FOOD AND DRUG ADMINISTRATION (FDA)

CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)

PUBLIC MEETING ON PATIENT-FOCUSED DRUG DEVELOPMENT FOR NEUROPATHIC PAIN ASSOCIATED WITH PERIPHERAL NEUROPATHY

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WELCOME

MS. GIAMBONE: Well, good afternoon, everyone. Let's go ahead and get started. My name is Soujanya Giambone, and I'm with the Center for Drug Evaluation and Research, here at the FDA. And I'm with the Office of Strategic Programs. And on behalf of all of my FDA colleagues here, we'd like to welcome you all to the D.C. Metro area, for those of you that traveled outside of the Metro area, and for all of our local neighbors, thank you for coming to our nineteenth patient-focused drug development meeting on neuropathic pain associated with peripheral neuropathy. We have a really great day of discussion ahead. And what I'd like to do is just over a few housekeeping items, go over the agenda and then we'll get started.

So, next slide, please. Okay. So we're going to start off with some presentations from my FDA colleagues. They'll provide an overview of the FDA's patient-focused drug development

initiative, some background comments on neuropathic pain and therapeutic options. We'll have a presentation on clinical trial endpoints and then I'll come back and go over the discussion format for the day.

So as you know, we have two topic questions, two topics today for today's discussion. Topic one is on disease symptoms and daily impacts that matter most to patients. So we'll have a panel discussion, followed by a larger group facilitated discussion. And then, we'll take a break. We'll come back and we'll do the same thing for topic two, which is on patient perspectives on current treatment options. So again, we'll do the same thing. We'll have a panel discussion, followed by a group discussion. And that'll take us to the last half-hour of the day, which we've reserved for open public comment.

Open public comment is a time for anybody in the room, not just patients or caregivers, but others in the room to share some comments that come to mind. So we have a sign-up

for open public comment out on the registration desk. I believe we've already had several people sign up for it. We'll take sign-up through break time and we'll see how many people signed up and how much time each speaker will have. And then, we'll wrap up the day with closing remarks from my FDA colleagues.

And so, you can see it's a pretty packed agenda. But it will be a really, really great day of listening to you and definitely learning from you. So thank you for being here. So what I'd like to do is quickly do a round of introductions. If I could look at my -- turn to my FDA colleagues here and if you could please state your name and your office?

DR. EGGERS: Good afternoon. I'm Sara Eggers. I'm in the Office of Program and Strategic Analysis here at FDA.

DR. HERTZ: Hi. I'm Sharon Hertz. I am currently the director for the Division of Anesthesia, Analgesia and Addiction Products, here at CDER.

DR. HORN: Hi. I'm Pamela Horn, and I'm a clinical team leader in the same division.

DR. GALATI: Hi. I'm Steven Galati. I'm also a clinical reviewer from the same division.

DR. PATEL: Hi. Nikunj Patel. I'm a clinical outcome assessment reviewer in the Office of New Drugs.

DR. PARKS: Hello. I'm Mary Parks. I'm deputy director in the Office of Drug Evaluation II.

MS. GIAMBONE: Thank you. And then, I'm going to turn to my colleagues to my right.

MR. THOMPSON: Graham Thompson, CDER.

MS. WOODWARD: Shannon Woodward, CDER.

MS. GIAMBONE: Great. And we have a few others that are floating around and they are Yewande and Meghna. So you'll see them throughout the room too. And so, just a few last-minute housekeeping items. Bathrooms are back out into the lobby area. If you go down to where that registration desk is and make a right and go all

the way to the end of the hallway, you'll see bathrooms there. And there's also a kiosk out there that sells basic sandwiches and snacks and drinks. So this is definitely a more informal -- I want you to feel very comfortable to be here. So if you need to get up to have a snack break, to have a stretch break, bathroom break, whatever it is, please feel free to do so. We want you to be as comfortable as possible.

And last but not least, this meeting is being recorded and transcribed. And just about a week after the meeting, the recording and the transcript will be posted onto the meeting webpage. Okay. So with that, I would like to turn it over to Pamela for opening remarks. Thank you.

OPENING REMARKS

DR. HORN: Good afternoon, everybody. Welcome to the meeting on patient- focused drug development for neuropathic pain associated with peripheral neuropathy. As I just said, I'm Dr. Pamela Horn, clinical team leader in the Division

of Anesthesia, Analgesia and Addiction Products. And that's in the Office of New Drugs in FDA. Our division reviews drugs for the management and treatment of pain, including neuropathic pain. So we're happy to see so many patients, caregivers and advocates in the audience today. I understand that we also have a lot more of you joining us remotely on the Web, and I want to thank you all for being a part of this meeting and sharing your experiences with us. We're excited for this opportunity to engage directly with all of you. In our discussion today, we will be focusing on the symptoms that matter most, the impact that neuropathic pain has on your daily lives and what factors you take into account when selecting a treatment.

We understand that neuropathic pain associated with peripheral neuropathy is a serious condition with physical, emotional and social impacts and that there is an unmet need for treatment for patients. Dr. Steven Galati, from our division, will provide a bit more background

in a few minutes on neuropathic pain associated with peripheral neuropathy and the current treatment options.

It is FDA's responsibility to ensure that the benefits of a drug outweigh its risks. Therefore, having this kind of dialogue is extremely important and valuable for us because hearing what patients care about can help lead us in figuring out how to best facilitate drug development for neuropathic pain and understand how patients view the benefits and risks of treatment for neuropathic pain. So I know that we also have representation from industry, from academia and some healthcare professionals today. And while FDA plays a critical role in drug development, we're just one part of the process and I'm glad to see a high level of interest from those of you who also play an important part of the drug development process.

FDA protects and promotes public health by evaluating the safety, effectiveness and quality of new drugs. But we do not develop drugs

or conduct the clinical trials ourselves. Drug companies, sometimes working with researchers or patient communities, are the ones who conduct trials and submit applications for new drugs to FDA. It is then FDA's responsibility to ensure the benefits of a drug outweigh its risks. This benefit-risk decision-making is an integral part of our review process. We look forward to incorporating what we learn today from all of you into the agency's thinking and understanding of how patients view benefits and risks of treatment for neuropathic pain.

Once again, we are all here today to hear the voice of the patient. So thank you for your participation and coming to share your experiences, your personal stories and your perspectives. I'll now turn it over to Sara Eggers, who will provide background on the FDA'a patient-focused drug development initiative.

OVERVIEW OF FDA'S PATIENT-FOCUSED DRUG DEVELOPMENT INITIATIVE

DR. EGGERS: Thank you, Pamela, and

welcome. I am happy to tell you a little bit more about the initiative that brings us all together today under this large umbrella we call patient-focused drug development initiative. This initiative is something that has stemmed out of years of conversation and a growing awareness that -- by FDA that the use in having a more systematic way of gathering patient input and perspective on their condition and available treatment options, you and your caretakers, as the experts of what it's like to live with your disease, it helps inform our understanding of the context of the benefit-risk assessment and decision-making for new drugs, as Pamela mentioned.

It can also, as she mentioned, help inform our oversight and advice during drug development and review of the marketing applications of those -- of drugs that want to go on the market. Patient-focused drug development is a program that came out of a commitment FDA made as part of the Prescription Drug User Fee Act, or PDUFA V, which is a series of commitments

that we make to advance drug development, drug review and FDA's role in that. As part of that commitment, we are convening more than 20 public meetings on specific disease areas over a five-year period. As Soujanya mentioned, this is the nineteenth meeting. So we have learned a lot from the meetings that we've conducted and we continue to learn as we go along this journey. We hope that the meetings will help develop a systematic approach to gathering patient input. What we're learning from you can help translate to how we engage with patients and caretakers and advocates and other stakeholders in the future.

In the selection of -- and the identification of the meetings, we went through both a public process and an internal look at the areas that -- disease areas where a meeting would be extremely helpful. We announced a preliminary set of meetings approximately five years ago now and collected input on the nominations for the meetings and we've reviewed the public comments and all the input we received to come up with a

final set of 24 meetings that would be the focus of our efforts for this five-year period. And here you have the meetings that we have conducted. You can see since 2013, we have conducted meetings on a range of conditions, a range of severity, a range of the types of populations they have -- that they -- that they mean and in the challenges that the patient community has faced. Now, we've learned a lot of similarities across these disease areas. And so, what we hear from you will help build on -- not only will we learn more about what it's like with your condition at this time, but we are building on what we're learning from others and their conditions as well.

Each meeting -- these meetings are quite unique for a public meeting at FDA, and I gather elsewhere as well. As Soujanya mentioned, they are designed specifically to listen to patients and their caretakers and hear your input. We focus on a set of questions, as she mentioned, that elicit patients' perspectives on the disease and treatment approaches and we have a general set

of questions that we built upon and tailor, as needed, to the type of meeting that we're having and the topics that were most important to our review colleagues and others today.

We have learned through this meeting that active patient involvement and participation is a key to the success of this meeting and we want to thank anyone who has spread the word about the meeting, who has helped engage with patients or caretakers in helping them navigate through FDA and getting here and all of the other things that it takes to come here on a Friday afternoon. So we thank stakeholders, advocates and you, patients, and your families as well.

Following each meeting, we publish a "Voice of the Patient" report that summarizes what we hear today and what we learn from the folks on the webcast and what we learn from those of you that we hope will continue the discussion through our docket process, which Soujanya will describe in a few minutes. We try to capture in these reports your words and your thoughts in a way that

is most successful for our FDA colleagues to understand your perspectives and your experiences. They do serve an important function in communicating to our colleagues here at FDA, but also we hope as a resource for you as you continue to engage with yourselves as patient communities or engage with others throughout the drug development process.

We believe that the long run impact of this program will be a better and more informed understanding of how we all might find ways to develop new treatments for these diseases. And with that, I would like to turn it over to Steven to give a bit more background on peripheral neuropathy.

BACKGROUND ON PAIN NEUROPATHIES AND AVAILABLE TREATMENTS

DR. GALATI: Thank you. Good afternoon, everyone. Thank you for being here. So I'm Steven Galati. I'm a medical reviewer in the Division of -- DAAAP. And what I'm going to do today is go over very briefly what peripheral neuropathic pain

is. It's a very complex issue. So, but I'll keep it simple and brief for today. So peripheral neuropathy is -- and the pain associated with it is associated with damage to the actual nerves themselves. And when we refer to the peripheral nerves, we think of the central nervous system as the brain and the spinal cord. The nerves that come out through the rest of the body, that would be the peripheral nerves. And we all have sensed pain in our lives, whether we have peripheral neuropathic pain or just living our lives.

So for example, pain can actually be adaptive. If you put your hand on a stove and you feel the heat, your body then signals that there's damage going on to your tissues. You then pull away. That's an adaptive, appropriate response. But people who suffer from peripheral neuropathic pain, the damage itself is to the nerve, not to that tissue. And it falls underneath chronic pain and chronic pain is exactly how it sounds. It's been going on for a specific period of time, and we divide it into different descriptors.

So you may or may not have heard of nociceptive pain. And no nociceptive pain would be, for example, you break a bone. And in the bone, the injury is to the bone, to the tissue and in those nerves will then sense that there is injury or inflammation to the brain and you can react or you can go to your physician or however you were meant to respond. When there's neuropathic pain, the lesion is not in the bone. It's in the nerve going to the bone. And that's what causes an abnormal function, so people who will have pain without a stimulus. So you may just be sitting there in bed and feel pain. That's why it's happening is because it's damage to the nerve itself. And like I said, peripheral, peripheral is because it's in the peripheral nervous system. So it's outside of the brain and spinal cord.

So how does this get diagnosed? So those of you who suffer from peripheral neuropathic pain know that you go through certain procedures. Usually you go to your primary care

physician. And although peripheral neuropathy is associated with a number of different symptoms, pain is one of the main complaints because of the discomfort. So you go to usually your primary care physician, for example, and they may initiate a treatment or workup. But often, it can be referred to a specialist. Neurologists typically are specialists that see these referrals. It also can be a rehabilitative doctor.

And then, a number of different tests in addition to a physical exam can be performed. There are those of you who may recognize some of these terms. So a nerve conduction velocity that measures the speed of the nerve. EMG, which is when they stick the needle into the muscle fiber to see if it's firing appropriately. Lab tests are often done. For example, can test for different types of infection, can check for blood sugars because diabetes can be associated with this and many other studies. And it may even go to a nerve biopsy where there may take a piece of the nerve and send it off to a pathologist to look

at it under a microscope.

So based on this combination of symptoms, history and physical examination and any other tests that were needed, a physician can come to a determination as to cause of the peripheral neuropathic pain. Now, here's a list of a number of neuropathic pain syndromes that deal with neuropathic pain and the most common tends to be painful diabetic neuropathy. And the reason why that's the most common is because diabetes is so prevalent. And as you can see, 10 to 20 percent of diabetic patients may have neuropathic pain and that's a pretty large number. But there's also a number of other causes and this just lists some of the main ones, but there are others. And it can cause from infections. It can cause from trauma. It can cause from other drugs. It can be induced by substances such as alcohol and cancers and even autoimmune disorders.

