremely difficult to follow because most of the foods I ate to help with weight loss were high in potassium. And I eventually began gaining weight once I started substituting more unhealthy foods.

Between 2017 and 2019, my treatment remained the same, besides the short remission, though with low levels of proteinuria and blood creatinine levels that fluctuated from normal to high. The doses of losartan and the two or so additional blood pressure medications – they did adjustment when my blood pressure fluctuated too much. At its worse, the blood pressure reached 150 over 90 in the office and lower at home. Edema typically in my legs never fully went away. The cyclosporine also typically caused nausea within an hour of taking the dose, even when I took it with food.

Gout has been a recurring issue for me throughout my disease. When I received my undergraduate degree, I walked across the stage on crutches because of the gout flare. In 2019 because of the recurring gout, I was prescribed a daily dose of 10 milligrams of prednisone and a hundred milligrams of allopurinol. Prednisone caused some sleep issues so I started taking it early in the morning, which helped. I also noticed I was more hungry than normal.

Soon after starting prednisone, I began moving towards remission, the PLA2R tests and related labs were within normal limits, so I was weaned off the prednisone and then the cyclosporine. That was almost a year ago and this is the longest I've ever been in remission.

Besides allopurinol, I currently take losartan, chlorthalidone and diltiazem to control my blood pressure which has been in a good range for a while.

Eric (03:34:20):

Finally, the mental health effects of my MN are the single most important aspect of my disease experience, especially when I was young, but they were never treated. Being diagnosed with such a serious and rare illness at a young age forced me to confront my mortality before my brain was ready.

My mental health suffered enormously. I was 15. And when my friends were worried about what they were getting for Christmas, I was trying to figure out how we can afford medications or whether or not I was on my way to kidney failure and ultimately death. The disease definitely put a dark cloud over my teenage years and beyond. I take Lexapro now to help manage my anxiety and it changed my life.

I really wish the patient's mental health played a larger role in treatment because it's just as important as treating the physical symptoms of membranous nephropathy.

Thank you.

James Valentine, JD, MHS (03:35:19):

Incredible. Thank you, Eric, and our entire panel number two for sharing your treatment journeys and so much more than that embedded in sharing those experiences. Exactly what we needed to hear.

And we'll be now expanding on that. And this is our second opportunity to bring in all of you and our live audience, individuals living with MN, direct caregivers and care partners for that. To get us all thinking

about these different treatment approaches, which is of course, this topic that we're continuing to discuss.

We're going to go to a pair of polling questions to start us off. So this is your chance to open that phone or to open up your phone and go to that browser that you've had or go to that tab in your web browser on your computer. If you just joined us, if you're a patient or a caregiver, we invite you to answer all of these polling questions throughout the session at PollEV.com/PFDD.

James Valentine, JD, MHS (03:36:19):

Our first question for you this afternoon is, we want to get a sense of the different medications that you use or have used for your MN. And here, we want you to select all that apply. So here the options are A an ACE and ARB, a beta blocker or diuretic sometimes referred to as a water pill or some other drug for your blood pressure, B allopurinol for gout or high uric acid, C a statin or some other drug that you're taking for cholesterol, D VELTASSA or some other drug that you're taking for high potassium, E sevelamer or some other drug that you're taking for high phosphate, F antidepressant or antianxiety drugs, G drugs affecting immune system such as anti-inflammatories or immunosuppressants, H some other medication including non-prescription medications that you're taking for your MN or have taken.

James Valentine, JD, MHS (03:37:17):

And I, if you have not taken a medication for your MN, select I. So these, as a reminder, we're seeing percentages displayed. These are percentages of responses like in the morning when a polling question allows for more than one option to be selected. It's not the percentage of people that are being shown, but the percentage of total responses. So think of these as rankings, when we see the bars here on the slide. So, I want to welcome you all into selecting all those different medications that you or your loved one either currently use or have used to help treat your MN and its symptoms.

James Valentine, JD, MHS (03:38:10):

So I'll give you a few more moments here to get in this question. We want to make sure everyone is in the polling system for the afternoon session. As it stands it looks like blood pressure medications are the most prevalent medication being used in our audience today, followed by drugs for cholesterol. And after that, anti-inflammatories and immunosuppressants. We do have also see fairly high rates of antidepressant and anti-anxiety drug use, as well as other things that are not listed on this slide.

So we certainly want to hear from you, hear what it is you've tried, whether you're using it now, or you've used it in the past, we're all past. We're also seeing for B, some people reporting that they're on medications for their gout or high uric acid. No one is reporting that they're on drugs for high potassium or high phosphate. And no one is reporting that they are not taking any medication at this time.

James Valentine, JD, MHS (03:39:12):

So if we move to our next polling question, so thinking about the treatments that you're using, we want to know how well have your treatments reduce the most significant symptoms of your disease. The options are: A very well, B moderately well, C somewhat, D not at all, or E you do not currently take any treatments for your MN. So please think about this. Pick the response option that best reflects how well these your current treatments are reducing the most significant symptoms of your disease. Give you a few more moments here.

So as it stands, it looks like the majority of our audience is reporting – about two thirds reporting that their current treatments are helping moderately well manage their symptoms. And then we're seeing

after that a more of a minority, either reporting that it's helping very well or only somewhat. No one has reported that their treatments have – do not help at all.

James Valentine, JD, MHS (03:40:32):

And we do have a few people who are not currently taking any treatments.

So when you're thinking about this, whatever made you select the response option that you selected, we want to know why you picked that. When it's helping moderately well, what does that mean in your mind? And so, we want you to reflect on that.

And to that point, I want to invite you to call in and help share your impressions and treatment experiences. So as with this morning, you can call in that phone number for you is +1 703-844-3231. Again, dial in at +1 703-844-3231. We'll get you in the queue, just let us know the topic you'd like to share. And we will invite you to share that live. And we'll have a little bit of a discussion.

But to expand now we want to – I want to welcome our Zoom panel who's joined us today – some of your peers in the MN community who are going to also be sharing their experiences with treatments on this panel.

So if I could start with Katrina, as you were thinking about those treatment approaches, maybe let's start with what has worked the best or maybe something that has helped at all. Thinking through your list of not only just medical treatments, which was more of the focus of that one polling question, it could be any treatment approach, even medical procedures, it could be more holistic or alternative approaches, it could be diet, exercise, even lifestyle modifications, kind of everything's on the table, so to speak. So, Katrina let's – we'd love to hear from you.

Katrina (03:42:20):

Well, mine was all of the above. I haven't been on too many medications, mainly high blood pressure. We've been monitoring the progression of the disease. I have tried weight management, diet management and holistic approaches. My weight would go up and down. I'd always gain back a little bit more than I lost. Recently in May we took a fairly drastic step. I just had a gastric sleeve done. Okay. And I have found that the weight is definitely coming off. I have had to really increase my protein intake, but the swelling and edema is dramatically reduced. As in almost gone. So, right now, along with exercise and diet, I would say that was one of the more beneficial things that I've done.

Katrina (03:43:23):

We just had a full workup done. And we're noticing some of the values I'm gaining there. Do another workup in eight months and we're hoping to possibly go into a partial remission, but that's the goal right now. I'm not sure what else other than diet and exercise at this stage. I did kind of go kind of extreme from the, from the start but I didn't see where anything was working or reversing. And the potential side effects of the medications that were being used were scary enough that it was not worth it to me.

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

Yeah. So if you don't mind Katrina, I'd like to ask you a little bit. You've talked about the weight really coming off. I want to get a sense of what that has meant for you. I don't know if you're able to maybe share an example of when you had the weight on, how that impacted your life and maybe how that compares to now, even where you're at this moment in time.

Katrina (03:44:27):

Okay. I'm still fairly early on in that journey. As I said, my surgery was beginning of May. So I am fairly early on, I have lost 53 pounds and I have gone from it being a battle to get up in the morning. I have to get up four, five times a night. That's actually down to about three right now, which is yeah. A big bonus. I'm actually getting some sleep these days, rather than getting up and down and I can move.

Katrina (03:44:57):

I can walk, I can walk my dog rather than just avoiding that. I've actually been asked to slow down rather than the reverse happening. Historically, it's me tailing and dragging along. And it's not that I'm running or racing. It's just, I'm enjoying moving. And that is really talk about a goal and a win. That is a win for me – that I'm able to move. I'm able to live my life. I'm able to play with the grandkids rather than just watching them, It's been a great three months. I'm looking forward to the rest and hopefully going into remission. But I don't think we'll be taking a look at medications and leaving all my options open there.