So despite all the numerous causes of peripheral neuropathic pain, the symptoms tend to be similar. And pain, of course, is a big portion

of the neuropathic symptoms. But common symptoms that people might suffer from would be burning sensation, shock-like pain, numbness and tingling and it could be a combination of these symptoms. It's not usually just one. There's some other terms, such as allodynia and what allodynia is -- would be described as something that's normally painless can induce pain in people who have peripheral neuropathic pain. An example would be if you're in bed and you rub your foot or your hand across a sheet, all of a sudden that might induce pain. Hyperalgesia is another term where you may have increased sensitive to a normal painful response. For example, if you were getting an IV or you were giving a blood draw, that's normally uncomfortable for the average person. But these patients may have an extreme response to that, where it's even more painful.

So all of this is beyond the scope of the talk, because we're at the FDA, I thought I'd say something about what FDA approval is. And what happens is -- and the reason why I'm putting

this up here is because I want people to know that you may be prescribed or given a treatment that doesn't technically say FDA approval. It doesn't mean it's not an effective treatment. It doesn't mean it's not appropriate.

But when a company wants to get FDA approval, they have to go through a rigorous process. And generally speaking, there has to be two successful trials. It also has to be replicated. And what we're here today also is to hear, well, what are the endpoints. What's the most important things we want to hear from patients is that what symptoms are bothering them the most, that then a company can target to improve. And then, there's more a general indication, which isn't done as often, but it's treating all different types of neuropathic pain.

So here's just a list of some of the FDA or the FDA-approved medications for peripheral neuropathic pain. As you can see, diabetic peripheral neuropathy and postherpetic neuralgia are the most common kind and these medications --

for example, Nucynta and Lyrica and Cymbalta are all approved. And what that means is they met those FDA requirements. And you can see there's a range of different types of treatment. Some of these started off as antidepressants. Some are anticonvulsants, used for epilepsy and some are just pain medications.

The reason I put this slide up here is this is an expert review panel from 2015. They got together and they provided guidelines and these are just guidelines for physicians. These are not hard and fast rules. These are just general recommendations that physicians can go off of, here from an expert panel who's reviewed the literature and also given their own experience. And what they recommend, when they call something first line, what they're meaning is there's effectiveness that's been shown in their experience or through proof of literature. And then, that is balanced against the risk of treatment, so the side effects and potential risks.

So what they're saying in these strong recommendations is that this is what they would consider trying first because they think that in most patients, the benefit would outweigh the risks. And then, they have some weaker recommendations. And that doesn't mean they don't work. The reason why they put that was it means that maybe the evidence wasn't as strong. So maybe they don't have as much proof that a medication might work or a medication might work but their concern is you don't want to jump to it because maybe there's a lot of side effects that make it difficult for a patient to tolerate. And then, a lot of times, in reality, combinations of treatments are used.

So for example, they may use two different types of drugs or you may use one drug and another treatment modality such as acupuncture. The problem is that's much harder to study and there's less evidence to prove it. However, it's used commonly in practice and physicians may even tell you when you see them

this is what I've used and this is what's been shown to be effective in your case. Then, there are other types of anticonvulsants that are used sometimes and them there are also immunoglobulin that's sometimes used for treatments, for certain specific types of treatments.

Other components of therapy -- so one of the most important things is to treat your underlying cause and condition. So for example, if you have peripheral neuropathic pain and your diabetes isn't well-controlled, your physician is going to of course want to control that as a portion of it. Another component of therapy, which can be very helpful, is exercise and/or physical therapy, although it seems counterintuitive because you may be in pain and saying, I don't really feel like I can move or I can do this activity because of pain, depending on where it is. It's been shown that, well, in diabetic peripheral neuropathy, for example, the pain may improve with the exercise.

And then, there's cognitive behavior

therapy, which is a type of psychotherapy, which has limited number of side effects, of course, but it has been shown to have some evidence of improvement. And then, there's other modalities and these modalities may have limited evidence or support from placebo-controlled trials. It doesn't mean that they don't work. But it may be that there's just not as much proof of them because maybe there's been faulty studies. But I've seen a lot of people, both physician's recommending and patients, who have had success with acupuncture, for example. Then you can see some other ones here, spinal cord stimulation, massage and TENS units are also used fairly commonly. And when they are used, a lot of times they're used in concert with another treatment.

So we all know that peripheral neuropathic pain is a very serious condition and it has a significant impact on the quality of people's lives. So the key to success would be to diagnose appropriately, identify it, find what is modifiable, modify that the best you can and

then maximize the effectiveness of the treatments, while keeping in mind the long-term adverse events. Because peripheral neuropathic pain is often chronic -- it's not something that happens in a couple of days and then goes away -- you want to make sure that the long-term plan, one, is flexible and also you have to consider what the long-term implications of treatment would be; for example, consider long-term adverse events or side effects.

So there are a number of challenges to drug development. So although we've talked about drugs being FDA-approved in all sorts of modalities that may be effective, many patients still are not completely satisfied with treatment. So efficacy is incredibly important that we have to target. Most trials compare single agents. So as I mentioned, some people are having multiple modalities of treatment. There are so many causes of neuropathic pain. So although one medication or one treatment might work for a specific type, it doesn't work for others. And that has to be

proven over time. And also, medications have their side effects. So although a medication, for example, may be effective, it may not be tolerated by that person or it may not be suitable long-term.

So the overall conclusion, the FDA is aware of the unmet need and that is experienced by patients with peripheral neuropathic pain and one of the points of this meeting today is to gain input from the patients and caregivers that helps us then communicate the appropriate information to drug companies trying to design these trials. So thank you very much. I appreciate it.

[Applause.]

THE ROAD FROM PFDD MEETINGS TO CLINICAL TRIAL ENDPOINTS

DR. PATEL: Good afternoon. Excuse me. Good afternoon, everyone. My name is Nikunj Patel. I am a clinical outcome assessment reviewer here at the FDA. Our team, Advisory Review Divisions, on matters concerning clinical outcome assessments such as patient

questionnaires, which we commonly refer to as patient-reported outcomes or PROs. We evaluate these PROs to ensure that they are assessing the most important signs, symptoms and impacts to patients and that they are assessing these concepts in an accurate and reliable manner. Today, I will briefly go over how we use information from these patient-focused drug development meetings and how we intend to incorporate patient input into clinical trial endpoints. Here is my disclaimer.

You may be wondering, we have these PFDD meetings where patients such as yourself are here to discuss. But where do we go from here? What's the end game? How do we take what we learn today and generate clinically relevant, patient-focused endpoints to incorporate in clinical trials? So I hope in the next few slides I can answer some of these questions.

One of the main advantages in having this meeting is that it gives all stakeholders, patients, drug companies, questionnaire

developers, clinicians, FDA and others the opportunity to listen to your voice, patients' voice, your experiences, particularly to hear what's important from your perspective and how you describe your symptoms and impacts in your own words. These meetings also inform us on how we at FDA review PROs in drug applications to ensure they are adequately assessing your perspective. PFDD meetings also help us to think about incorporating patient-focused endpoints in clinical trials, as appropriate.

So what is an endpoint? In the context of a clinical trial, our goal is to measure key disease-specific outcomes of interest, reflecting how patients feel, function and survive. To do this, we sometimes use PROs, patient questionnaires. In this case, the study endpoint would be how the patient questionnaire will be measured and analyzed in a clinical study to address a particular research question reflecting specific outcomes of interest and these outcomes can be safety, can be efficacy-related. There are

many things that are important to patients that are discussed during PFDD meetings. However, not all of these things lend themselves to being measured in clinical trials for drug approval, as they may be impacted by many factors beyond the treatment itself, such as socioeconomic factors, so therefore, making it challenging to interpret as results.

Here at FDA, we focus on safety and efficacy. So for example, financial well- being may be an important factor, an important concept to patients, but may not be impacted by treatment in a clinical study setting. So we encourage drug sponsors, drug companies to consider selecting the most important and relevant concepts to support key study endpoints that are likely to change as a result of a treatment. Financial well-being and other important concepts that are unrelated to treatment can still very well be assessed and measured, but perhaps for exploratory purposes.

While there are many benefits of having PFDD meetings, I want to underscore this is just a

starting point. We also have to be mindful about considerable amount of work that needs to be continued after we are done today. We encourage -- we strongly recommend that drug companies or other researchers who are developing these patient questionnaires to engage additional patients, those patients who are not here in the room today, as well as gather input from physicians, other experts, as appropriate. Such an engagement may help confirm the questionnaires, include patient-relevant information and to ensure the questions and instructions in the questionnaires are clear and understandable across patient populations before they are incorporated in clinical trials.

So my job here at FDA as a reviewer is to apply our drug laws and regulations. Within these regulations, there are regulatory standards for assessments such as patient questionnaires. Our goal is to make sure these PROs are well-defined and reliable. In other words, are they measuring what they are supposed to measure, both accurately and reliably? We want to make sure they

are not misleading in any way.

So not only do we recommend drug companies to engage patients to develop questionnaires using qualitative research, we also recommend them to perform quantitative studies as well -- statistical testing, for example -- to show that they are well-defined and reliable. In addition, patient input can be quite valuable and powerful, along with other methodologies in determining how to interpret what is clinically meaningful change in the context of a clinical trial. Therefore, we recommend that sponsors to engage the agency early and throughout drug development for FDA input.

So how can we help you and other stakeholders who are involved in this area of drug development? So there are three pathways to provide advice on clinical outcome assessments such as PROs. The first one is within the context of an individual drug development program while the other two are outside. This is where an individual, an organization has opportunity to

engage the agency.

In the first pathway, the IND and the BLA pathway, we encourage drug companies to begin this discussion as early as the pre-IND stage. So if they have -- if any work needs to be done on proposed questionnaires, there is time to do so before the pivotal studies are conducted. The second pathway, this is through our drug development tool, or DDT qualification program, through this pathway, we work with questionnaire developers to develop and qualify PROs for use across multiple drug development programs in a pre-competitive space. The last, the third pathway, this is relatively new. This is through another avenue to engage the agency through our critical path innovation meetings program. Through this program, a person or an organization has opportunity to discuss and receive general feedback on questionnaires such as PROs. It could be any other subject as well. But in this case, a PRO or other clinical outcome assessment.

In conclusion are three key takeaways.

First, PFDD meetings are a starting point for developing and using patient-focused outcome measures and endpoints. Second, the outcomes of PFDD meetings will support and guide FDA's assessment of clinical benefit in drug reviews. And the third point is patients' input ultimately helps determine what is measured to provide evidence of treatment benefit, how best to measure what matters most to patients and what amount of change is meaningful to patients. With that, I conclude my presentation. Thank you so much for your attention.

[Applause.]

OVERVIEW OF DISCUSSION FORMAT

MS. GIAMBONE: Okay. Great. Thank you to my FDA colleagues for your presentations. And now, you have a background on why we're all here today and you've heard that your input is very important to the work that we do here at the FDA and the work that others do to really give us a good understanding of what matters to you most in your management of neuropathic pain. So what'd

I'd like to do now is to go over the discussion format. So as I mentioned early on, just a little while ago, that there are two topics. And so, topic one is one disease symptoms and daily impacts. So here, what we're going to be listening for is what are your most bothersome symptoms of living with neuropathic pain. How does your pain manifest and how does it -- you know, what's a good day like? What's an average day like? What's a bad day like? How does it impact your ability to do certain activities or to not do certain activities? And really, what worries you most about your condition?

And then, in topic two, we're going to be listening for your perspectives on treatment approaches. So what are you doing currently to treat your neuropathic pain and is it working and what's not working about it? What are the benefits of your treatment? What are the downsides of your treatment? And how has your treatment regimen changed over time since you've been diagnosed? And then, lastly, we're

definitely going to be spending some time on what you look for in an ideal treatment. What are the aspects of an ideal treatment that are important to you? And we'll also spend a little bit of time on what factors you consider when deciding whether or not to participate in a clinical trial. So we'll have a scenario question that we'll pose to you and we'll get your immediate -- you know, your initial thoughts when you hear this type of scenario.

So here's how this is going to work. And as I mentioned earlier, we're going to have a panel discussion, followed by a group facilitated discussion. So we're going to first hear from a panel of patients. And on that note, I'd like to invite our topic one panelists to come on up and have a seat at the panel table. So I'd like to make a quick shout-out to our amazing panelists that we have today, topic one and topic two panelists. They've worked very hard to get their panel summaries together and we're really grateful that they're here and we're looking forward to

hearing from them.

So the purpose of the panel discussion is to set a good foundation for our discussion. Those panelists, they reflect a range of experiences in living with neuropathic pain. And so, they'll each have about three to four minutes to present their comments. And once they've completed presenting their comments, we're going to then broaden the discussion and open it up to other patients and caregivers in the audience to build on what you've heard from the panelists.

So periodically, I will ask some questions along the way. I'll turn to my FDA colleagues to ask some questions along the way. And we invite patients and caregivers in the audience to raise your hand and share your perspectives with us. We'll have microphone runners around the room and they'll come to you with a microphone. And so, if you're interested in sharing some comments, just raise your hand, and if you could state your first name, that would be most appreciated.

So along the way, we have some other ways that we'll be hearing from you. So in addition to the group facilitated discussion, we'll have some polling questions along the way. And you should have -- for patients and caregivers in the first two rows, where we encouraged you all to sit, you should have these little clickers that we've passed out. And we're going to test those out in just a bit. And actually, Shannon, would you mind passing clickers out to our panelists also? Thank you.

So this is not a -- these are not scientific surveys that we're going to be doing. It's entirely voluntary. It's just a way for us to learn more about the perspectives in the room, and also on the Web, which I'd like to make a shout-out to. We have about 150 people joining us on the webcast today. So we can't see you, those of you on the Web. But you are a very important part of our meeting. We're going to be hearing from you shortly. We'll do some phone comments along the way. So those of you on the Web, please

participate in the polling. Please continue to submit your remarks through the webcast and we'll -- it's a very big part of our meeting today.

So we do ask that for the polling questions, that it's only patients and caregivers. I'm not sure why that says parents of patients only. It should say patients and caregivers only to participate in the polling. So -- and so, that'll be another way for us to learn about perspectives in the room and on the Web. And then, Sara had mentioned earlier that we have a public docket. And what this is, is a space that we have online. You see the website here. We highly encourage you to submit comments to the public docket, which is basically another way to continue this discussion. We can't possibly cover everything about symptoms, impacts and treatments that are important to you within a four-hour meeting.

So we have a public docket that will be open for two months after this meeting. So it closes on August 10th. And it's a huge and very

important part of our -- you know, our understanding of neuropathic pain. So please continue to submit your comments there. And all of those comments are going to be incorporated in our summary report that Sara had mentioned, the "Voice of the Patient" report. So we will look for very helpful information through the docket as well. And anybody is welcome to comment, not just patients and caregivers.

So we have some resources here at FDA that we always like to share during these public meetings just to let you know of other ways that you can sort of interact with the FDA, especially as it relates to, you know, patients and what matters most to patients. So within the Office of Center Director, we have the professional affairs and stakeholder engagement team, or PASE. We have Chris Melton here, who is the primary contact that you can contact for this meeting. And so, that's one very helpful office that we collaborate with. And the second very helpful office that we work closely with is the FDA Office of Health and

Constituent Affairs, or OHCA. FDA is full of acronyms. So we call this one OHCA. And there's -- you can see their email address right here and you can feel free to contact them. Again, they serve as a liaison between FDA and stakeholder organizations.

So we do have a few discussion ground rules for the day. This is a meeting where we are really focused on the patients and caregivers and advocates. So we encourage patients and caregivers and advocates to contribute to this dialogue. FDA and industry and academia and other government entities who are here, we're really grateful that you're here. We know that this meeting is going to be really important for you too. But we ask that you stay in listening mode, as this is really a day to hear from the patients and caregivers.

The discussion will focus on symptoms and treatments. We are going to do our very best to stay on topic. We know that there's so many aspects and so many considerations that you as

patients live with and think about as it relates to neuropathic pain. But we're going to focus on symptoms and treatments for today. So we'll stay on topic. We do have the open public comment period, which I had mentioned earlier, for aspects or considerations that are outside of the scope of topic one and topic two. So I hate to be a stickler for time and a stickler for staying on topic, but I will have to direct you to the open public comment period or, more importantly, the public docket if there are aspects that you'd like to share that are outside of topic one and topic two.

So the views expressed today are personal opinions. And so, on that note, respect for one another is paramount. And last but not least, very importantly, we will have evaluation forms that we'll pass out closer to the end of the meeting. We read through each and every single one of them. They're very important to us. So let us know how the meeting went for you today and it helps us as we prepare for our next one.

Okay, so what I would like to do now is a quick test of our clickers to make sure that everything is working. And we -- and those of you on the Web, you can also participate. So the first question, so patients and caregivers, if you could please grab your clicker, the first question is where do you live. Press A for within Washington, D.C. Metro area or B for outside of Washington, D.C. Metro area. Is it up? Okay. All right. So it looks like two-thirds of you are our neighbors, so welcome again. And it looks like a little over a third of you are traveling from outside of the D.C. Metro area. Thank you for coming. We are so glad this is not a rainy day because we went through a stretch in May where it just rained for about three weeks straight, which was no fun. So glad it's a sunny day and that you're here for it.

Okay, let's do the next question. Have you ever been diagnosed as having neuropathic pain associated with peripheral neuropathy? Press A for yes or B for no. Okay. So the majority of

you in the room, almost 90 percent have been diagnosed as having neuropathic pain. So we know that it's not easy to come here and to travel. And so, it really means a lot to us that you're here to share these perspectives with us.

And I think we have one more. Okay, your age, A, younger than 18; B, 18 to 29; C, 30 to 39; D, 40 to 49; E, 50 to 59; F, 60 to 69; G, 70 or greater. Okay. So it looks like -- it looks like we have a pretty good spread. The majority of you are in the age 60 to 69. We've got 50 to 59, 70 or greater and then we also have some representation between 30 and 49. So lots of perspectives in the room.

And lastly, do you identify as, A, male, or, B, female? Okay. So we -- almost kind of the same -- okay, so almost half and half, equal spread of male and female. Great. What is the length of time since your diagnosis of neuropathic pain associated with peripheral neuropathy? So A, less than a year ago; B, one to two years ago; C, two to five years ago; D, five to 10 years ago; E,

more than 10 years ago; or F, I'm not sure. Okay. So we definitely have a nice spread of experiences and perspectives here, which is great. Everywhere from one to two years ago all the way over to more than 10 years ago and some that have identified that they're not sure when the actual neuropathic pain was diagnosed.

Okay. Okay. What is the underlying cause of your neuropathic pain? Check all that apply. A, trauma, physical injury or surgery; B, metabolic or endocrine disorders such as diabetes; C, medication toxicity; D, viral or bacterial infection; E, other condition not mentioned; or F, I'm not sure. Okay. All right. So it looks like we have a few that identified some sort of trauma, physical injury or surgery. We have medication toxicity. We've got viral and bacterial infection. There are definitely other conditions not mentioned. So I will just point out now that when we do our large group facilitated discussion, if you could -- if you're comfortable to do so, if you could mention your underlying cause of

neuropathic pain, that'll help us a little bit understand the context of your comments also. And then, F, I'm not sure.

Okay. Okay. We have a lot of polling questions, don't we, to test these out? Okay. What comorbid conditions do you have, if applicable? Check all that apply. So A, depression or anxiety; B, diabetes; C, cancer; D, kidney disease; E, chronic bacterial or viral infection; F, other comorbid conditions not mentioned; or G, I don't have a comorbid condition that I'm aware of. All right. So we have depression mentioned. We have cancer, other comorbid conditions not mentioned -- again, I'll just, you know, put a plug in for, if you're comfortable to do so, to share that with us and many others that said they don't have a comorbid condition that they're aware of. Let me check in with the Web. I know we just went through a lot of polling questions. Can you give us an idea of who's on the Web?

MR. THOMPSON: Very similar. We have a

50/50 male/female split, a range of ages, with the majority in 60 to 69 range, a similar range for the length of time since diagnosis and similar results also for the underlying cause and comorbid conditions.

MS. GIAMBONE: Okay. Great. Thank you. And I think -- is that our last one? Okay. So thank you so much for going through those polling questions with us. We know that the technology works because every once in a while we get a little, you know, unexpected clickers don't work type thing. But I'm so glad it worked. All right. So now, we're going to get started with our -- the highlight of today, which is to hear from you all, from patients and caregivers. So once again, we have four panelists on topic one. And we're going to start with Adam. What I'll ask you to do is when it's your turn to speak, just press the red button on your microphone and you can go right into your comments. And then, when you're done, just hit the red button again to turn the microphone off. Okay, so Adam, it's all

yours.

PANEL #1 DISCUSSION ON DISEASE SYMPTOMS AND DAILY IMPACTS (TOPIC 1)

MR. HALPER: Hello. First of all, before I dive in, I'd just like to thank all of you for having us here. I can probably speak on behalf of a lot of neuropathy patients in saying that it's wonderful to get this type of publicity for the range of disease processes that cause peripheral neuropathy. For me, in terms of the sensations I personally experience, I really -- I primarily experience three different types of sensations. The first is what I would describe as sort of a deep muscular soreness. And that is primarily activity-dependent. So for example, as I sit here right now, my legs feel almost entirely normal. But if I were to stand for, you know, let's say 10 minutes or, you know, walk a half to three-quarters of a mile, I would start getting a deep muscular pain down the back of both legs, which primarily manifests in my calves, back of the knees and hamstrings.

The second sensation that I experience with some regularity is -- it's almost like a heaviness. So I think the easiest way to think about it would be almost like if you're riding an exercise bike with resistance turned up and every step would require some additional effort. And that's also very much activity-dependent. So you know, if I were to go walk to the exit sign, I wouldn't feel it. But if I went and walked a mile-and-a-half, I certainly would. The third sensation that I experience is not activity-dependent and that's -- it's more of a classic burning sensation. So very much on the surface of the skin, and I get that up and down both legs and in my hands as well and it sort of comes and goes. And that is, you know, very much this classic sensation where you feel like your legs are on fire, to a degree. And it can be at times quite uncomfortable.

In terms of the specific activities that peripheral neuropathy affects for me, you know, as a young guy, I developed peripheral neuropathy

about two years ago at the age of 28. At that time, I was very physically active, you know, running 40 miles a week and in the gym seven days a week. So within about a 24-hour period, post onset, you know, that ability to really move in a sense was dramatically reduced. So today, I would say with some variation, you know, I'm able to walk about a mile-and-a-half to two-and-a-half miles over the course of a day with breaks. And at any one time, you know, I can generally walk about a mile comfortably. In terms of standing, for me, it'd say it's within 10 minutes I'll start to get uncomfortable. And within about a half an hour, it's really time to find a seat.

And so, you can think about how that plays out within one's daily life. So some very routine activities like, you know, riding the subway, if you can't find a seat, going food shopping, anything that would require one to stay on their feet for an extended period of time can be dramatically impacted and it requires a lot of strategic thinking in order to plan out one's day.

In terms of the fluctuation for me between the best and the worst days, for me, on the worst days -- and for me, it's not really a day-to-day fluctuation. It's more of a week-to-week or a month-to-month fluctuation. But on the worst days, I've had problems, you know, taking a five-minute walk from my home to a subway station. So it's gotten to that point at times. And in terms of the burning, you know, I've had nights where, you know, it can really impact my ability to sleep comfortably. Conversely, during the best stretches, you know, I'm able to walk, you know, well over three miles in one day. So there is -- or there has been some variability in my experience.

In terms of the change over time, since onset, I would say there isn't one long- term trend, either positively or negatively. There certainly have been fluctuations over the period -- over a period of months. But if I look back a year-and-a-half, I would say I'm in roughly the same position that I was in. And for the final

question, in terms of my biggest fear, I think it would be that there might be some dramatic uptick in symptoms which would, you know, quite literally disabled me or require, you know, some heavy hitting pain medication, which would, you know, dramatically impact my quality of life.

MS. GIAMBONE: Thank you so much, Adam. Okay, next we have Susan.

MS. WALDROP: Good afternoon. I'd like to echo Adam's thanks to the organizers of this meeting, for coming and listening to all of us. My neuropathy resulted from the chemo I received for colon cancer in 2009. Throughout my treatment, peripheral neuropathy is a very recognized and anticipated side effect of oxaliplatin, which is one of the drugs I was treated with. And so, throughout my treatment, I was monitored very, very carefully for the development of neuropathy, pain level, function level. And my neuropathy stayed within expected range. So I was able to get my entire -- my full course of chemo, which is of course what I wanted.

But I completed that chemo. I was on the home stretch and six weeks after is when I was struck with this debilitating pain of peripheral neuropathy. My feet were on fire. My lower legs, my hands. It was what others have described, that burning sensation. You feel like you're stepping on frying pans and electric shocks going up my arms, my legs, the sides of my feet. I certainly couldn't walk and I certainly couldn't sleep. My oncologist started me on gabapentin and promised that with time, it would get better, and it has.

So nearly seven years now, I'm cancer-free, which is a good thing. I'm on 3,300 mg of gabapentin. Without it, I couldn't function. My pain level today is greatly reduced. It's that sort of constant numbness, unpleasant numbness. Tingling's not pleasant. I can't feel my feet. They sort of feel wooden. So my balance is lousy and it's something that I work on all the time. I have an increased sensitivity to cold. I love a good, crisp winter day. But I can't take my grandkids ice skating or teach them how to ski.

And the summertime, like today, normal air conditioning, particularly on my feet, just turns them into blocks of ice. If I sit -- I can stand and walk okay -- but if I sit for long periods of time, the pain is worse. So travel in a car or airplane has become for me very difficult.

And even on my very, very best days, when I'm able to do what it is I want to do, I constantly have to be mindful not to do too much. Don't have too much fun because if I get over tired or stressed, that for me is when the neuropathy kicks in. so after one of those really good days, I sometimes have a really bad night. And in that bad night, the pain intensifies. It's what I described on my worst days. It's impossible to sleep. And I'm not a heck of a lot of fun on those evenings. And as I lie in bed, the neuropathy reminds me that I'm living with cancer. It's a constant trigger in my mind that I'll always be living or battling my cancer.

I know I'm lucky. I can function. And plenty of people out there can't. They have a

much harder time. The disease for them is much more debilitating. But I bet there's hundreds, and I bet thousands of people like me. They probably aren't even in this room because they've accepted peripheral neuropathy as a consequence of the chemo. They just -- you just accept it. I'm happy to be cancer-free. But yet, ironically, the drug that may have cured my cancer has left me with peripheral neuropathy. And it's the neuropathy that makes me unable to really fully enjoy the life that the successful cancer treatment has given me and that's what makes me really mad.