James Valentine, JD, MHS (03:45:56):

Yeah. This is incredibly helpful. So thank you so much Katrina for sharing that kind of a positive treatment experience that you're currently in the middle of experiencing. So, it's so wonderful to hear that.

Why don't we come over to Taylor on this same topic of thinking through all of the treatments that you've tried or currently employing. What seems to have been the most successful?

Taylor (03:46:23):

Hey, everybody. I am Taylor. I'm from Parkersburg, West Virginia. I'm a registered nurse and I've had membranous since I was 19. I'm almost 24. As far as treatments go,. we tried just about everything to avoid cyclophosphamide because I'm so young and we didn't know necessarily how that was going to affect me in the future. So we tried some ARBs, the immunosuppressants, just diuretics, and symptom management, blood pressure medication. I did resort to cyclophosphamide which essentially did put me into remission, but the side effects of that were absolutely terrible with the nausea, I lost a bunch of my hair, just not being able to do what a normal 20-year-old should be able to do. I couldn't fit in my clothes because I was so swollen. I was in nursing school at the time as well. So, keeping up with 12-hour clinicals and going home and studying was very difficult. I required a lot of sleep.

James Valentine, JD, MHS (03:47:42):

So that's a lot to have to manage and certainly dealing with this while studying to be a nurse. That's a lot to manage. And looking back at all of that, did anything provide you kind of relief from some of – you mentioned the swelling. Even if it didn't help a lot, even if something sometimes helps a little, it's good to know about that too.

Taylor (03:48:13):

Yeah. I feel like almost everything that helped me sort of hurt me in a way as well. I would take the Lasix, which helped tremendously with. I had gained 35 pounds and I lost it very quickly with the Lasix but I was constantly going to the bathroom, I had to take breaks and I just feel like everything that I tried to help me also hurt me in a way.

James Valentine, JD, MHS (03:48:40):

Right. Well, thank you Taylor for sharing that. I think that's a theme that we've already heard quite a bit, but we really want to hear these personal experiences. Oftentimes things help, but they hurt, as you said. And I so appreciate you sharing that. I see that we have a phone caller. We have Mary from New York who wants to share some of her treatment and experiences. So we'd like to bring her into the conversation. So we'd like to welcome Mary, are you with us?

Mary (03:49:16):

Hi there. Yeah. Yes. How are you?

James Valentine, JD, MHS (03:49:18):

Hi, welcome. We'd love to hear some of your treatment experiences and have a dialogue about that.

Mary (03:49:26):

It's great. Thank you. I started with prednisone and as I'm sure you are all familiar, it's very intense drug. It allows you to get very little sleep. You're up late into the night. Then the sleep is not quality. When you do sleep it's like having 20 cups of coffee on a hundred milligrams per day. So, naturally if you're trying to hold down a job, and I was working on Wall Street at the time when I was diagnosed, it – yeah, it's virtually impossible because you're not sleeping. So how do you function without sleep? So it's – from a treatment standpoint, the steroids was extremely difficult, obviously not to mention the weekend and when you're on them long-term, my cholesterol shot up.

Mary (03:50:24):

There were things that were going wrong. Obviously, there could be bone density issues if you're not on top of taking calcium and vitamin D and even still, it can still affect long-term. So it really wasn't a long-term solution. Although I did cycle on and off of them. I tried cyclosporine, as well and also on the prednisone, I – not to mention the – what it does to your memory and your cognition and your mood. It's just a very difficult drug to function on.

James Valentine, JD, MHS (03:51:04):

And Mary when you -

Mary (03:51:05):

But then I -

James Valentine, JD, MHS (03:51:07):

That's very important for us to hear those experiences you have had with the steroids. Is that – even with those side effects, is that something that you continue to take or did you have to – ultimately, did you have to decide to stop taking it given some of those things you were experiencing?

Mary (03:51:27):

Well, it's a great question, but the sad truth is that that happens to be the lesser of the evils that are the current treatment options that are out there, which are very limited at this time. The current treatment options, the side effects are not as obvious, but they're scarier because they all – and they're just worse in some ways to where I did resort back to taking the steroids because the other options were so terrible.

James Valentine, JD, MHS (03:52:04):

Sure. And do you mind mentioning what you tried but – and then had to go back, just so we know.

Mary (03:52:06):

Yep. So I did cyclosporine and that was very high maintenance in terms of monitoring to make sure it didn't get over certain levels, took a lot of time and energy to even make sure and even when it wasn't in toxic levels, I was getting very bad migraines. I had been following my labs for 10 years. My lymph cells were doing some very strange things.

Mary (03:52:32):

There was a lot of activity in my lymphatic system. I was having night sweats, things of that nature. It's in the label that it causes lymphoma. I happened to know someone personally taking cyclosporine that got lymphoma. I mean that could be obviously anecdotal, but the point is, it is the label, so just taking this stuff is very scary because with the toxicity of this drug and what it can do, I would much rather go with something like a prednisone where you at least you know what you're getting with that.

James Valentine, JD, MHS (03:53:11):

I see.

Mary (03:53:11):

You know what to expect. You know you might have some [inaudible 03:53:14]

James Valentine, JD, MHS (03:53:17):

Right. Well, Mary, thank you so much for calling and sharing that. I think it's really important to hear that there are these downsides to existing treatments and as you put it, it's kind of you're choosing between the kind of different sets of negative consequences and picking the lesser of the two. So thank you so much for sharing that perspective.

I want to come back to our Zoom panel here for just a minute and still on focusing on treatment successes, see with if – from a show of hands, if anyone on the panel wants to share something that's worked for them or has helped even a little bit for them, before we move on to some other questions that we have for you. Yes, Eileen

Eileen (03:54:10):

I'm Eileen from Pennsylvania and for me so far, the rituximab has been the one that has put me in remission. So, that's the best drug that I've had so far. I was on the cyclosporine previously. That put me in a partial remission, but until I did the rituximab, that's the one that actually put me through to the remission.

James Valentine, JD, MHS (03:54:37):

Yeah. Can you maybe talk about that treatment decision to switch from cyclosporine to rituximab? Was it – you were in partial remission, you weren't moving any lower and so you made that decision, or were you starting maybe to go in the opposite direction, and maybe just what were the considerations that you had to make you make that switch?

Eileen (03:55:01):

It just felt like with me, it was like every two years I would be coming out of remission. So, it was like each time I came out of remission, there was more damage being done to my kidney. And my doctor and I both decided that, try the rituximab since that has worked, now I'm on a maintenance type protocol with it that I get it every nine months. And that so far has been working and has not reduced my kidney function anymore.

James Valentine, JD, MHS (03:55:30):

And how long have you been on rituximab and the maintenance?

Eileen (03:55:35):

So, I started back in 2018 with the rituximab and now it's been like every year now, every nine months I go.

James Valentine, JD, MHS (03:55:43):

And how long were you living with MN before your diagnosis, maybe before finally getting to rituximab?

Eileen (03:55:51):

I was about eight years.

James Valentine, JD, MHS (03:55:54):

Eight years. Okay.

Eileen (03:55:55):

Yes.

James Valentine, JD, MHS (03:55:56):

And so over eight years nothing has helped to the same degree rituximab has now.

Eileen (03:56:00):

Exactly.

James Valentine, JD, MHS (03:56:02):

Sure. Well, thank you so much Eileen for sharing that.

So I want to also expand the conversation. We've already – I think it's inherent in talking about treatment approaches. We've been hearing about some of the downsides of these treatments that you have. So we want to hear both how much it's helped, but also maybe things that haven't worked or things that work and provide still some downsides that either you tolerate or maybe you've given up a treatment that's worked because the side effects are too much to bear.

I'd like to perhaps start with Daniel on this. Thinking through all the treatments you've tried, is there something that hasn't been so great of a treatment experience for you?

Daniel (03:56:49):

Currently well, thanks for having me, Dan Holmes out of Palm Bay, Florida. I have been battling membranous nephropathy now for a year and a half. So I'm a little new to the game, but I feel like a seasoned veteran because I've been through so much in just 18 short months. I have almost abandoned all of my treatment programs because of the side effects that they entail. So, just like Taylor said, right, you take something and it causes something else. You take a water pill and you're up all night peeing or you can't get sleep so then you need to take a pill to go to sleep better. Then you take – so you – I found myself taking pills to take pills which made no sense to me. I came very in touch with my nephrologists, my doctors. I'm a veteran so I have the VA behind me as well, monitoring my labs.