So what do I worry about? I worry that I take a heck of a lot of a drug that was developed to keep people from having seizures. And if I'm really lucky, I may be taking it for a really long time and who knows what that's going to do and how it's going to impact, you know, where I go in this next sort of chunk of my life. So anyway, that's where I am today. I'd like to thank again the people on the panel who are

joining me and the organizers of the committee. And I look forward to our discussions this afternoon.

MS. GIAMBONE: Thank you so much, Susan. Next, we have David.

MR. MORROW: Yeah, hi. I'm David Morrow, and I'm senior vice president of the Neuropathy Support Network. And I have a very similar story to Susan. My neuropathy started in 2009 as well as a result of chemotherapy and surgery I received for colon cancer. And my symptoms started probably -- I had 12 sessions of chemotherapy that were scheduled. And it started probably on my ninth session. And by my tenth -- my eleventh session, my doctor stopped me and wouldn't let me take the last session of chemotherapy.

It began -- the symptoms began slowly. They were sort of mild, more of tingling and numbness in my hands. And I would get this weird sensation that I was wearing socks, even when I wasn't. And then, before I knew it, I began

fumbling with things. And it was -- you know, when I dropped my first cup of coffee, I thought it was because I was just being clumsy. And then, I dropped another cup of coffee. And then, I was seasoning my food and I dropped my salt shaker. And I would drop my keys. And it wasn't because I couldn't feel things. It was like I could put my -- if I could put my hand in my pocket and I scraped my fingers up against my keys, it almost felt like I was scraping them up against shattered glass. It was very painful. But when I would pick something up like a cup of coffee, I couldn't feel how hard I was gripping it. So ultimately what would happen is when I would pick something up, it would slip through my fingers.

But as bad as it got for my hands, it really became worse with my feet and my legs. What would happen is at night I'd be woken up in the middle of the night with like these stabbing pains in the bottom of my feet that would shoot up my legs. And then, it felt like I was walking on rubber pads, rounded rubber pads, which is a very

weird sensation. And ultimately what that resulted in was it affected my balance. I couldn't really balance. So like, for instance, if I was taking a shower and I was rinsing my hair and I closed my eyes, I would fall. I would fall against the wall. Or if I -- you know, when I'd get up in the morning, first thing when I'd get up in the morning, I'd have the pain also in my feet and tried to move around. But if I tried to put my pants on and I lifted one leg up off the floor, I would fall. So what I learned to do was I learned that I would have to lean against the wall or sit down and do certain particular things.

And where this became a problem was at a certain point I realized I couldn't really tell where my feet were. And this manifested in a situation where I was driving to a restaurant to meet a friend and I pulled into a parking space. And I hit the gas pedal instead of the brake and I ended up on top of a cement bumper. And at that point, luckily there wasn't a car in front of me. But I realized at that point how a person could

actually drive through a store window. So ultimately what ended up happening was I had -- in my worst times, I had to get people -- you know, someone to drive me because I couldn't drive myself. And then, because of the balance issues, when I would get out of the car, there was like an instance where I got out of the car, because I couldn't feel where my feet were, I was in a parking lot, got out of the car and my feet were up against a curb and I ended up falling flat on my face. I fell a couple of times because not knowing where my feet were.

So as far as specific activities that -- you know, that I wasn't able to do, you know, through the symptoms I described to you, pretty much all those were due to the chemotherapy. But also, because of the surgery that I had, I had abdominal surgery, I lost sensation in my stomach. So I have no feeling in the top layer of my stomach, which is -- which is -- it's a very strange feeling because I can feel underneath it but I can't feel on top. So in an intimate

situation like with my girlfriend, if you have stomach-to-stomach contact, it's not painful. But if there's any friction, there's a great deal of pain underneath my skin and I don't know how to describe it. The other thing that occurs is that occasionally I'll develop itching on my stomach that's down below my skin that I can't reach. So I could scratch all I want, but the itching is not going to go away.

So basically, over time, a lot of these symptoms have dissipated. Now, the neuropathy in my hands, I really don't feel it or notice it unless I think about it. I do still have the feeling on walking on rubber pads sometimes and sometimes it's painful when I've been sitting for a long time and get up. And I still have the issues with balance, which still bothers me. You know, if I try to climb something a little steep, it's not going up that's so bad. It's coming down. You know, it gets scary. And it's hard for me to run and -- because of the balance issues and stuff. As far as the surgery goes, you know, my

stomach is always going to feel the way it is. I don't have any hope that that's ever really going to change.

So the thing that really worries me the most is as I get older, I'm a little worried about the balance issues because I'm afraid the balance issues may end up affecting my mobility. But I have to admit I really feel a little guilty sharing this because I'm getting better. And I know that there are so many people out there that are so much worse off than what I am. And I just wanted to share something that I think is very important and really impacts this and really speaks to this one question about what worries you the most about your condition.

The Neuropathy Support Network just recently did -- with the Western Neuropathy Association, just recently did a comprehensive survey. And we received a great deal of responses from people. And we asked this very specific question, what worries you most about your condition. And we found that there was a common

underlying thread that was very similar to all age groups within the people that responded. But there was one response that really stood out for me and I think really underscores the need for meetings like this that we're having today.

And it was from a young woman who had just turned -- as she says in her own words, she's just barely 20 years old. And she had been diagnosed with diabetes 1. But her diagnosis for her peripheral neuropathy was idiopathic. And so, when she reached the survey question, what worries you most about your condition, she simply answered, my future. Now, understand this is a 20 -- this is a girl who's just turned 20. She answered, my future. I'm still very young and the prospect of being in this kind of pain the rest of my life makes me not want to live it. And that was a common theme through many of the responses that we received.

MS. GIAMBONE: Thank you, David. And last, we have Beth.

MS. LANNON: I'm glad I'm old when I got

this. I do feel bad for you young people. My problem began with minor bilateral pain in my feet in 2009. I was a triathlete. I noticed it when I was running. It was such a slow progression that I didn't even think of going to a neurologist. I saw an orthopedist and podiatrist. And it wasn't until my hands started tingling and going numb that I said, oh, neuropathy. I need to see a neurologist and --

MR. THOMPSON: Could you move your mic a little bit?

MR. LANNON: I'm sorry. So it wasn't until I actually started feeling some tingling in my hands that I went to a neurologist. But for like 18 months, I was just -- had no clue. I describe my pain as sharp, constant, bruised, like somebody took a hammer to my feet. I know that's not typical and most people don't describe it that way. It's true whether I'm sitting, standing or laying down. And when I'm walking, it's kind of like I'm walking on rocks. So I wouldn't say this is just bothersome. It's debilitating. You know,

I spent 16 hours a day laying down. And not -- actually not all at once. I intersperse it with what I need to do to live. So I just do things in short bursts.

Besides the pain, I do get electrical shocks. It's like sticking your finger in a light socket. I get them in my toes, my hands, my feet, my hips, my eyes. That's the worst. Doctors don't know what that's -- what causes that. They just say it's progression. So I don't know. And they go away. I'll be plagued with them for a month and then they disappear and I'll be fine for a few months and then the electrical shocks start up again. At least they're short, you know, short bursts.

The other bothersome thing is that one doctor described it as he doesn't think my nerves know how to open and close my veins and arteries because they can't find anything wrong with my veins and arteries. But my lower half of my body takes on the temperature of the air. So my toes -- first it started with my toes. They would be

freezing. Then, you know, my feet. Now it goes all the way up to my hips. So in winter, I do not want to be outside during the winter. Let me see. Oh, and I do understand the tingling and burning. That's on the top of my feet, the not wanting to wear socks, the brushing of the sheet against your feet that sends you jumping. I know those are -- those are kind of the common neuropathy feelings.

It usually happens when I'm overtired, you though. You know, I've been standing or walking for more than a few minutes. And that's when I tend to think of my feet as being on fire. It's like, oh yeah, they're on fire. Need to get them in ice. And like I said, I do have the numbness in my toes in particular. So my feet, they've got the pain at the bottom, the tingling, the burning at the top and my toes are numb. My hands are, you know, typical neuropathy, the tingling and burning, numbness there.

Things that I can't do, gee, well yeah, sleeping's a problem. Everybody knows that. How do you sleep in pain? How do you fall asleep in

pain? And it wakes you up in the middle of the night. But you know, I struggle through every -- I struggle to make it through every day. I know I look really normal to most people, you know, especially when I'm at work. So people don't realize that no matter what I'm doing -- what, in the foremost part of my brain, is what I'm thinking, my feet hurt. And they will be hurting so bad by the end of today that I will probably be in bed all day tomorrow. I just know that. If you're going to do something, you plan for a day and then you pay for a day. That's okay.

I lost my ability to do just about everything. I think I mentioned I was a triathlete. I worked 50, 60 hours a day. I can't -- I can't sit for long periods of time. So even just going to movies or plays or, you know, a game are uncomfortable. I do it sometimes. I'm untreated. None of the medications worked or gave me such bad side effects that the doctor said, nope, you can't take that any longer.

I can still do daily hygiene. But it

makes me tired. You know, I have the shower handles and the seats. But you know, okay, then you've got to sit down and rest for a while before you go onto the next thing. I also have a rolling walker to get around the kitchen. So even preparing -- oh, I changed my diet. I guess that's for a good thing. I now only eat things that can be prepared in less than five minutes. You know, raw fruits and vegetables, nuts, peanut butter sandwiches, anything that doesn't make me have to stand on my feet and cook. I live alone, so that's a problem.

I used to be a veterinary technician. I worked 50 to 60 hours a week. I loved the job. It's a job I took -- got late in life. I'm glad I quit corporate America in my forties and went back to school and got a chance to do it. So that's what I said. I'm really sorry for those of you that are young. A lot of people think that's a very strange profession for me to have. But I only work two hours a day. I work Monday, Tuesday, Thursday and Friday, two hours a day.

This job's good for me because I can stand when I want to, sit when I want to and walk when I want to. There aren't many jobs that let you come in for two hours a day and do that. But I've been working there for a very long time, so that helps. But I miss it. Gee, what have I not said? One more -- one more thing.

MS. GIAMBONE: Beth, you want to tell us what worries you most about your condition?

MS. LANNON: Oh, I fall. I live alone. So I guess that's --- you know, that's the worst thing. I've had some really bad falls. I've torn my MCL. I've broken toes. I end up bruised. I knocked myself out once falling down the stairs. So living alone, that's the main thing that I worry about.

MS. GIAMBONE: Thank you.

MS. LANNON: And who's going to take care of me? I don't know.

MS. GIAMBONE: Thank you so much, Beth. Thank you for your comments. Okay. Is this on? Yeah. So let's give our panelists a round of

applause for putting together -- [Applause.]

MS. GIAMBONE: Thank you for preparing so well and for writing and sharing such personal stories with all of us. So it really means a lot to us. And I want to ask to the audience, how many of you feel as though, you know, the experiences that you've had, that what the panelists have said -- how much of that resonates with your own experiences? Yeah, so a lot of the patients in the room are able to have similar experiences. And I know there's different experiences too.

I did take a few notes as the panelists were talking. And so, I just want to do a really quick show of hands. Adam, you mentioned that you feel like your legs are on fire. Do others share something similar, that your legs are on fire? Okay. And then, Susan, you mentioned that you have an increased sensitivity to cold. Others? Okay. Yeah. David, you mentioned balance issues. Balance issues, others? Absolutely. Okay. And then, Beth, you mentioned -- so while you were

talking, you said that -- you said -- I think you said you're not sure how many others feel this way. You said you feel like a hammer on your feet. How about others, a hammer on your feet or walking on rocks I think is what Beth said? So there are others that share your perspectives.

So that's -- glad to see so many similar experiences. Looking forward to hearing some of the different experiences in here as well. I do also want to ask how many of you are in pain right now as you're sitting here sharing -- you know, ready to share your experiences with us? Let's see, almost 12 or 13 hands that I see raised for those of you in pain right now.

Okay, so let's -- actually, we're going to do another polling question to sort of kick off our discussion now. So everybody get your clickers out again. Okay, what parts of your body do you experience your most severe neuropathic pain? Check all that apply. A, head, face or neck; B, hands or arms; C, feet or legs; D, trunk; E, back; F, genital area; or G, other areas not

mentioned. Okay. So it looks like those of you answering have said that C, feet or legs is where you experience your most severe neuropathic pain. We also see some hands or arms and trunk, genital area. And let's see, are there other areas not mentioned? Not too much. But please be sure to tell us if there's anything else that comes to mind. How about on the Web? What do we see there?

MR. THOMPSON: We see 95 percent for feet or legs, 38 percent for hand or arms and between 15 to 20 for all the rest.

LARGE-GROUP FACILITATED DISCUSSION, TOPIC 1

MS. GIAMBONE: Okay. Okay. So would somebody like to start us off with feet or legs? Now, we've heard different ways our panelists mentioned how they're experiencing it in their feet or legs. But would somebody in the audience, other patients or caregivers like to tell us how you experience it in your feet or legs? And what do you experience? What is that sensation that you feel?

MR. KLITZMAN: Well, one thing that we haven't talked about, and maybe it's not within the scope of this discussion, but I experience more numbness than pain. To the extent that I'll be walking or standing for a long time. And then, I lose the contact with the ground, which David referred to, and I have to hold on to something or shake my foot. I was in a department store with one of my kids, buying clothes for him, and we finished that and then we met some family that we knew. And we started talking in the department store area and they kept chatting away and chatting away. I had to go on -- I had to look for something to hold on to. I found the tie table and I sort of looked like I was looking at ties, holding onto the edge of the table so I could shake my foot.

It was a very scary sensation if you feel you're losing contact with the ground. You don't want to fall. And I know that numbness is not on the agenda necessarily. But it often gets overlooked. And you know, if one day there could

be a medication to cure numbness or to regenerate the nerves, you know, that would be a real blockbuster, instead of just focusing on pain all the time. But numbness shouldn't be disregarded.

MS. GIAMBONE: Steve, thank you so much for your comments. And actually, we will be talking some more about numbness. I know it's a very important aspect of how you experience the neuropathy. And can I just ask actually, while we're on the topic of numbness, is it the numbness that leads to the balance issues that we've heard David describe, and now, Steve, that you've described? I see heads nodding. Would somebody like to -- sure.

MR. SHROUT: Sure. I'll speak up on that. My name is Gary Shrout. I've had this for a very long time. It's idiopathic. Nobody knows why or what. As Dr. Galati was going through his thing, it's like, yep, yep, yep, yep, both all the pains and everything. So all the symptoms. I certainly identify with the numbness and --

MS. GIAMBONE: We're going to see if

your mic is on. It doesn't sound like it's on.

MR. SHROUT: Oh. Okay, how's that?

MS. GIAMBONE: No. Go ahead and use mine. Use mine.

MR. SHROUT: Okay. All right. Name's Gary Shrout. I've had this for probably over 30 years, so not diagnosed officially until 13 years ago. Idiopathic. Nobody knows why. All the pain symptoms you could possibly have, I've had. I've been very blessed. I'm still able to function pretty much normally. Balance is a big deal. Numbness is a big deal. I've classified my nerves into three categories and I'm determined to hang onto the ones that I really need. The good guys, the normal ones are still doing fine. Hi, happy Friday. The dead ones, it's like, dude, I'm gone, you're not going to hear from me again and then other ones that are screaming for help. And it's the ones screaming for help I think that are partially damaged, that are still communicating that cause the problems.

Numbness is a huge deal. I've had the

feeling of wearing socks. That's like it right now. And I'll make some comments later at a more appropriate time about some interesting things that I think are happening. But yes, numbness is a deal. Balance is a deal. My pain has been everything that you guys have listed up there, including the ice pick going through the top of the foot, which is real nice in the middle of the night. Sleep is an issue. Get up, go the bathroom. You may have been exhausted from the day and, you know, you finally pass out, despite the pain. Get up, go to the bathroom when you've had a little bit of rest. Well, guess what, getting back to sleep is not an option. So I hope that contributes to what you're looking for.

MS. GIAMBONE: Yes, thank you.

MR. SHROUT: Thank you guys for doing this.

MS. GIAMBONE: Thank you.

MR. MORROW: I do think there's something also --

MS. GIAMBONE: Thank you.

MR. MORROW: -- that needs to be said about the numbness so that people who don't have this understand. Because you are numb doesn't mean you don't feel pain.

MR. SHROUT: Right.

MS. GIAMBONE: Okay.

MR. MORROW: You can have numbness and still feel severe pain.

MS. GIAMBONE: Okay.

MR. MORROW: And that's a -- it's sort of a weird condition when you first experience it.

MS. GIAMBONE: Okay. I heard a lot of people agree to what you just said, David. Okay. Let's take one more comment. We'll -

UNIDENTIFIED AUDIENCE MEMBER: Okay. I had Guillain-Barrsyndrome, or GBS, 42 years ago and for the last 42 years, the first thing I want to do at the end of the day or even in the middle of a day is rip off my shoes and socks. My feet, barefoot I feel a lot better. I was an aspiring drummer and I had to kind of give that up due to -- if you know anything about drumming, your feet

are a very important part of that. And my feet simply didn't work and I'm up on stage trying to do some drumming and everybody's kind of looking at me like, you know, dude, what are you doing up there. So but just numbness and pain. The only way to really get rid of the pain is an ice bucket, an ice bucket filled with ice water for about 10 or 15 minutes and I'm good to go for a little while, so --

MS. GIAMBONE: Okay. Okay, so numbness in the feet is what I'm hearing a lot of, then. Okay, other experiences that you'd like to share? Right here, Meghna.

MS. CHARLESTON: Good afternoon. I had a thyroid storm that led to Guillain- Barrsyndrome and I have the pain, the numbness and the tingling all over my entire body. There is not a specific area that's worse than the other. I t's all bad, all the time. So for me, I'm a very active person. And in order to stay active and doing the things like volunteering and things like that, I have to not be on medications. So if I stayed on

the Lyrica and the tramadol and all the different ones that I saw on the screen, then you're sleeping 24/7.

MS. GIAMBONE: Okay.

MS. CHARLESTON: So the numbness and I think the tingling together has me off- balance --

MS. GIAMBONE: Okay.

MS. CHARLESTON: -- because it seems like a lot of times, it's a connection issue when my body's in motion and I'm walking and I'm walking and I'm looking at you and I'm coming over to see you, I have to constantly say keep moving, keep walking, pick up your legs, go, shake hands. But if I look to the left, I just stumble. I would fall before I get to you because I've taken my sight off of where I'm going. And it's kind of like that.

MS. GIAMBONE: Okay.

MS. CHARLESTON: So the balance issue is tied into focus, concentrate, lift your feet, move your arms, stay, go in one direction. Don't try to do something else while you're going over there

because you just lose balance.

MS. GIAMBONE: Okay. So let's do a show of hands. How many others feel -- and sorry, I didn't catch your name.

MS. CHARLESTON: Tonya.

MS. GIAMBONE: Tonya. I saw some heads nodding while Tonya was speaking. How many others relate to what Tonya just said about having to sort of focus and make sure that you're concentrating on your next step, just so you can keep your balance? Okay. Okay. So let me bring us back to this polling question because what I want to ask is can you -- can you tell us about differences in how you experience the pain or the tingling or the numbness in different parts of your body? So how is it different, for example, in your feet or legs than it is in your hands or arms? Can -- is there -- is there a difference between how you experience it in different parts of your body?

MR. MURPHY: My name is Tim. I have a chronic inflammatory demyelinating polyneuropathy,

specifically Lewis Sumner syndrome. And so, I have symptoms in all my arms and legs and they all differ. So with my feet, it's mostly a numbness, maybe some tingling that's led me to several falls, limited some activity. At its worst, I'll take the elevator instead of the stairs. But my worst symptoms are in my arms and that's where it had started. And so, it's a dull, like somebody hit me with a hammer, pounding. It feels like my right arm is made out of wood. And then, the best -- in addition to medication, I've had it all, but I'm currently on Motrin and Neurontin and biweekly IVIG treatments. But actually the best thing is exercise, as much as I can do it, because the persistent -- I like to swim -- pounding of the water takes probably 50 percent of the symptoms away, as long as everything else is working.

MS. GIAMBONE: Okay. Thank you, Tim. Are there other areas that you'd like to share with us before we move onto the next question? Yes?

MS. LANNON: You asked about diagnosis.

I have CIDP too. That's probably why we have such similar symptoms. And the thing about exercise is I went to a physical therapist and I made him realize the importance of letting me do exercises where I didn't have to stand because they all wanted to make me stand. I'm like, no, you don't understand. I can't stand. I won't stand and do exercises. We need to do them laying down. I need to be able to work every muscle in my body laying down and it works great.

MS. GIAMBONE: Okay. Okay. Thank you, Beth. Let's take one comment here.

UNIDENTIFIED AUDIENCE MEMBER: It's sort of a generalized question. We're telling all our stories and so it's all very experiential. My major question -- well, I'm a science writer -- what's it leading toward? What are these individual stories -- where are they leading to in terms of research priorities? What is the status of the research that is going on? What do we need to do about that research as it applies to our individual problems? Because all of this is so

individualized.

Is there a field theory yet of neuropathy? Some of you know what a field theory is in science. But what are the generalized questions that we need really to know about where things are going? So we can tell our stories, you know, on and on and on and on. But where is it leading and how do we know, how do we keep track of it? Where's the place to go to really get to understanding? What are other areas of research? By who? Where? Who to talk to if you really have a real question, stuff like that would be useful.

MS. GIAMBONE: Thank you. Thank you for bringing that up. And I think that's exactly why we're here today, to hear from patients because you're really the experts. You're the experts in how you're living with the pain and the sensations of pain and numbness and tingling. And I think what we -- what you tell us is really important to the work that we do and to the work of drug developers. And as my FDA colleagues identified, you know, at the start of the meeting, that's

exactly why we're here, is to learn from you so we can move forward with this in drug development. Okay. So I think we have -- let me check in with the Web really quick because we're going to move on to the next question, which I think is really the bulk of our discussion.

MR. THOMPSON: So some of the symptoms that have been mentioned on the Web, people having issues with balance and coordination, for people with pain in the face or head region, it's common to also get migraines. Many people mentioned feet issues, such as numbness in their toes, burning feeling like sunburns, pain in the ankles or feeling like you're walking on nails. A few people mentioned sleep problems. And there's also mention of Charcot disease, which is a syndrome of bone deformation caused by peripheral neuropathy.

MS. GIAMBONE: Okay. Thank you. And actually, before we go on, I did want to ask one question. Can somebody describe to us what is the different between numbness and tingling or can you describe separately how these terms are different

from one another? We've heard burning, shocking pain. We've heard tingling, of course numbness. Can somebody tell us how -- what's the difference in how you experience it? Can we come to -- oh, yes. Tonya, let's start with Tonya.

MS. CHARLESTON: Hi. The numbing part of it I guess best described is when I put my hand in my bag and I want to pull out lip gloss or a pen or something, I cannot feel it.

MS. GIAMBONE: Okay.

MS. CHARLESTON: I can't distinguish what the item is without physically dumping the back out and looking and saying, oh, there it goes. The tingling is like something that's creepy, crawling all through under your skin, every which way. And you just feel like every nerve end is yelling out you because it's like, sit down, sit down, you know, put a blanket on, warm up or be still, don't move, because you're hurting so much. So the tingling is creepy, crawly things just all over, in you, through you, everywhere.

MS. GIAMBONE: So tingling is sort of an all-over feeling. Numbness is maybe more localized or is it --

MS. CHARLESTON: You can't distinguish the feeling or it's like -- like with my hands, I can't distinguish what the item is.

MS. GIAMBONE: Okay.

MS. CHARLESTON: With my leg, if you were to squeeze my leg, I can't really tell. I can see you're squeezing it but I can't initially feel the pressure like that.

MS. GIAMBONE: Okay. Okay. Thank you, Tonya. And I think Lou wanted to say something.

MR. SCHMITT: The best way I can describe the difference between the numbness and the tingling is the numbness -- we've all had the sensation of our feet or legs going to sleep. That's what the numbness feels like to me. It's you can look at your foot, you can wiggle your toe and you can't feel that you're wiggling your toe, if you're able to do that. And it's the same thing when your foot goes to sleep and you try to bring

it back. You move your foot and wiggle your toes and you can see it but you can't feel anything. That's kind of how the numbness is for me.

The tingling is kind of when you do -- your foot does fall asleep and you move it around. And all of a sudden, the sensation starts coming back. Then you start getting those pins and needles and kind of the tingling feeling as the sensation returns to your foot. Now, I don't get that anymore because my feet are numb. So I don't get sensation that comes back. But I still get the tingling feeling. So it's -- so the numbness is sort of like when the foot's asleep. The tingling is sort of like when the sensation is starting to return and you start getting that first feeling that the sensation's coming back and it starts to tingle. And that's kind of how my numbness and tingling feels.

MS. GIAMBONE: Okay. So I'm hearing you say that with numbness, it's not that it -- it doesn't go away. It stays numb whereas the tingling is sort of like an on and off type thing?

Okay. Do others feel that same way or is it different for you? How about with --

MS. WALDROP: You know, one thing I'd just like to emphasize is that numbness and tingling as words don't sound so bad. You know, it doesn't sound like it's that bad. But it really is bad.

MS. GIAMBONE: Sure.

MS. WALDROP: It really is painful. It's really uncomfortable. And it -- and I wish there was another word that could better describe what we all feel because I think we know what we all feel.

MS. GIAMBONE: Okay. Let's take a comment over here. Yeah? Sure.

MS. PAGETT: I'm Cherie, and the numbness is like a block, like your foot -- it is on -- like your foot is a block. But at the same time, numbness is so dangerous. It's like -- it's having your big toenail ripped off and not knowing it for 10 minutes when you look down and you see the blood. That's numbness. So I mean, it's --

you can really injure yourself because you can't feel what's going on with your feet.

MS. GIAMBONE: Okay.

MS. PAGETT: The tingling, it can be like jabs and darts and that Lyrica commercial that we've all seen with the foot with all the stuff going on all over it, that's the tingling part and the -- there is a difference.

MS. GIAMBONE: Okay. Okay. Yeah. Okay. And do you feel that there -- is there a part of your body where you feel -- I know Tonya said tingling was more of an all-over body sensation for her. Is that the same for others, where tingling is more of an all-over sensation or do you find that it's more localized for you and in a certain area of the body? We have a hand raised back there. I'll just take one comment here.

MS. COOK: Hi. I'm Evelyn and I have CIDP. I went into relapse about three months ago. And I get the tingling mostly in my hands and my feet, although I have had it in my face. And

again, I just want to emphasize it's not mutually exclusive. So when you're numb, you may also be feeling tingling at the same time.