Daniel (03:57:55):

And basically, we got to a point where my kidney function is above 60. It's really good, actually, right now. A lot of my labs are really good where they should be and we've made the decision to stop the cyclosporine. So I've been off of that now a couple of months. Right now, the only medical regimen I'm on is water pills and that's to help alleviate and drain some of the water storage, of course, maintaining a low sodium diet and things like that. But I know this thing is going to come and go. There's going to be waves, right. There's going to be ups and downs and partial remissions. I could not prove to myself that the treatment plans that I was on were actually working or not. I knew that the side effects I had were created by the medications, but I could not prove the opposite.

Daniel (03:58:57):

So I did not. And nobody could prove it to me either that, hey, the cyclosporine is what has got your eGFR to where it is today. Well, let's stop the cyclosporine and see what happens. So we've done that now for several months and the eGFR maintains pretty high. Am I one of those one in three that could go into a spontaneous remission? Possibly, hopefully. That would be awesome. But, again, without taking the medication out of the mix, I won't know.

So at this point in my treatment plan, we've – me and my medical team have basically decided to pull away from a lot of the medications and then evaluate and see what happens and see what's going on. I still deal with the edema. I still have the proteinuria and those kinds of things but the blood pressure is normal. The eGFRs are normal. The white blood cell counts are normal. Those things are normal. You still deal with the water pill side effects of the cramping, the significant charley horses that you get when you take water pills. So you got to take potassium or eat a higher potassium diet to counteract some of those kinds of affects as well. But everything you put in your body has got an opposite reaction that you have to fight and it's just a never-ending story.

James Valentine, JD, MHS (04:00:26):

Yeah. Daniel, can you maybe help us get a picture of, when you came off of some of these medications because of the side effects and this taking pills to – other medicines to help with the side effects, have you noticed any improvements in your quality of life? What has that looked like by coming off those things?

Daniel (04:00:50):

Yeah, I have and I haven't. Right. So like you come off of the prednisone and I dealt with about six months of significant body pain because the prednisone I was taking at such a high dosage had masked so many different things. I was new to Florida. When I moved here, I was on prednisone. I didn't know that I had allergies here. You stop taking the prednisone and boom, you have allergies to things that you never knew you had before. So you deal with those kinds of things. I got myself onto Gabapentin

because of the chronic pain that you deal with when you come off of a steroid but I have to go to work and I have to drive and I have to coach football and I have to do these different things that you can't just be on a narcotic pain med forever.

Daniel (04:01:43):

Right. So, I was on that. Being off the medication, yes, I can go to the beach, right. I can have a great day in the sun and not have to worry about the cyclosporine making me feel completely immobilized. I couldn't stand out in the sun for more than 10 minutes. You would throw up and you would feel dizzy and you get these weird stomach cramps. I don't have that anymore.

So the enjoyment of being able to go to the beach. I live right next to some of the best beaches in the planet and being able to go there and enjoy that, has given me and my family some satisfaction, but there's always how long is it going to last? What's next? So we just kind of take it day by day and enjoy what you can take now. You know what I mean?

James Valentine, JD, MHS (04:02:36):

Yeah. Now, thank you so much Daniel. It sounds like it's not an easy landscape to navigate and with knowing which things to try to stay on, it sounds like there's really no right answer and so thank you for sharing that.

I do see that on the topic of treatment successes that we did have some written comments come in on that. So, before we go too far down the road or talk about also the downsides, we want to check in with David on some of the things that have helped for those that have been writing in with comments.

David Feldman, PhD (04:03:10):

Right, James. Betty from Massachusetts writes, "I made vast dietary changes after learning that I was now a kidney patient. I learned about the importance of water, exercise and I have been on a plant-based diet for four years, which has improved my overall health. I then saw a renal dietician for further suggestions and I avoid NSAIDs."

Nina from Texas writes, "I work out every day to stay in shape and eat very little protein and salt which helps a great deal."

And Janet from Washington writes, "Although the rituximab treatment was successful and I'm technically in remission, I still have reduced kidney function, which was stable, but has started to drop recently."

James Valentine, JD, MHS (04:03:56):

Sure. Well, thank you all for writing in with that. Please continue to write in whether it's treatment successes, treatment downsides. We want to hear about your treatment experiences. Similarly, if you would like to call in, we don't mind you to call in at +1 703-844-3231. Again, that's +1 703-844-3231.

I see we have a caller who would like to share some of her experiences with treatments that she's tried. We have Jamie from Maine. So I'd like to welcome Jamie and see, Jamie, are you with us?

Jamie (04:04:32):

I am. Thank you.

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

Hi, welcome.

Jamie (04:04:37):

Hi. So, I have – the cycle of meds I was on as we started with prednisone, then it was prednisone and tacrolimus. And then I ended up on ritux and every six months I get four infusions. And that's finally what worked, but the prednisone made me gain a hundred pounds because I was on the max dose for so long it caused a tendon to rupture. They've had to completely reconstruct my foot and all these things, but the Rituxan is finally what got me into remission. It's horrible that prednisone is the first line of defense. You know what I mean?

James Valentine, JD, MHS (04:05:26):

Yeah. Yeah. Is that something that you're still on or have you discontinued prednisone now?

Jamie (04:05:35):

I discontinued it. Now, when I'm on it, it's during my infusions. They give me 50 milligrams of prednisone and then they give me Benadryl and Tylenol. Then, I get the Rituxan infusion.

James Valentine, JD, MHS (04:05:49):

I see.

Jamie (04:05:51):

But even then, I still have, what we call, chemo brain. Because by the time I'm finally feeling pretty normal again, I have another infusion scheduled. With a four-year-old daughter, it's really hard to keep up when you have this condition. You're constantly sick because of your medication. It's almost like what's the lesser of two evils constantly.

James Valentine, JD, MHS (04:06:13):

Right. That chemo brain you described; can you help me understand that? Is there an example that maybe you can give in your daily life of what that looks like?

Jamie (04:06:26):

Yeah. I can have something in my hand; it'll be a glass of milk and I'll call it a couch. I'll be driving to my parents' house and all of a sudden, I'm like, "How did I get here?" Things like that. I forget plans. I used to have a memory where I could remember everything. Now I'll look at someone and I know their name, but I can't get it out.

James Valentine, JD, MHS (04:06:54):

Wow. The chemo brain, is it most severe right after your infusion and it slowly gets better, or right up until the time of your next infusion? Or is it really variable or hard to predict?

Jamie (04:07:12):

It can be difficult to predict, but it definitely usually is much worse, much more acute during my infusions and just after my infusion. But the sickness from the infusion – that can even take a couple of months to wear off.

James Valentine, JD, MHS (04:07:34):

I see. Well, Jamie, thank you so much for sharing this. Not something we've heard a lot about yet so far. Really want to encourage others to call in, write in as well. In fact, I see we have some written comments on some treatment downsides as well. I want to see, David, what's standing out to you?

David Feldman, PhD (04:07:56):

Yeah. Mark from Massachusetts is just basically concerned about having to be on multiple medications. Obviously, because nothing's really working that well.

Seferiana from Seattle writes, "I had a few treatments that made things a bit better, but never went into remission."

Charles from North Carolina writes, "In spite of my proteinuria, which has been as high as 40 grams per day, which is very high, though it seldom stays that high for long, many of my symptoms have been controlled using statins and ACE inhibitor, and an SSRI. That's a selective serotonin reuptake inhibitor. However, these drugs are hard on the body and the ACE inhibitor causes some dizziness, and low blood pressure for me."

James Valentine, JD, MHS (04:08:45):

Sure.

David Feldman, PhD (04:08:45):

All lots of important side effects.

James Valentine, JD, MHS (04:08:47):

Yes. Important to hear these, I know. Not only are there lots of different side effects we've been hearing about, but they impact people differently. It's so important to hear that there's personal impacts and stories. Again, encourage you to call in if you have a treatment experience to share, good or bad, or mixed. That number is 1703-844-3231.

James Valentine, JD, MHS (04:09:13):

But want to come back to our panel here exploring existing treatment options a little bit more with you. Maybe come to Eileen, as you're thinking about some of the most significant downsides that you've experienced, is there one that sticks out? Something that maybe has had the greatest impact on your daily life?

Eileen (04:09:36):

I remember when I was on the cyclosporine. Taking that, the main side effect that I had was hair growth on my face. Being a female, that was very, very embarrassing. Swollen gums, that was another side effect that I had. I don't know if anybody else had that, but that was two of the main things that I had to deal with.

James Valentine, JD, MHS (04:10:01):

Sure. Were those things that were there and pretty persistent? Maybe, can you share an example of a time that you remember it having an impact in your life?

Eileen (04:10:17):

Well basically, every day looking in the mirror, it had an impact on my life, at least for me. I don't know if anybody else would even say something to you that it was that obvious, but to me it was so obvious.

James Valentine, JD, MHS (04:10:29):

Right. Sure. Thank you, Eileen, for sharing that. Taylor, how about you on this topic? Anything that sticks out as the biggest downside that you've encountered in trying different treatments?

Taylor (04:10:46):

A lot of these treatments have really nasty side effects. Everything was just thrown at me because we were so desperately wanting something to work. But as I had mentioned earlier, what impacted me most emotionally was when I took the cyclophosphamide, my hair falling out. Sad truth, I guess I have an emotional bond with my hair; that falling out impacted me a lot.

Just not being able to do things that I had done before. I was pretty active. The medication, it makes you very tired. As the caller mentioned a little bit ago, the brain fog. As I had mentioned earlier, I was in nursing school. I had to be able to remember the things that I was learning and a lot of times I couldn't because of the medication.

James Valentine, JD, MHS (04:11:56):

Wow. Yeah. All of those are really significant downsides. When you said that maybe you got an attachment to your hair, that it has a really big impact on you, did that affect you socially? Did that affect maybe your mental health? Help me understand when you say it had a really big impact. What was that impact?

Taylor (04:12:23):

It definitely affected me. My mental health made me very self- conscious about my image. Also, going out with my friends, I was constantly trying to cover up the spots in my hair that were missing. Definitely impacted my mental health the most.

James Valentine, JD, MHS (04:12:47):

Yeah. Thank you for sharing that. I know it's not always easy to acknowledge that aspect. To round out our Zoom panel, I want to also ask Katrina this same question. Thinking about the downsides, is there one that has had the greatest impact on your life as you think through different treatments that you've experienced?

Katrina (04:13:12):

The limit, the limiting of my life. I wasn't able to go out and do anything. Let me also just say that being female, the hair on the face and the loss of hair, the self-image that a person gets, it's affected by that greatly and that affects every aspect of our lives. My goodness. My goodness, girls. The weight gain also affects that. It's not just physical; it is mental. There is the swelling and the bloating. You end up feeling like the Stay-Puft guy and when it's hard to physically get moving to try to correct it. Then with the hair issues, it's really hard to live your life. Yeah. I guess that's all I have to say about that.

James Valentine, JD, MHS (04:14:14):

No, that's a lot to say and it's all very important to hear. Thank you, Katrina, for adding to that. I think it's important to hear that it's not just providing physical limitations, energy. You've talked a lot about lack of sleep and other impacts impacting physical or activities in daily life, but it really is emotional and psychological, too.

Katrina (04:14:39):

Yes.

James Valentine, JD, MHS (04:14:40):

Thank you. I see we have a phone caller. Eric from Alabama who actually wants to share one of his treatment experiences, a positive treatment experience. We'd like to welcome Eric to the show. See, Eric, are you with us?

Eric (04:14:56):

I'm here.

James Valentine, JD, MHS (04:14:57):

Welcome. We'd love to hear the treatment experience that you were hoping to share.

Eric (04:15:04):

Sure. There's been a lot of talk about prednisone and all of the things that go along with that. I was on cyclosporine for many years. Mostly under control; never really a remission or anything to that extent. We never really attempted using prednisone along with that, although my understanding is that's a pretty common thing that's done.

James Valentine, JD, MHS (04:15:30):

Sure.

Eric (04:15:31):

The combination of the two when I started it, it was very quick after that. Probably my next appointment, a few months later, we started seeing reductions in the proteinuria. We started seeing the PLA2R test, came back as negative. I very quickly moved towards remission to where I was eventually taken off cyclosporine, which is awesome, given the long-term side effects. You worry about that. I've been in remission for a year now and I've never been in remission for longer than a couple months max. I guess that's the point that I wanted to hammer home is it really worked for me. Obviously, now that I've seen that that does seem to have helped, I wish that would have been something we would have at least given a shot a number of years ago just to see if there would have been some success.

James Valentine, JD, MHS (04:16:25):

Sure. Just to make sure I understand. You were able to go off the cyclosporine and are still on prednisone, or have you tapered off that as well?

Eric (04:16:37):

No. I'm sorry. I left that piece out. We actually tapered both of them. The only thing I really take now are some blood pressure medications and a few others, but I'm off both prednisone and cyclosporine for a year now.

James Valentine, JD, MHS (04:16:49):

Wow. That's wonderful to hear. When you were on those two, obviously there's the long-term effects that you referenced that are always a concern. Did you experience some of the more acute side effects as well? It sounds like maybe you're able to tolerate those if you did.

Eric (04:17:09):

I did. It was certainly worse early on in the cyclosporine treatment because I was on higher doses initially to try and get everything under control. There's a lot of things that folks have mentioned with cyclosporine: nausea, cramps, things like that. All the side effects that come from that. We reduced the dose a little bit over time and that did help as things were under control. I was able to more or less remain stable. I think that helped to get me to a point where the actual side effects weren't as bad, perhaps as they could have been, but yeah.

James Valentine, JD, MHS (04:17:56):

Yeah. Well, Eric, you've been so gracious to let me probe. If you don't mind me probing, one more question for you. Now that you are in remission, have you noticed corresponding changes in the direct, not side effects, but direct symptoms of your MN? I don't know what you might've been experiencing beforehand. But since this has got you into remission, has that also helped with the other symptoms and health effects of MN that you might've been experiencing prior to remission?

Eric (04:18:33):

I think so. Definitely. The obvious physical side effects like edema and foamy urine, things like that, they're just not around anymore. The cyclosporine used to give me upset stomach anytime I would take it; so every single day, twice a day, no matter if I took food with it or whatever. I don't have any more; that's gone. The side effects that some folks have talked about, not being able to sleep with prednisone and perhaps more hunger, that sort of thing, that's gone. Just in general, I feel better mentally because it's like, yeah, there's a good chance that it could come back one day. It just feels good for right now to be in remission and not having to take those medications that I've had to take forever. Just enjoying it right now.

James Valentine, JD, MHS (04:19:22):

Yeah. Well, Eric, thank you so, so much for calling in and having this conversation about your treatment journey. I'm so glad for you are where you are right now. Thank you for sharing that.

Comments are just rolling in with regard to this discussion around treatment experiences and particularly the topic we've more recently gone to, which is the downsides of some of the existing treatments. David, I want to see and check in with you again.

David Feldman, PhD (04:19:53):

Yeah. Amy from Illinois writes, "I was started on cyclophosphamide and prednisone as well as Lasix, a blood thinner, and a blood pressure medication, and a cholesterol medicine. My blood pressure hasn't been affected by this disease; so I had to stop taking that because I was getting dizzy and fainting spells.

I also had to stop taking cyclophosphamide because I had a rare bladder reaction to this medication about three months into it. I was then put on tacrolimus. I was not working during my treatments and I don't think I could have with all the side effects of the drugs, and the disease itself."

David Feldman, PhD (04:20:37):

Amy from Illinois writes, "I was on prednisone and cyclophosphamide. As a female, they messed up my period and I'm still not over those two and a half years later. I lost it for six months." She lost her period for six months. "When it came back, it was irregular and abnormal. I thought I had gone into early menopause."

Safa from California writes, "While I was on steroids, my hands shook so much that while taking notes or drawing a picture, I would hide my right hand with my left to avoid having others see and ask questions. Even though I was weaned off steroids a couple of years ago, the hand tremors have never gone away. I still struggle with simple tasks like painting my nails and sometimes even holding a spoon filled with liquid because the tremors prevent my hands from ever being still."

James Valentine, JD, MHS (04:21:32):

Wow. Yeah. Incredible. Still more things we'd not yet heard. So, so important to have those experiences be shared today. I want to continue to have these treatment experiences shared and come in, phoned in and comments, but I would want to continue to broaden the dialogue as well while we have everyone today.

As I mentioned very early, one thing and often particularly in rare diseases, that when we're thinking about treatments, we're also thinking about trials and participating in clinical trials as a possible way to supplement the current standard of care. Obviously, that has also the important benefit of helping us understand the benefit and risk profile of investigational treatments for our community, but may also be part of your own personal strategy for thinking about your approach to treatment.

James Valentine, JD, MHS (04:22:32):

To get us thinking about this topic of participating in clinical trials and your thoughts in decision-making around that, I'd like to go to a pair of polling questions that we have on this topic. This is a chance to pull your phone back out, open up the browser, go to that tab that you have opened. If you're following along on your computer, go to PollEV.com/PFDD and join us in this third polling question for this session, which is on factors that you would consider for participating in trials.

The specific question we have for you is: of the following factors related to a test drug or an investigational drug that's being studied in a clinical trial, select up to five that are most important to your decision about participating in a clinical trial.