MS. GIAMBONE: Okay. Thank you, Sharon. Sharon, right? I hope I got your --

MS. COOK: Evelyn.

MS. GIAMBONE: Evelyn, I'm sorry. Okay. Thank you, Evelyn. And now, let's look to my FDA panel. Sharon, you have a question?

DR. HERTZ: So by way of background, I'm a neurologist and I actually was in practice prior to becoming a bureaucrat. And so, what I would like to know -- I certainly do understand the difference between the numbness and the tingling, the paresthesias, as we would call it, versus the sensory loss or hypoesthesia. And you may have heard some of those terms or seen them even in your doctor's notes or in materials that you've read.

When you think about treatment and when we think about what we see coming in for treatment, we tend to see two things that

sometimes overlap but also sometimes are independent of one another. For painful neuropathy, we also will see symptom management. And what typically that refers to is a positive symptom, like the occurrence of these pins and needles, tingling sensations, what I will call painful paresthesias --

MR. KLITZMAN: Can you speak up a little bit? I can't hear you.

DR. HERTZ: Sure. Sorry, is that better?

MR. KLITZMAN: Very.

DR. HERTZ: So we typically see one of two approaches, two therapeutics. We see drugs being developed to treat the positive symptoms that you've been describing, predominately the painful tingling, the painful pins and needles sensations. But we also see people who are -- or companies that are interested in what we would call disease modifying treatment, trying to fix what's wrong with the nerve and that would try to either slow the development of the numbness or the

lack of feeling or even try to restore it, depending on the nature. If you had a pick, what was important to you, is it more important to decrease the positive symptoms that are associated with pain or is it more important to try and restore the lost function, the numbness?

MS. GIAMBONE: So why don't we do this by a show of hands then? So is it more important to -- you said the first is decreasing the pain, right? So who thinks between decreasing the pain and restoring the function -- the sensory function, who thinks decreasing the pain is more important? Okay. So we have one, two, three, four, five, six -- we have about 10 hands raised, 11 hands raised. And how about the flip side, which is restoring some of that sensory function? One, two, three, four, five, six, seven, eight, nine, ten, eleven -- about twelve. So it seems about the same for both.

MR. MORROW: You know, I think it's sort of a misleading question though.

MS. GIAMBONE: Okay.

MR. MORROW: It's the wrong question to ask. And the reason I feel that way is because it depends at what level you're experiencing the neuropathy. We have a tremendous amount of people that contact us that have debilitating pain. You know, it affects the way they function and the way they react with people and just affects their lives overall. It puts them into a deep depression because it's pain all the time and it's the type of thing that never goes away. And because it never goes away, it may seem tolerable in the beginning. But over time, it gets worse and worse and worse. And at a certain point, some of these people reach a breaking point.

And so, to ask that question -- I think by all means -- I think pain has got to be very important in this, that to alleviate the numbness, that to me is after the pain is gone. And for those people that are at that level, yeah, that's important. But I think for the people that are out there, there's too many people out there suffering through the pain right now that really

need help getting rid of the pain.

MS. GIAMBONE: Thank you, David.

UNIDENTIFIED AUDIENCE MEMBER: [Off mic} -- why is that an either/or aspect, why is --

DR. HERTZ: I'll just say why I was curious about that piece of the question is because it impacts how the products are developed. Symptom management could be an earlier measurement, reducing pain can happen quicker because what we know, and I'm sure you all know as well, is trying to see healing of a nerve is an incredibly slow process. And it can take years even in situations where it's possible.

So it helps me to know in the context of when they are both present because I definitely understand the concept of the progression in certain types of neuropathic conditions where early on it's predominately positive symptoms. And then, as the damage progresses, it's more that negative loss of feeling. But when we discuss this with companies that are trying to develop products and we're trying to see what makes sense

in terms of staging the clinical study and what to try and get out of the study, it's just helpful to hear some feedback on that.

UNIDENTIFIED AUDIENCE MEMBER: Can I make a general --

MS. GIAMBONE: Yes.

UNIDENTIFIED AUDIENCE MEMBER: I think it's a no-brainer on the question. Forgive me for barging in. But yes, you do have to relieve pain. There are products out there that relieve pain out there now. How many products that are out there actually cure neuropathy? I mean, you know, let's get real, because once it's curable, you don't need to worry about the pain.

MR. MORROW: Yeah, but I don't think there's that many products out there -- I think there's a lot of products that will help the pain. But from what I'm hearing back from patients, it doesn't completely alleviate it and there are too many patients out there that have the pain so severely and they can't get any sort of relief from it. And the other aspect of it is for most

drugs that are available to them that they can get some relief, the side effects for some of them are awful. And so, it really comes down to I think, again, is what situation, where you're at in regards to where you're at with the neuropathy. And the people that suffer from the pain and they're in the severe pain are not here today.

MS. GIAMBONE: Okay.

MR. MORROW: You know, I think it's great that Elizabeth made it because I know how difficult it was for her to get here. But you're not going to hear from the people that have the really severe pain, you know, as much as you're going to hear from the people that have maybe just the numbness like myself.

MS. GIAMBONE: Thank you, David. And you're all bringing up some very, very good points. And I want you to hold onto the topic -- the points on treatment because we do have the second session really dedicated towards what you're looking for in treatment. So they're all important and we are going to get to them, I

promise you. However, I do want to check in with the Web because it sounds like we have some updates coming in from the Web. And I know that we have some -- to David's point, some people that couldn't travel to come here today joining us on the Web. And Adam, I promise I'll come to you right after.

MR. THOMPSON: So we have a few people who have called in. but before that, we've had a couple of comments on numbness and tingling. Some people described it as a confusing sensation, like ants crawling or small cramping localized over the body. Numbness has been described as just having a lack of sensation or feeling in certain body parts or localized tingling. And some people describe tingling as mild to moderate electric shocks.

MS. GIAMBONE: Okay. Thank you. Adam, would you like to share your perspective?

MR. HALPER: Yeah. I just -- maybe I misinterpreted the question. But the way I interpreted it is almost like there's two separate

questions there, right? And so, I think if you were to break it apart a bit and phrase it as, you know, if we're thinking about priorities, should it be symptom management or figuring out a way to actually alter the underlying disease process, I think you might -- and I could be wrong, but I think you might get a different set of answers because I think for people who have a progressive form of neuropathy, you can treat the symptoms to a degree. But if it's going to keep getting worse and worse and worse, there's only so much you can do. So speaking from my point of view, if you were to phrase the question that way, I would personally say unequivocally that modifying the disease process would be my priority.

MS. GIAMBONE: Okay. I see some head nods with what you just said, Adam. Thank you. All right. Let's --

MS. LANNON: Yeah. I think that's really true because I first chose to stop the progression. I have CIDP. I could stop the progression. We spent a long time doing that.

But once the progression was stopped, I don't have any pain relief. So right now, yeah, my brain thinks nothing but pain, pain, pain. But you're absolutely right. When I was first -- started getting the symptoms, I wanted it to stop progressing. That was my -- the main thing, stop the progression. You know, and if I don't just think about myself and the pain that I live with, yes, I would want them to stop the progression and be able to stop the progression for anybody that it happens to.

MS. GIAMBONE: Okay. Thank you very much, Beth. Leslie, you have been waiting very patiently. Can we bring a microphone over to Leslie?

MS. LEVINE: I think I've been on both sides of this. I have autoimmune small fiber. It took three years to get that diagnosed -- diagnosis. But when my neuropathy came on, it came on quite quickly and I went from being a high functioning professional to being on disability, practically unable to do anything. It felt like I

was having a blowtorch applied to my - - first my feet, but then it went up my legs and my arms and hands. And I don't know how long I could have taken it. None of the drugs worked except for opiates and my doctor -- I wouldn't have stood it for three years without that. And there's a lot of people now with the opiate issues that can't get that.

For the last seven years, I've run a support group for neuropathy patients of about 60 people. And the people who are in this level of pain can't get to the group very often and they usually drop out because they end up not being able to leave their homes. They can't drive. They can't function. I was in that status and finally I got on IVIG and my symptoms largely went away. And it was my life back. People are paralyzed by depression after being in this level of pain for very long. It pickles your brain. It -- my -- well, I won't go into all the effects on my life. But it was devastating and it was agony. And I can understand why some people commit

suicide because of this. And so, I'm on both sides of this issue. The pain control, when you're in that level of pain, you can't go on without it. But the disease modifying, where all of a sudden you don't need the pain control, is definitely worth research dollars, of which neuropathy gets very few.

MS. GIAMBONE: Thank you very much, Leslie. Let's do a polling question.

[Applause.]

MS. GIAMBONE: It sounds like your comments really resonated with a lot of people in the room.

MS. LEVINE: Thanks.

MS. GIAMBONE: So let's do a quick polling question, if we could get our clickers out again. How do your neuropathic pain symptoms typically manifest? A, pain appears suddenly and progresses rapidly; B, pain appears subtly and progresses slowly; C, pain comes and goes; D, pain is continuous; E, pain worsens over time; F, other manifestation not mentioned; or G, I don't know.

Okay. So it looks like we have the majority of people said that pain is continuous, which you all highlighted early on when I asked how many of you were actually in pain right now. Many of you said you are. So pain is continuous. And C, pain comes and goes. And we also have pain worsens over time and other manifestation not mentioned. So whoever answered that, I definitely want to encourage you to share your comments.

So on this note, what I'd like to ask is, you know, some of you have described -- and I know that even some of you that provided your comments and so forth mention that sometimes you experience a flare-up or a time when your pain is significantly worse than your average day of pain. So I don't know if that's the right word to describe it and I want you to tell us if flare-up is the right word to describe it. But can you share with us, you know, what an average day of experiencing the pain or the tingling or the numbness, what that is and then what your really worse -- you know, what it feels like on your

worst day or your -- is there a flare-up and what does that feel like. Oh, we have Lou and then we have --

MR. SCHMITT: The way I describe -- my pain's constant. It never goes away totally. But the way I describe my pain is that it's as if you're in a room and somebody comes in and turns on a radio at kind of a low volume. When they first turn it on, you hear the radio. But after a while, you don't really pay that much attention to the radio any more. So a good day for me is the pain's there, but it doesn't get my attention all that much. I go through my day. I do what I need to do.

On a bad day, when there's a flare, it's as if then somebody turns the radio up as high as it can go and then now all you can hear is that radio. And so, the pain becomes really, you know, a kind of focus of my day when it's that bad. I really can't focus on other things because the pain is just so severe, you know, that it really kind of takes over my consciousness at that point.

So that's kind of the way I experience the flares. And by the way, when we talk about pain and we talk about the symptoms that we get, my pain isn't just different day to day. It's different moment to moment. It is never exactly the same.

It becomes greater in intensity. It becomes lesser in intensity. It moves to other parts of my body. The sensations themselves go from perhaps stinging then to stabbing, you know, and burning. And it never is exactly the same from moment to moment. Btu when there's a flare -- that's what I call them. I call them flares. When there's a flare, it's as if somebody just turns the volume up on the pain way up and I become much more consciously aware of it.

MS. GIAMBONE: And is it a certain aspect? Like you mentioned stinging, shocking. When you're having a flare, is it -- which one of those is worsening or are all of those worse?

MR. SCHMITT: It becomes -- it becomes -- instead of more -- instead of kind of a stinging, a tingling, it becomes more of a

stabbing type of a pain. You know, it's as if -- when it's at its worst, it feels as if somebody plunges a knife into my leg and just drags it down my leg. And it's much more -- it's much more focused in a certain area than the kind of generalized stinging and tingling that I usually get. It'll feel like somebody's pounding spikes into my feet. You know, that sort of thing. And that's how I describe the difference between, you know, a flare and just the normal stinging and tingling that I have pretty much all the time.

MS. GIAMBONE: Okay. Thank you, Lou. Sharon, I know you had a question.

DR. HERTZ: We're hearing a lot of similar descriptions or a spectrum for the painful type of symptoms. And one of the things that we try to do in clinical trials is have a consistent endpoint to measure so that we can tell if the drug is working. And because there are many terms associated with the pain that is experienced with painful neuropathies, it's challenging to know what is the right question to ask so that the

effect can be measured.

So what I'm hearing, for instance, with this last gentleman is that when the pain intensity changes, there may be -- and this is -- I'm not sure if I'm hearing one or the other -- either just a much greater intensity that goes from a pin to a knife or does it actually change in quality? And I think what's important about that is hearing that kind of feedback, when you -- if you were to be asked to keep a diary every day as part of a pain study, how -- what is your experience of trying to rate -- we usually ask for like if you have multiple symptoms, what is the most bothersome symptom and how would you anticipate trying to rate that over time to see if perhaps a new medicine was working?

MR. SCHMITT: Well, I mean, I do agree that it's -- this pain can be very difficult to describe. I mean, there are times when I have sensations I really can't describe to other people. And it would be very difficult and maybe misleading for me to try and do that. But in

terms of a -- in terms of a pain diary, you know, I think that I would obviously describe the differences in the intensity of the pain and not so much the location, because I can get it anywhere, but more the intensity of the pain and it seems when I get a flare, that the pain becomes much more -- it becomes much more perceived in a certain -- in more of a limited area.

I mean, usually I have pain and numbness all over. But I'll start to get it, for instance, for some reason on the outside of my right foot. It will just feel like somebody's pounding a nail into that over and over and over again and just in that one location. And I may never have felt pain like that ever in that location before. I may never feel it in that location again. But it's just at that point, that's what it -- that's what I perceive. And that, to me, is something that I could -- I'm sure I could catalog in some sort of a diary and indicate where I'm getting it. And it doesn't seem so much the location. It just seems more of the change in the nature of the pain that

indicates a flare-up for me.