These factors that we want you to consider are: A, whether you might get placebo or a sugar pill; B, whether you may need to stop your current treatment; C, potential side effects of the new drug; D, how the drug is taken, whether it's by mouth, intravenous injection, or a subcutaneous injection in the muscle, E, in earlier trials, was the study drug effective for specific benefits that are most meaningful to you; F, knowing if you can make the commitment to participate in the trial, knowing that there are study site visits, other tests, and procedures that you may need to undergo; G, the frequency of exam appointments more specifically; H, distance to the trial site; I, the length or duration of the trial; J, whether a kidney biopsy is required; K, negative things that you've heard about clinical trials more broadly; L, whether your own nephrologist recommends enrolling in the trial; or M, some other factor that's not listed on this slide that would be important to your decision to participate in a clinical trial.

Again, there's a lot of options here. We want you to try to narrow this down to the top five most important factors to you that will inform your decision about whether to participate in a clinical trial.

James Valentine, JD, MHS (04:24:57):

We'll give you a few moments to think about this. I know there's a lot of options for important factors.

As it stands, it looks like the one that is the top factor that would be important to our audience today is what are the potential side effects of a new drug. That's likely, I think, informed by the fact that we've heard so much about all of the side effects that existing drugs provide and a desire to perhaps avoid drugs with similar degrees of side effects. We also see a bit major consideration whether you might get placebo or sugar pill. Participating in the trial, you might not actually, at least for the randomized proportion of the trial, get the investigational drug. Then after that, we're seeing whether you need to stop your current treatments and whether your nephrologist recommends it as two major factors for you. I would say maybe the fifth most prevalent response is whether in earlier trials, this study drug was effective for the specific benefits that are most important to you.

James Valentine, JD, MHS (04:26:06):

What we're seeing though is, across the board, many of these are in your top five. We're only seeing a couple of options that aren't in some people's top five.

We'd like for you to call in and share about what it is that would be most important to you in considering whether you would participate in a clinical trial. Even if maybe you aren't eligible right now, I know many of you have talked about being in remission. Perhaps you can think about in a situation where you have a relapse, would you consider a trial? If so, what factors would be important to you?

James Valentine, JD, MHS (04:26:44):

But we do have another polling question on this topic. Let's move to our next polling question. This is specific to the biopsy factor. What we want to know is would you enroll in a clinical trial if it required any of the following frequencies of kidney biopsy. We'd like you to select the greatest number of biopsies that you would be willing to accept.

The options here are: A, no kidney biopsy, so you would never enroll in a trial unless there was no biopsy required; B, you would enroll if there was only one kidney biopsy in a year; C, if there were two kidney biopsies in a year; or D, if there were three kidney biopsies in a year. What's the greatest number of biopsies that you would accept? We'll give you a few more moments to think about this.

James Valentine, JD, MHS (04:27:55):

All right. It looks like there's a bit of a spread here – different tolerance for kidney biopsy in order to participate. It looks like a little over a third of you would only tolerate one kidney biopsy per year and a little under a third of you would not accept any kidney biopsy within a year. Whereas about a third of you would either accept two or three kidney biopsies per year. We're seeing a spread there of different tolerance for number of kidney biopsies for participating in a trial.

James Valentine, JD, MHS (04:28:29):

I want to thank you for participating in these polling questions. Of course, we welcome treatment experiences still, but if you have something to share on your thoughts around participating in trials or maybe if you have participated in a trial, you can share that experience. We invite you to call in at 1703-844-3231. Again, 1703-844-3231. But I'm going to start this discussion with our panel. My understanding

is Taylor and Eileen, you have participated in observational clinical trials. No interventional drug as part of that, but you still had to commit to some degree of follow-up and perhaps testing. Maybe we can start with Taylor. As you were thinking about either participating in that trial or maybe a hypothetical drug trial, thinking about those factors in the polling questions that we posed, what would be most important to you or was most important to you, and why?

Taylor (04:29:38):

Well, I am in remission; no active disease right now. But if my symptoms were to come back and I would relapse on this disease, I think the important key points of a clinical trial for me would be A, reducing the symptoms because they are so intense. B, the accessibility of the medication. I had to travel a couple of hours away for my rituximab infusions when we tried those the first time. I would like that to be closer to home because I do have a life here and have to move on with my life. Then C, would be side effects of the drug. Again, with the rituximab infusion, I did have a pretty severe allergic reaction in the chair while getting my infusion, hives all at my face. I would like that to not happen again. If the drug had little side effects, that would obviously be a plus, too.

James Valentine, JD, MHS (04:30:41):

Sure. In fact, I guess the one point of that is if you did go into a relapse, you would be interested in participating in a potential clinical trial given those -

Taylor (04:30:53):

Right. I definitely would. I even picked up to three kidney biopsies a year because in all of my disease, the kidney biopsies were the easiest.

James Valentine, JD, MHS (04:31:05):

Wow.

Taylor (04:31:05):

As far as relating it to the symptoms and everything, it was one of the easier things that I did during those years that I was in active disease.

James Valentine, JD, MHS (04:31:14):

Right. Sure. Thank you, Taylor.

Eileen, maybe coming to you again, whether it's about your actual experience in a observational trial or the hypothetical clinical trial for investigational drug, what's important for you for participating in a study?

Eileen (04:31:33):

I just feel that the more people who actually do participate who have this disease, the better they can narrow down a drug that will actually work for everybody.

James Valentine, JD, MHS (04:31:45):

Yeah. Yeah. You would be interested in participating for that -

Eileen (04:31:52):

Absolutely.

James Valentine, JD, MHS (04:31:53):

- community for the greater good. Obviously, that is the key reason for doing studies. So important that people would be willing to participate and volunteer for that greater good.

Is there anything in terms of, if you were looking at a potential study, is there a deal breaker for you whether it's, you saw the list, to a certain degree of travel or number of visits, or biopsies that you would say, "Well, I really want to. I just can't do that"?

Eileen (04:32:25):

I would think the side effects would be the one for me; that would be the downfall.

James Valentine, JD, MHS (04:32:28):

Yeah. Would you be willing to tolerate any side effects? What's your tolerance for side effects?

Eileen (04:32:37):

There's usually a point that you'd like, "I can't do this anymore." You would try to tolerate it as much as you could. Then, once it's affecting your everyday life, then I would have to stop.

James Valentine, JD, MHS (04:32:48):

Sure. Sure. Well, thank you, Eileen. Daniel, would you be willing to consider a clinical trial at any point? At what point would you consider that?

Daniel (04:33:03):

Absolutely. Hundred percent. I would consider a clinical trial side effects. The current medication that's out there right now, you got to deal with every side effect on that list. I wouldn't really care about the side effects because if it's going to be for the greater good, if there's going to be some positive coming out of it, I'm good with that. You want to do a kidney biopsy three times a year? Let's get it done. It's trying to find the trials that are there. I've tried my hardest to involve myself in trials. I came up blank; I got nothing. [crosstalk 04:33:48]

James Valentine, JD, MHS (04:33:48):

Is that because you don't qualify or there's not been ones near you?

Daniel (04:33:55):

I don't see why I would not qualify. I'm membranous nephropathy, right? Why wouldn't I qualify if you're doing a membranous nephropathy trial? I've never been offered to get on a plane, to go fly anywhere, to go test, to do anything or talk to anybody, but yeah. Would I? Absolutely. I absolutely would.

James Valentine, JD, MHS (04:34:14):

Wonderful. Well, thank you, Daniel.

Katrina, do you have any thoughts on this topic of trials? Would you consider one if your disease was at a place that warranted it and what would that be for you? Is there anything that would be a deal breaker? We're just interested to hear your take. Oh. I think you're on mute still, Katrina.

Katrina (04:34:40):

I would definitely sign up for a trial. In fact, as soon as I was diagnosed, I went looking for a trial after being told about it. The one I found was a few states over. I was in Minnesota at the time. It had closed. It was nothing, but I still signed up. I think that's how you all contacted me, now that I'm out in Oregon.

Yes, definitely. I would be willing to talk to my nephrologist who would be my number one. Then, I would go side effects and effective. As far as the biopsy, I was thinking anywhere between one or three. I've only had one biopsy. It was not a pleasant experience, but if it's going to make life easier for myself or anyone else, sure.

James Valentine, JD, MHS (04:35:32):

Yeah. Well, thank you so much. Want to check in with David across any treatment experience, comments that have come in. I know we've covered so many different discussion questions. Things might be coming on in on different topics, but anything that you would like to share at this point?

David Feldman, PhD (04:35:51):

Yeah. Well, of course, for preferences for future-

James Valentine, JD, MHS (04:35:58):

Any pre-existing treatment experience topics at this moment?