MS. GIAMBONE: Thank you. Thank you. Graham, I'm going to look to you. How many people do we have that want to dial in? we're technically right into our break time. So if you don't mind, can we take a few minutes of break just to hear a few more comments, and then we'll get right back on track? Okay. So can we take one caller from --

CALL OPERATOR: Yes, the first comment or question in the queue is from Eugene Richardson. Your line is now open.

MR. RICHARDSON: Yes. Hi. I'm Colonel Eugene Richardson, retired from the U.S. Army. I have CIDP due to exposure to Agent Orange. And I would be there today, except I'm in a wheelchair most of the time, and I wanted to share about the numbness if I walk more than 10 feet and attempts to walk. I eventually become so numb, I will collapse and then become so exhausted, I must go to sleep. My legs are just basically gone, even though I am on IVIG. But I didn't get that until

maybe 35 years after I was exposed and had symptoms. And I'm grateful for IVIG because otherwise I wouldn't be here talking to you. But I am grateful for what you're doing and the work of the FDA.

I remember that nortriptyline was the only drug that helped me. The others, I ended up tossing into the closet, which was not good. I had nortriptyline until I got my IVIG started, which I get every three weeks, go to the hospital and get it and that's a godsend, but it's not a hundred percent. It's not a cure. And to answer that doctor, I would love have healing of the nerves. I don't know whether that's realistic because I'm 77 now, but would love to have the healing and I'm fortunate now, even though I've had hellish pains all over my body, including screwdrivers being pushed out of my fingers, I don't have quite as much pain anymore, I think mainly because the nerves are pretty kind of damaged. But I'm grateful for IVIG because that keeps me going every 21 days. But I just wanted

to thank all of you for what you're doing today. God bless.

MS. GIAMBONE: Thank you, Eugene. There were a lot of heads nodding and -- [Applause.]

MS. GIAMBONE: And I hope you heard and are seeing on the webcast that we are clapping for you for sharing that personal story with us. So thank you very much. And do we have -- Graham, do we have a few more polling questions or is that it? Okay. So as I mentioned, we are right into break time. And just so we stay on time, what I'd like to do is at least get your responses to the polling questions so we capture those perspectives. And we'll come back right after break time to dive into more detail about treatments.

So if you could get your clickers out, and we did talk about this a bit, but just to sort of I suppose revalidate it, what terms best describe the most bothersome aspects of your neuropathic pain, and you can choose up to three terms. Numbness; B, tingling; C, burning; D,

stabbing or shooting pain; E, prickling, pins and needles; F, electric shocks; or G, others not mentioned. Okay. Oh, a nice wide spread here, from numbness to others not mentioned. Okay, I see a little bit of everything except for the electric shocks and then we do see a lot of others not mentioned. Can we quickly have somebody share, if you identified others not mentioned, can you share with us what you meant by that? Let's --

MARY: [Off mic] -- aching, which is --

MS. GIAMBONE: Aching --

MARY: -- not there.

MS. GIAMBONE: Okay. Thank you. And your name?

MARY: Mary.

MS. GIAMBONE: Mary. Thank you, Mary. Anybody else? Did you select others not mentioned? Yes?

UNIDENTIFIED AUDIENCE MEMBER: Just real quickly, cramping, migraines.

MS. GIAMBONE: Cramping, okay. Do others experience cramping? One, two, three,

four, five, six, seven -- I'm seeing about seven, eight -- eight hands raised. Okay. Anybody else, other symptoms or other manifestations not mentioned? Okay. I think we have one more polling question. Okay. What are the most bothersome impacts of your neuropathic pain on your daily life? A, ability to participate or perform activities; B, ability to fall asleep at night; C, ability to stay asleep through the night; D, ability to concentrate or stay focused; E, ability to care for self, family or others; F, impacts on sexual intimacy; G, emotional impacts, such as fear or hopelessness; and H, other impacts not mentioned. And you can choose up to three.

MARY: [Off mic] -- all of the above.

MS. GIAMBONE: All of the above, okay. If we had an all of the above, would you select that? How many of you would select that? Okay, so we had about five hands raised for that.

MR. THOMPSON: Go ahead.

MS. GIAMBONE: Okay. So, okay, once again, a wide spread. Let's see here. Really

everything, and it looks like we sort of captured these biggest buckets of impacts. And on the Web?

MR. THOMPSON: Seventy percent said ability to participate or perform activities and 50 percent emotional activities or ability to fall and stay asleep.

MS. GIAMBONE: Okay. Thank you. All right. So before we go to break, FDA panel, are there any final questions that you'd like to ask? I know that it's impossible to cover everything that you're feeling about how you experience the sensations of neuropathic pain and other sensations in this timeframe. But we thank you for what you've contributed. FDA, any final questions? Okay. All right. So let's take a -- shall we say five-minute break or 10-minute break? Let's take a 10-minute break and we'll be right back.

[WHEREUPON, the foregoing went off the record at 3:05 p.m., and went back on the record at 3:18 p.m.]

MS. GIAMBONE: All right. So let's go

ahead and get started with our topic two discussion. I know that topic one -- we had such a robust and rich conversation in topic one, and once again, I know that it's really impossible to cover everything that you want to tell us and there's so much I know to cover when it comes to the way that you're experiencing the aspects and sensations of your peripheral neuropathy. And so, I'm going to put a plug in again for that public docket. It is very, very important that if we didn't get to -- that if you didn't get to share what you wanted to say in topic one, please submit it to the public docket. It is a very important part. It is part of the public record. We will read your comments and they will be incorporated into the "Voice of the Patient" report. So please don't feel that we didn't come to you. It's that we're trying to stay on time, as best as we can.

Before we continue with topic two, I want to look to Graham to hear from what came in through the Web from the polling results. I know that you mentioned there were some other aspects

not mentioned during our discussion.

MR. THOMPSON: In terms of when looking at the terms that best -- most describe the bothersome aspects of neuropathic pain, there was a lot of focus on electric shocks and stabbing and shooting pains and then for the question on the most bothersome impacts of neuropathic pain on daily life, 71 percent of people focused on their ability to perform physical activities and mentioned things like fly fishing, dancing, driving and just basic social interaction.

And then, for -- whoops, hold on -- for the question on how do neuropathic pain symptoms typically manifest, I think we had zero percent in the room saying these first two options, but on the Web, we had 30 percent saying that the pain appears suddenly and progresses rapidly and another 30 percent saying that the pain appears suddenly and progresses slowly and also a lot of focus on how the pain has been worsening over the duration since their diagnosis.

MS. GIAMBONE: Thank you, Graham. Yes,

Sara?

DR. EGGERS: Yes. So going back to the comment that the gentleman on the panel made about that maybe some of the people who are in the worst pain aren't in the room, what I will suggest is if you're on the webcast and you're -- and particularly if your experience is different, that's what makes the docket so important. If you can -- if you're able to just write even a few paragraphs and submit that in, it becomes very helpful evidence that helps balance what we get from folks who are able to come today in person and folks who are not able to come today in person. So --

PANEL #2 DISCUSSION ON CURRENT APPROACHES TO TREATMENT (TOPIC 2)

MS. GIAMBONE: Thank you, Sara. Absolutely. Okay. So let's get started with topic two, which is on patient perspectives on current approaches to treatment. Once again, we have a panel of four. Our fourth panelist will be calling in. but we're going to start first with

Linda. So once again, if you could press the red button and start your comments?

MS. SPINELLA: Hi. I'm not as good as the others. I'm going to read mine. I am 47 years old and I have had chronic neuropathic pain for over 30 -- 13 years, excuse me. I have had two low back surgeries. I work full-time and I have a family. I am here to provide a summary of my treatment journey, as I have had intermittent relief from the pain that I experience and it interferes with my activities of daily living, my sleep and overall function.

Currently, I have multiple herniated discs in my spine and my pain, on a scale of 1 to 10, ranges from six to eight while taking the following medications: tramadol, diclofenac, cyclobenzaprine, Lyrica, over-the-counter supplements for bone and disc support, Tylenol as needed and prednisone to reduce the inflammation, as needed. I'm also seeing a chiropractor and an acupuncturist twice a week.

I recently stopped physical therapy

because it was aggravating the pain in my neck and lower back. I have a cervical traction unit that I use at home. I had a cervical epidural in February and I just had a lumbar epidural in May. The following three days after the epidurals, I had almost complete relief. The epidurals have helped tremendously, but they usually wear off and my pain goes back to between six and eight. The current treatment regimen has been able to reduce my pain as well. However, it causes drowsiness, dizziness, lightheadedness.

I have trouble concentrating and remembering information. I have gained weight. I have swollen hands and feet. I have dry mouth and a metal taste in my mouth. I also have occasional leg cramps. I am so exhausted, yet I'm unable to sleep through the night unless I take these medications. Each time I roll over in bed, I wake up from the pain. These were not the only treatments that I've had. I got to where I am today through a journey of treatments, beginning over 13 years ago and it has included Percocet,

OxyContin or Vicodin, diazepam, cyclobenzaprine, naproxen and prednisone. The dosages were frequently tweaked and the side effects were hard to manage. I was anxious, jittery and extremely agitated. Under this treatment regimen, I had difficulty driving a car, concentrating and functioning.

I was also under chiropractic care, which included traction, electrical stimulation, ice and adjustments. The treatments would reduce the pain, but it was temporary, meaning only a few days to a week. I've also had multiple trigger point injections, cortisone shots and epidurals, which gave me temporary relief, meaning only maybe a few months. But those procedures are limited, if they actually worked. I've tried massages, a therapeutic bed and pillows, ice, heat, acupuncture, hydrotherapy, exercise, yoga and even an inversion table.

Over time, the L5 herniation would heal, but then reoccur maybe within 6 to 12 months, with lower back and leg pain. Each time I went through

the same treatment process all over again, trying to find relief and avoid surgery. But eventually, I needed it.

In 2009, a discectomy was performed and during recovery, I was on the similar medications as before. After roughly six months, I achieved a good level of pain relief and I was off all medications and functioning well for almost two years. In 2011, I herniated the disc again and I was placed on the similar treatments. The pain meds helped, but I was lightheaded, dizzy and it was hard to concentrate. I also had the sensation of feeling high. The anti- inflammatories made me jittery and agitated and anxious. I was extremely tired and I woke up feeling groggy. I had more trigger point injections and was still under chiropractic care. I was also in physical therapy, but that aggravated it. I was unable to get any relief from my back and leg pain. The MRI showed that I was bone-on-bone in my lumbar spine.

So I finally underwent a lumbar fusion in 2012. After the surgery, I was in physical

therapy, taking Vicodin, then Percocet and then I began to feel better. About four months after the surgery, I was medication-free and feeling good. I was able to rejoin my bowling team and take long walks with my dogs. However, I limited my movement based on my own fear of reinjuring the back. It took a while, but I began to feel confident and started working out and exercising.

Just this past July, while exercising, I herniated two discs in my cervical spine. I started the same medication therapy all over again. I also began cervical traction. I had slight reduction in my pain. And in October, just three months later, I herniated three more discs in my lumbar spine. Same treatment continued and physical therapy was added. I received a cervical epidural in February, of this year, as well as a lumbar epidural in May. The doctor has also prescribed Lyrica for my lower back, neck and leg pain. At the beginning, my pain was at an eight or a nine. Now, I have days at five or six.

I have been on Lyrica since March,

starting at a low dosage. I am now up to 300 mg a day. It has relieved a great deal of pain, although I hope I can endure the side effects of the medication, as it might be a long-term treatment for me. It will hopefully give me enough relief so I can sleep comfortably through the night, walk and maybe endure some exercise so I can lose weight without the drugs and I can avoid another surgery. I realize this is my life and the prognosis isn't great. The possibility of reoccurrence will always be there. I hope there is a treatment or a drug out there that can give me some improvement in my condition and help me consistently feel better and help me function at the same time.

[Applause.]

MS. GIAMBONE: Thank you, Linda. Next, we have Cherie.

MS. PAGETT: My diagnosis -- my diagnosis is idiopathic small fiber peripheral neuropathy recently expanded to autonomic neuropathy. Although they say it's idiopathic,

there is some consideration given to the fact that when I was 23, I had radiation therapy following ovarian cancer and which resulted in radiation ileitis. So you know, there's some doctors who really like to make that connection. I experienced my first neuropathic symptoms 18 years ago, surrounding a 125-mile walking pilgrimage in Northern Spain, beginning with neuroma symptoms and toe numbness, then nerve pain, which have increased over the years. I am now numb up to my knees and in soul sapping pain at least three to four nights a week, not as intense during the day, and I'm totally unaware of foot injuries.

I've now begun having symptoms in my fingertips and my left cheek. My current treatment includes daily minimum prescription medications: 3,000 mg of Neurontin, tramadol 600 mg and Mirapex 0.5 mg. I also take various over-the-counter supplements. I sometimes use prescription lidocaine ointment now that Medicaid no longer covers the lidocaine patch, although I'm not sure why, because that was helpful. I use

OxyContin and hydrocodone, cannabis oil and my non-drug therapies include massage, ice packs and heat pad for leg cramps. I meet twice a week with a personal trainer, focusing on balance and core strength, and I've recently begun an aqua-fit class.