David Feldman, PhD (04:36:03):

Yeah. Nina writes that, "MN is something I can never escape from because of all the drugs I take every morning and evening. I try and stay positive because it's so many worse things, but the drugs I will take and have remission cause other symptoms that are serious as well. It's not just about the kidneys."

James Valentine, JD, MHS (04:36:34):

Right.

David Feldman, PhD (04:36:34):

Alma writes, "My daughter takes an ACE inhibitor and she gets dizzy at times with the medication. She also gets nausea with medicine while at school and has to run to the bathroom because she feels like throwing up."

Susan from California says she has been on several medications and has suffered with uncontrolled blood pressure, edema, and cholesterol. " I tried several statins for the cholesterol. However, myalgia, muscle pain, was so severe I could not tolerate them. Living with MN been hard on my self-esteem due to edema and fatigue."

James Valentine, JD, MHS (04:37:15):

Sure. Yeah. So many treatment experiences and we're continuing to get more of these experiences here as David was sharing with downsides. I want to really thank you all for those comments. If you haven't

heard your comment read, I promise you we are getting them. There's been quite a few that have come in and we will be including all of those in the Voice of the Patient report.

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

At this point, I want to move to our final topic for this for the day. Now that we've explored all of these approaches to treatment that you've tried, things that you've tried and stopped maybe because of some side effects, maybe because you reached remission, things that you're currently on, we want to now look towards the future and think about what is it that you still need, and what are your priorities for those future needs.

For our final polling question of the day, we're going to get all of you thinking about this topic. For one last time, please pull out that phone, open up your browser, go to that tab. If you're following along on your computer, go to PollEV.com/PFDD.

We have a question for you on deciding on what it is that you would most want from a future treatment. Here we want to know without considering the side effects of a drug, which one of the following would be most important to you in a future therapy?

James Valentine, JD, MHS (04:38:45):

We're going to ask that you select the one that most closely reflects your top treatment goal, which would be: A, reversing or halting decline in kidney function, meaning halting the progression of your MN and delaying the need for dialysis; B, improving your quality of life and symptoms or preventing a future reduction in your quality of life and in those symptoms; or C, prolonging your life.

Again, please select one. Which of these three treatment goals for a future treatment reflects the one that you would view as most important to you? Or if you're a caregiver or care partner, the one that would be most important to you to consider, or rather that you would desire?

As you would expect, as with all of our polling questions, we want you to think about this when you're picking this response and think about the answer of why did you, when given these three options, choose that the option that you did?

So we'll let final results come in, but as it stands, it looks like about three quarters of our participants today – actually it's inflating a little bit more – as more results keep coming in – most want a reversal or halting in the decline of their kidney function. The second choice, at about one fifth of our audience today, most want a drug that improves their quality of life and symptoms or prevents a future reduction in their quality of life or symptoms. And no one in our audience today would say that prolonging their life is the most important goal for a future therapy.

So, I know that wasn't an easy question. So thank you for thinking about that.

I'd like to go to our Zoom panel, perhaps to get us to think about this, although I want to invite you for one last time to call in. If you have thoughts about future treatments, what it is you would look for in a future treatment? Please call in at +1 703-844-3231. Again, +1 703-844-3231. We'd love to hear from you live, what your preferences for future treatments are, essentially if short of a cure for your MN, what would be meaningful for you and a future treatment? So, we'd love to hear that.

James Valentine, JD, MHS (04:41:42):

Of course, you can also write in using that Comment Box under the live stream. Many of you have been writing in today. I know you know where to find it but we encourage that as well.

So, I want to come to our Zoom panel here and maybe this time, we'll start with you, Katrina on the topic of thinking about short of a cure for your MN, what would represent an ideal or a meaningful future treatment for you?

Katrina (04:42:15):

I'm still muted.

James Valentine, JD, MHS (04:42:19):

Oh, we can hear you.

Katrina (04:42:20):

Oh, okay. A, reverse or halt, because that was my goal. And it is my belief that that will lead to B and then C. But to reverse or halt the progression of the disease, because that is the gold ring out there.

James Valentine, JD, MHS (04:42:44):

Sure. So, since you said that, it actually reminds me, I want to maybe pull up a slide and then I'm going to come back and ask you to follow up on this. So if we can actually show Dr. Beck's slide on partial remission, this was a slide that Dr. Beck shared where he described how we have, of course, complete remission, but then we have this idea of partial remission, something that's short of complete remission. Dr. Beck, I think, defined it as estimating around proteinuria value that's 50% less and that gets you below a 3.5 grams per deciliter per day. As Dr. Beck discussed, this is a drug outcome that might come sooner than complete remission, although the long-term consequences of that might be more uncertain. We don't know if that partial remission will translate to complete remission, whether it will just stay as partial remission, or if ultimately, there might still be a relapse.

James Valentine, JD, MHS (04:43:48):

So, when you were talking about being able to halt or maybe even reverse progression, if you were in a situation where, perhaps you were in a relapse, would partial remission be a goal for you as well?

Katrina (04:44:05):

Yes, it would. Without a doubt, because I still stand by that. I believe that that would lead to an improved quality of life. If you're in a partial remission, your symptoms are lessened, which leads to an improved quality of life. Ultimately prolonging life. But yeah. I've already gone to pretty drastic methods to try to get things from progressing and getting worse. So, yes, that would be my goal and I would be happy to participate.

James Valentine, JD, MHS (04:44:45):

Yeah. Thank you, Katrina. Taylor, I want to bring you into this dialogue. Short of a cure for your MN, what would represent a important or meaningful future treatment for you?

Taylor (04:45:02):

For me, like Katrina said, it's mostly about quality of life. I was miserable for two years, two and a half years, and like her, I think even partial remission is absolutely worth it. Just because you go through so much for so long, you feel like you can't do it anymore and even just the littlest bit of relief is beneficial.

James Valentine, JD, MHS (04:45:31):

And that's been your experience when you've been in, maybe not quite complete remission, but partial remission zone, you've also had relief from symptoms and other issues in daily life?

Taylor (04:45:45):

Absolutely.

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

Yeah. Great. Daniel, how about you? As you're thinking about all the things you could ask for, is this on your wish list? The only thing I'm not allowing you to put on your wish list is the complete cure but that's because it's on everybody's wish list. What would you ask for, for a future treatment?

Daniel (04:46:09):

I chose in the polls, quality of life. I've accepted the fact that I have a non-curable kidney disease and I've mentally accepted that, so looking for a treatment program is exactly what that is. It's a treatment program, it's a program to treat your current symptoms and illnesses. I understand if they develop the cure, that would be awesome, but it's a treatment program. And in a treatment program is quality of life because the current treatments for MN take away that quality of life, even though they're treating the kidney, they're taking away the quality of that life.

Daniel (04:46:50):

Prolonging life, I don't care as much as how long I'm here, it's about what I do while I'm here. And I wouldn't want to prolong life if the life that I have here is full of trash. So, it's about the day-to-day. Let's improve the day-to-day, let's get up and still go to work, let's be able to hang out and have fun with our friends and family and enjoy the days that we are here. And if we can do that pain-free, that'd be awesome.

James Valentine, JD, MHS (04:47:32):

Yeah. Thank you, Daniel. And we'll give, on the Zoom panel, the final word to Eileen, your thoughts for preferences for a future treatment.

Eileen (04:47:42):

Mine would actually, be to reverse or decline the kidney function because my function has gone down so much that anymore, I'm on the border of dialysis. So that would be my main, main concern, my goal, for that.

James Valentine, JD, MHS (04:48:03):

Yeah. So, prevent, or perhaps delay needing dialysis would be actually a very important thing for you.

Eileen (04:48:10):

Absolutely.

James Valentine, JD, MHS (04:48:11):

And what about that question of partial remission? If you could get something that could at least get you there, would that be a value?

Eileen (04:48:20):

Absolutely. Because again, when you're at least even in partial remission, you'll still feel much better than if you're in a full-blown episode.

James Valentine, JD, MHS (04:48:31):

I see. Yeah.

I want to thank our Zoom panel so much for contributing to today. It's been terrific talking to you about your experiences and thanks for bearing with me as I probed you so much on so many different issues, but I do see that we have a phone caller, so I want to go to the phones. I see that we have Mary from New York who wants to share some of her thoughts about what she would want from a future treatment. Mary, are you with us?

Mary (04:49:03):

Yes. Hi.

James Valentine, JD, MHS (04:49:03):

Hi. I would love to hear your thoughts on what it is you would look for in a future treatment.

Mary (04:49:12):

Okay. So, I think I agree with much of what's been said. There's far too much emphasis, not only in kidney disease, but other diseases as well, and finding a cure, finding a cure. But I think a lot of it comes down to a partial remission is a win because at the end of the day, some or many of these, maybe even genetic, where the genes are always going to be that way. So, what are we going to do to remediate what's going on would be my thing. [inaudible 04:49:54]

Mary (04:49:55):

So getting that partial remission to me would be most helpful because it's addressing the eGFR, it's addressing the kidney decline, it's going to help with that. It's going to help with all of the side effects of the disease, so things going in the wrong places, and then protein being in the wrong place.

Mary (04:50:28):

So if they can target something to address the filtration and the resulting proteinuria, I think that would be a win. And then also something that's minimally toxic, so maybe something a little more biosimilar that would, in essence, not only would it reduce your toxicity, but it should cut down on some of those terrible side effects that the body is tolerating it better because it is more similar to things we already produced endogenously.

James Valentine, JD, MHS (04:51:03):

I see what you mean. So, I think I hear you, both treatment goals in terms of, at least, partial remission, but definitely want to see improvements on protein spillage and eGFR, but also a treatment approach that helps reduce the side effect burden that you're living with in dealing with.

Mary (04:51:28):

Right. And just to add, there are other treatments and even newer ones on the market already that are for preventing eGFR decline. So, I mean, there's always going to be ACEs and ARBs and things that we can use the further help the eGFR decline, and my thing would be more the proteinuria and partial remission.

James Valentine, JD, MHS (04:51:48):

Okay. Well, thank you so much, Mary. It's so great to get another voice in the here around preferences for future treatment. And I do have to commend our audience.

I see we have also been getting written comments on this topic. So, I want to give the final word to those of you who have been writing in and check in with David for written comments here.

David Feldman, PhD (04:52:11):

Right. So, Amy from Illinois writes, "Looking back, I'm not sure I would have chosen to take the medications that my doctor gave me because of all the side effects, even though I reached remission very quickly." That's pretty significant, I think. "The medications were very hard on me, physically and mentally and I'm so glad I was not working during that time."

Janet from Washington writes that, "My main focus in life has become preserving my kidney health, especially through diet and moderate exercise. I am always looking for new ways to improve my kidney health."

And finally, Kim writes "The toxicity of the medications are something that weigh heavily on my mind and heart and impact how I decide if I will ever choose to use a treatment. The side effects can take me from a functional individual to a non-functioning individual."

So the effect of side effects on people are very dramatic

James Valentine, JD, MHS (04:53:15):

Yes. Weighing on people's minds and their preferences for future treatment.

So this concludes the portion of our agenda, where we've been getting your input, and it's been a really powerful day. As your meeting moderator I just can't help but thank all of you for being so brave in a condition that you all have shared with me and with all of us, isn't one that you're always able to easily talk to people about, share with others as an invisible disease. You really stepped out and pulled back the curtain on living with MN and I just have to really commend you for that. It's really, really not easy to do. We often focus on persevering and prospering and what is working well and so to sidestep and instead talk about what isn't working well, I just want to thank you all for being willing to do that with us.

James Valentine, JD, MHS (04:54:18):

You've shared so many personal aspects of your life today but it's exactly the type of thing that we needed to hear. And I can tell you, as someone that works in this space and sees how the patient voice is applied in practice, how the regulators at FDA use it, I know that this is really going to help drive forward progress for developing drugs in MN.

So as your meeting moderator I just want to, from the bottom of my heart, thank you for opening up and sharing so much today.

James Valentine, JD, MHS (04:54:52):

So, now at this point, we're going to move into a meeting summary. It's an impossible task to try to capture all of what we heard today but what we're going to do is try to have a capture of some of the key things that our friend and colleague Larry Bauer has heard from today.

James Valentine, JD, MHS (04:55:11):

And, so Larry Bauer will be giving these summary remarks.

Larry is the perfect person to do this. He spent 17 years at the National Institutes for Health working in clinical research. He's worked for over 10 years at the FDA, he was one of the co-founders of the Rare Diseases Program within the Center for Drugs. And most recently he has been working to help work with groups like NKF and NephCure to plan these types of meetings, has been essential to the planning of this meeting, so, I would like to welcome Larry.

Thank you, Larry, for taking on this task of doing the summary.

Larry Bauer, RN, MA (04:55:54):

Thank you so much, James. Like James said, I'll be giving a high-level overview. I won't be able to make all of the points but all the points will be included in the eventual Voice of the Patient Report.

So, our meeting today on membranous nephropathy was opened by Dr. David Feldman, who's the medical project director of the National Kidney Foundation. This was followed with the presentation from Dr. Lisa Thompson, who's the deputy director of the FDA's Division of Cardiology and Nephrology and CDER.

Dr. Thompson shared that Patient Focused Drug Development meetings are valuable to the FDA and that she personally has used information from the Voice of the Patient Reports when reviewing drugs. Following her talk, we had a clinical overview, which was presented by Dr. Ashley Jefferson from the University of Washington School of Medicine. We heard that MN is an autoimmune kidney disease with antibodies attacking the cells in the filters of the kidney and causing membranous thickening. That's why it's call membranous nephropathy.

Larry Bauer, RN, MA (04:56:55):

Protein in the urine is a key sign and kidney biopsies are diagnostic of the condition. It causes fatigue, edema, kidney damage and can lead to thrombosis, infections and cardiovascular problems. The main antibody is the anti-PLA2R antibody. And treatment varies. It can include diet, blood pressure control, control of edema, vitamin D and prevention of complications as well as immunosuppression.

Larry Bauer, RN, MA (04:57:25):

So, we started then with two different panels. The first panel focused on health effects of MN and daily impacts. We heard from Marge who started gaining weight while training for a 5k race, and was soon after diagnosed with MN, as well as stage four kidney disease. She experienced exhaustion and brain fog and had to give up her pet therapy, which was one of her favorite things to do. She says, "On worst days I have to use a scooter to walk the dog. I have no stamina for the routines of daily life."

Larry Bauer, RN, MA (04:57:55):

Next, we heard from Taylor, who's a 23 year old nurse and developed swelling in her extremities that led to cracking skin and seeping fluid. She was diagnosed with MN at age 19, and her case has been difficult

to treat. She says, "I think about my loved ones will have to care for me if I need dialysis or transplant if I progress to end-stage."

Next, we heard from Alma whose oldest daughter, Lauren, was 12 when diagnosed with MN. Her eyes swelled shut at a camp, and she had fatigue and weight gain. Being a teenager, Lauren struggles to not have to share about her condition and why she can't participate in school activities. She likes to try to be private about it, which is typical for a teenager. She said, "Every day I wake up hoping today won't be the day Lauren's condition takes a turn for the worse."

Larry Bauer, RN, MA (04:58:45):

We heard from Dean who was diagnosed with MN at age 16. His early symptoms were extreme pain in the kidney region, swelling and a serious urinary tract infection. He also developed severe migraine headaches. He said, "In February of 2020, right before the pandemic started, my doctor said the scarring caused by the disease that damaged my kidneys to the point that I needed dialysis." And lastly, in this panel, we heard from Safa who's 18 years old and was diagnosed with nephrotic syndrome when she was in the sixth grade. She developed leg pain and swelling. She became very withdrawn and depressed. She used to enjoy sleepovers at her cousin's, but it became too complicated. MN has also impacted her fasting during the month of Ramadan and she says, "Now the years when I do fast, I worry about what my labs will look like afterwards and if my needs will need to be upped."

Larry Bauer, RN, MA (04:59:40):

Following this morning session, we took a break, and in the afternoon we came back. We began with an overview of challenges to clinical trial design by Dr. Lawrence Beck from Boston University School of Medicine. He shared the clinical trials are very important but challenges conducting MN studies include: there's few patients, we need a lot of time to measure the outcomes for the studies, and there's an evolving standard of care. So, it's kind of a moving target with just the basic standard of care.

Our panels discussion focused on different perspectives of MN treatments. We heard from Mark. Who's got advanced MN, has been on several immunosuppressant drugs, he had side effects of headaches, nausea, vomiting, high BP, joint pains, gout, and weight gain. With rituximab, he had temporary fatigue and minor headaches, but they subsided a couple of days after the infusions.

Eric H. took large doses of antihypertensives and developed dizzy spells as a result. He takes Rituxan and monitors the sodium in his diet. Any future ideal treatment for him is going to be one that's been vetted with lots of studies to the point where it's directly accepted by the FDA as being on label.

We heard from Seferiana who's 35 and has MN since the age of 30. She's taken quite a few different drugs. She said that cyclophosphamide caused severe facial swelling and immune suppression leading to many illnesses. Saferiana, at 35, said she would like to have children but, "I've declined Cytoxan twice and there are really no viable treatment options that don't risk my fertility. So, where do I go from here?

Larry Bauer, RN, MA (05:01:24):

Then we heard from Nina who had to resign from her dream job of teaching. She gets eye bleeds, if her blood pressure gets too high. She gives herself injections of Repatha into her leg, which she says is painful, like a wasp's sting. She also needs Prolia for osteoporosis and says, "I just wish there was a treatment that would put those of us with MN in long-term remission quickly and not cause other diseases or serious side effects."

We heard that over and over again about wanting less side effects.

And finally, we heard from Eric R. who's had MN since age 15. He developed gout and takes prednisone and allopurinol to treat it. Eric said, “The mental health effects of my MN are the single most important aspect of my disease experience, especially when I was young.” Once again, we heard that from numerous people as well, and he takes Lexapro to try to manage the depression related to having MN.

We've heard consistently today that there continues to be a great unmet medical need for people living with MN, and people overall, they'd be willing to participate in research and everyone would like more and effective treatments.

So, at this point, I'd like to turn the meeting back to David in the studio. Thank you all for your partnership.

David Feldman, PhD (05:02:39):

Thank you, Larry. That was a great comprehensive summary of today.

And now it's my great pleasure to introduce, for their closing remarks, two very good friends of the National Kidney Foundation and the membranous nephropathy community. Josh Tarnoff, the Chief Executive Officer of NephCure Kidney International and Kelly Helm, the Director of Patient Engagement at NephCure. Josh, would you like to start the closing statements?

Josh Tarnoff (05:03:13):

David, thank you. It is sincerely, and always a pleasure to work with you. Thank you for working so closely with NephCure and putting these on and Kelly and everybody today. It's just been an outstanding day and I thank you again, the National Kidney Foundation. Most importantly, I'd like to thank our patients. As you both had mentioned earlier in your comments, public speaking is not easy and whenever you ask somebody to, not only speak publicly, but now I'm also going to talk about my personal journey and things that are very sincere and deeply affecting my personal life and out to a public forum like this, that really takes courage and bravery. And so, thank you again to all of the panelists. You've done a great service to your fellow folks with membranous nephropathy and the medical community in general. So, thanks again.

Josh Tarnoff (05:04:02):

So, what did we hear? Boy, Larry did an outstanding job of summarizing the day in great detail. So I won't repeat a lot of what he said, but I think it's worth reiterating that there are several things that go on. There's physical symptoms, there's an impact our daily life, and we've heard stories of, "Man, this came on quick, rapid progression. And before I knew it, I'm exhausted and swelling." And those are probably the two greatest symptoms from the patient perspective.

Josh Tarnoff (05:04:32):

And so we often hear lab values of eGFR, or we hear things of protein levels, et cetera, but the patient perspective, really what today is all about comes front and center. We also heard about the side effects. None of the drugs that we've mentioned today were ever designed to be used in kidney patients. They're being borrowed from cancer therapies and other places that frankly, there's no free ride. Lots of side effects, and we've heard people say, literally, "Man, I have to choose between, do I take the medication to treat my disease or do I live with the disease?" Because sometimes the adverse events are equally great. And so, not an easy thing to do.

Josh Tarnoff (05:05:13):

But I think the number one issue, if we had to sum up today, one thing that rose to the surface and did a wonderful job by the way, with all of the surveys, was the emotional impact. And I think what we often forget is the impact on the family, the impact on, do I go out in public, clinical depression and everything associated with the emotional support around the patient. And that is something we need to think about. How does that now get incorporated into a clinical trial? Remember that's what today is, the patient incorporation of clinical trial. And we run clinical trials.

Josh Tarnoff (05:05:50):

We, in an academic sense, look at, "Okay, what's your protein level? Or what's your level of this biomarker we've called PLA2R, which are great things to have, by the way. But at the end of the day, are we looking at the impact of our depression? How do you feel?

And so I'll introduce a term today that I'm borrowing from Elisa Thompson. Dr. Thompson mentioned on many of her panels and discussions in the past, the thing called a PRO, stands for patient reported outcome and to all of the pharma companies listening today, I highly encourage you to take this message back and that it is imperative that we look at the patient in these trials; include secondary markers in addition to the lab values that look at, "Hey, how do you feel as a patient? Are you having swelling? Are you having depression? Are you exhausted? And what's the delta?" And we look at these and because that matters too.

Josh Tarnoff (05:06:50):

And I think that really expands today in terms of what we're looking at. And I would also end on what we heard from Dr. Beck and others, that there's a lag between the time we see this antibody response and the clinical response. We also heard that there's a thing called spontaneous remission. And that's complicated when you do a clinical trial, how do you measure effect of a drug when there's potential for somebody who was spontaneous to remit?

So all of these factors lead to, I guess, my final comment about the need to participate in these clinical trials and on behalf of National Kidney Foundation and NephCure, I'm pleading with you to please participate. There are 7,000 rare diseases out there and every one of the patient advocacy organizations are begging for the attention of the pharmaceutical industry. Please pay attention to my disease.

Josh Tarnoff (05:07:44):

So I'm happy to report that as of today, there are six significant clinical – meaning in human test phase – trials going on right now around the world. So, please do participate. Without that trial data, we don't get the drugs.

And so, thank you, today, for really making this all about what it should be, about the patient bringing things forward. We really can't thank you enough, to be blunt.

And with that, I'm going to turn it up to my colleague, Kelly Helm who has worked very closely with David on this program. And Kelly, by the way, is a patient mom herself of a daughter with nephrotic syndrome and really has the insight. So, Kelly.

Kelly Helm (05:08:23):

Thank you, Josh. I too want to start by thanking the patients who recorded their testimonies, joined us on a panel, emails, and even called in to share your experiences today. As Josh mentioned, I'm a caregiver myself and I know it's not easy to relive medical trauma, yet you all did so sincerely. So thank you very much.

Whether you are a patient caregiver, a regulator with FDA or an industry partner, I think we can all agree that after hearing the patient's journey today, two things are clear that membranous nephropathy patients live a difficult, sometimes invisible daily struggle, and they deserve better treatments. You as patients were loud and clear that the symptoms of membranous nephropathy and the side effects of your current treatments limit your quality of life. They prevent you from ideal participation in things like school, work, and most importantly, family time. Your fears and anxieties of relapse, inability to participate in important tasks and disease progression create an ongoing sense of uncertainty.

Kelly Helm (05:09:38):

And current treatments are often repurposed from other disease states, as Josh mentioned, and caused life altering side effects or comorbidities. Patients often don't even know which medication will work for them without trying all of them, which leads to added suffering and potentially sustaining permanent damage to their kidneys as they searched for the best option. The current way is not ideal.

So patients and care partners, please know that after the meeting today, if you think of additional comments or something that you maybe wanted to say today but didn't, the comment form will be available for 30 days from now on kidney.org. Post-meeting comments that come in after the meeting today are considered part of the meeting and will be incorporated. So, our next step today post-meeting is to gather all of the input that you provided and put it into what we call a Voice of Patient Report.

Kelly Helm (05:10:40):

And once that is completed, this report will be submitted to the FDA for their use whenever they're evaluating a potential drug for membranous nephropathy. This is also a public document that you too will be able to access. We also wanted to let you know that the live stream of today's meeting will be available for viewing both at kidney.org as well as nephcure.org. And I think everyone on today's call and those who will read the subsequent reports for years to come all have the same goal in mind, and that's to learn more about membranous nephropathy, develop and bring to market more effective treatments, specifically designed for membranous nephropathy patients, both to lower proteinuria, save kidney function and provide fewer side effects so that patients can avoid those freight train days we heard about earlier today and be an active part of society.

So, David, back to you,

David Feldman, PhD (05:11:44):

Thank you, Kelly. And thank you, Josh. This has been a wonderful meeting. Thank you for staying with us today and for painting such a vivid picture of what it's like to live with membranous nephropathy. You have been heard, and you can be certain that the FDA and pharma were listening carefully to the input that you gave today. Thanks again to our speakers and panelists. And we're particularly grateful to the FDA staff who took the time to listen to today's proceedings. I also want to thank my NKF colleague, Juan Perez for his expert help in organizing this meeting. And finally, we thank the incredible crew here at Dudley Digital Works for their expert and meticulous planning and execution of today's broadcast. So, thank you again for tuning in today and please watch for our Voice of the Patient Report, which will be available sometime next year. Stay safe and stay well.

PART 9 OF 9 ENDS [05:13:35]