Over time, my medication dosages have steadily increased, beginning with low- dose Neurontin, now up to 3,000 mg a day, as I mentioned, Lyrica, with which I gained 25 pounds in six weeks and I couldn't stand that, Cymbalta, I stopped after only a few days as I felt crazy and like I was outside myself, topiramate medication, which did help with weight loss, but made the top of my head buzz and kept me on the verge of tears.

Last year, I had four sympathetic nerve blocks, which in no way changed my unpredictable experience of good days and bad days. I've resisted repeated suggestions of a spinal stimulator trial and/or implant. It seems too risky and difficult to remove. I've focused more

on balance with my personal trainer and I'm contemplating the purchase of a TENS unit or the rebuilder recommended by my neurologist, who specializes in neuropathy.

How effective is all of this treatment? I don't feel that the pain's really under control. It attacks and abates when I least expect it. However, I imagine the medication takes the edge off. And despite the perceived side effects, I'm reluctant to reduce dosages for fear of increased pain. Massage and other therapies such as acupuncture provide temporary relief. So I'm thinking maybe it's time to explore meditation. It seems I've been chasing this pain, increasing medication dosages for the past 16 years or so. The prospect of continuing on this same trajectory not only contributes to my chronic pain-related depression but also causes concern about what I'll need 5 to 10 years from now.

For example, recently my peripheral neuropathy led to Charcot arthropathy, which is not Charcot-Marie-Tooth, in one foot, resulting in

a Lisfranc situation necessitating surgical midfoot fusion. There's a possibility that the same condition will develop in the other foot and the prospect of a fusion fail worries me. I'm also concerned that I'll be walker- dependent and ultimately wheelchair-bound before my time. I would say that my condition today is managed certainly, but not well-managed. Significant downsides to my current treatments include debilitating, discouraging and downright dangerous side effects such as weight gain -- 40 to 45 pounds since my initial diagnosis -- brain fog, both of which are attributable to the Neurontin, as well as drowsiness, difficulty focusing on my writing and translating and positional vertigo.

Travel to Baltimore for neurologist appointments and various clinical trials is time consuming. Plus, driving any distance is risky due to my tendency to drop off. Repeated nerve biopsies, and most of us have suffered through those painful nerve conduction tests. Numerous negative treatment-related issues weight heavily

on my family, especially my husband. For example, several years ago I asked my first neurologist if there was any relation between my meds and diminished libido and/or sexual arousal, to which he too quickly replied in the negative. I was curious then as to how the medication could block pain only in neuropathy-affected nerves below the knee. The connection is now recognized. I'm 70 and some might think it shouldn't matter so much anymore. But in a healthy 45-year marriage, it does continue to matter and we do lament that loss.

Although I found it necessary to sell my property management business five years ago due to unpredictable pain, sleeplessness and lack of focus and energy, I still have many regular responsibilities relating to our family investments and the care of our seven-year- old granddaughter. I must often choose between meeting these responsibilities or taking the time to accommodate my pain and the treatment thereof. We have an extensive wine collection, which is now

pretty much off limits to me due to the restrictions imposed by my meds. Not a huge sacrifice, but I don't think my husband will have time to drink it all alone. Peripheral neuropathy isn't going to kill me, in the short-term anyway. But some of these medications can cause me to entertain the idea.

I understand that my possession and use of cannabis oil for pain relief is not approved in the Commonwealth of Virginia, nor is medical marijuana in other forms. There are those whose constant pain is even more severe than mine. Even at my worst times, when I'm doubled over by the feeling of railroad spikes being driven into my foot or rolling back and forth in bed and beating the mattress because I can't tolerate the pain. Surely, if medical marijuana can help anyone, perhaps without the potentially devastating side effects of opioids, it should be available to peripheral neuropathy sufferers in all states.

[Applause.]

MS. PAGETT: And I think the rest of my

information here is pretty much shared by everyone else. So I'll let you go ahead because I've taken more --

MR. SCHMITT: Oh, thank you.

MS. GIAMBONE: Thank you very much, Cherie. Next, we have Lou.

MR. SCHMITT: 2009 seems to have been a bad year for a lot of the folks here, and for me as well. I was -- I was stricken with CIDP in the year 2009. I was diagnosed the following year and I underwent 20 months of high-dose IVIG, which sent my CIDP into remission. However, I suffered significant damage to my peripheral nerves as a result of my CIDP and the damage is permanent and the pain that I suffer is constant.

What I currently do to help with -- to treat my neuropathic pain is I do a lot. I think overall I don't just focus on my nerve health and trying to deal with my pain. I focus really on my overall health in general. I think it's very important to do everything you can for your overall general well-being to deal with the

problem of your pain because it doesn't just help with the pain, but it helps you feel better emotionally if you are living healthier. I always say that it's funny, I had to get sick to get healthy because I never worried about my health before I got CIDP. And once I got CIDP, it was really all that I worried about. And I changed my lifestyle. I became a vegetarian.

This lady mentioned meditation. I took a 10-day course in Vipassana meditation, which is a mindfulness mediation. And I highly recommend that to anybody who has chronic pain. There are studies I know that have shown that mindfulness meditation helps to reduce your pain. It also helps to reduce anxiety. It helps to reduce depression. And there's a cycle here. There's a mind-body connection between the physical sensations and the physical symptoms and the emotional and psychological components of it. If you feel less depression, you feel less pain and vice versa. If you feel less anxiety, you feel less pain and vice versa.

And I always say that you don't have to feel a lot better to feel a lot better. If you're in chronic pain and you have pain every day of your life, if there's a day that you feel even a little better, trust me, you feel a lot better. And that's a healthy spiral. And we can get into unhealthy spirals, because I don't know anyone who has chronic pain that hasn't suffered with a depression as well. And you know, we were talking earlier about would you rather have something that helps with the pain or would you rather have something that helps with the underlying disease. And I will tell you there have been times I've been in so much pain where I didn't think I could keep going. And at that point, I didn't care whether my nerves were healed. I just needed something to give me relief from this pain.

There were times when I would -- I paced for two or three days in a row. Forget about sleeping and lying in bed. I couldn't sit because of the pain. So some of the things I do -- some of the things I've tried have been successful.

Many have not. I've tried -- massage and acupuncture were not successful at all. Acupuncture was in fact quite excruciatingly painful. I don't know why I thought it would be a good idea when I had damaged nerves to have somebody stick a needle into them and twist it, like that would feel better. It didn't.

I tried some medications that did not help. I was on high-dose Neurontin initially, over 4,000 mg a day. And it did nothing for my pain. I will tell you all sitting here today that Lyrica saved my life. There was a time when my pain was uncontrollable and I could not sleep. I could not even sit down. I couldn't do anything but pace the house and vacuum the house. The house was never cleaner than when I was in terrible pain. But I tried Lyrica and almost immediately got relief from the Lyrica. I take 450 mg of Lyrica a day, which is a fairly high dose. I have been able recently to cut that back to 300 mg. I kind of did that on my own. So don't tell my doctor. But I wanted to see if I could

reduce it by doing some of these other things.

Another thing that I do that's very, very helpful is exercise. I feel very blessed that I don't have any physical limitations as a result of my CIDP. I work out. I lift weights three times a week. I hike four miles with my dog in the woods, you know, four times a week. I do those sorts of things and I found that those things are extremely helpful to me physically with my pain and mentally with the emotional aspects that come with having chronic pain. At the beginning, there was a time that I didn't know what was happening when I was first coming down with my CIDP and I had these symptoms, that all I could do was take Advil and walk constantly. It was the only thing that would allow me to reduce the pain.

I feel my pain is very, very well-managed. I do have days when I have significant flare-ups. They usually last a week to two weeks when I get a flare-up and they are quite uncomfortable. But I think my pain is very well-

managed with the Lyrica and the other things that I do. There are downsides, of course, to the medication. I always describe the mental effects as being in a speed boat and somebody throws an anchor over the side. That's kind of how your brain feels on Lyrica. It does cause drowsiness. The side effects for me were worst the first month that I took it. I felt intoxicated. I felt dizzy. I was drowsy quite a bit.

My body seems to have adjusted and those passed after about a month. I still am -- I get some drowsiness with it. There is a potential for weight gain. My weight's fluctuated a little bit. I have swollen hands and feet. Sometimes they're significantly swollen. A little bit of forgetfulness. There are times when I -- my short-term memory has been affected, I would say, significantly at times. The Lyrica, sometimes I'll be talking to people and in the middle of a sentence, I won't be able to finish it because I don't remember what I was saying when I started the sentence. So those things -- those things do

come with the medication. You pay a price for it. But it's been a miracle in my life and, as I said, I think it saved my life.

An ideal treatment for me would be something -- it would be a pill that I could swallow that would take away all my pain immediately and let me be the person that I was. I don't think that's realistic. But I think a medication that would control my pain, would perhaps eliminate the flares that I get and would have minimal to no side effects for me would be the ideal -- and would be cheap, would be -- would be the ideal, because Lyrica, by the way, is quite expensive. So it would be, you know, reasonably affordable, I think that would be -- that would be ideal for me.

And if I had an opportunity to participate in a clinical study, what would be the factors that would go into that. I would have to -- the first factor would be how I was feeling. If I'm feeling pretty well, and as I feel now with my pain, pretty well-controlled most of the time,

I don't think I want to be involved in a clinical trial. I think if my symptoms were significantly worse, I would probably be more receptive to being involved in a clinical trial. I also would want to know the potential side effects, of course, long-term and short-term of whatever the regimen would be in the clinical trial.

I am concerned, I will say, about Lyrica because I have heard some things anecdotally about long-term Lyrica use and perhaps an effect on dementia. So that does -- that does concern me, what effect it may have down the road. I know how it affects me with the brain fog now and I think long-term what might that do to me. So I am concerned about that. So yeah, any clinical trial, I would want to know what I was getting, what the possible long-term and short-term side effects would be and how effective it might be would be -- you know, if they could give me any kind of an idea how effective the clinical trial might be, I think that would also be very important to me.

MS. GIAMBONE: Thank you very much, Lou.

[Applause.]

MS. GIAMBONE: So our final panelist is Jackie, and Jackie's going to be joining us on the phone today. So here's a picture of Jackie. And Jackie, are you on now? Are you on the telephone?

MS. EVANGELISTA: Yes, I am.

MS. GIAMBONE: Great. Welcome, Jackie. And please go ahead with your comments.

MS. EVANGELISTA: All right. Well, greetings, everyone, from Ohio. I'm sorry I couldn't be there. My foot neuropathy is likely secondary to nearly life-long Lyme disease that was not uncovered until about five years ago when I was 68 years old. I was given various diagnoses over my life that, looking back, suggests that Lyme was affecting me at a young age. Perhaps my immune system was damaged, setting the stage for the Lyme after I had the Asian flu in 1958 with a high fever for 10 days. After that, my diagnoses included inhalant allergies, paroxysmal atrial tachycardia and adrenal fatigue in my 20s, fibromyalgia in my 30s, Hashimoto's and food

allergies in my 40s, chronic fatigue syndrome and osteoporosis in my 50s, CBO and Lyme in my 60s. All of these may have been caused -- may have caused a plethora of genetic defects to express, which I learned about recently from the 2-3 immunogenic test.

Okay. Wait a minute here. I got lost in my place. Okay. Foot neuropathy first appeared in my mid-50s with the sensation that a small child was standing on my feet and very gradually escalated to the point about five years ago that I was able to put the label of foot neuropathy on what I was feeling. Since then, my symptoms have included the feeling that I have a wide band across my foot at the base of the toes, numbness and tingling, as well as periodic stabbing pains or electrical shocks and foot and leg cramps.

Okay. My down arrow isn't working for some reason. Sorry about that. Okay. These however are only a small portion of those symptoms caused by the Lyme itself. The doctor who

diagnosed my Lyme via the Western blot test tried B-12 shots, which did not help. I don't recall him having any other suggestions for therapy. A Cleveland Clinic neurologist I consulted last fall gave me a list of supplements, including alpha-lipoic acid, which I had taken previously, and resumed taking with no significant improvement, as well as others which I was already taking. She said I would probably have a lot of inflammation and possibly the beginnings of an auto-immune condition. But I was not offered tests for inflammatory factors of Lyme disease or a possible auto-immune condition. She admitted to not knowing much about Lyme, and I suspect she's not the exception.

Regarding my approaches to treatment, I have generally eschewed drugs because of side effects, which I discovered from the 2-3 immunogenic test may have resulted because I have a gene that dictates I'd only need about half of the normally prescribed dose of any medication. I only started addressing my neuropathy a few years

ago because prior to that, it was an annoying but tolerable condition. It seems that my neuropathy continues to very gradually worsen and it's hard to say because the change happened so slowly that I think I get used to the new condition and can't recall exactly how I was before.

Of late, I have sought out therapies said to help the autonomic nervous system and vagus nerve, which is what it seems Lyme has most affected in my case, and that includes the heart, the stomach, bladder, et cetera. I go for acupuncture every two weeks in the summer and weekly in the winter and get craniosacral therapy as well as reflexology and chiropractic every two weeks. It has helped some of my other symptoms more than my foot neuropathy, probably because foot neuropathy isn't related so much to the autonomic nervous system. I take a number of the supplements that should quell inflammation, if that is the root of my neuropathy. But they have not made a noticeable difference. Before bed, to help with sleep, I use an essential oil foot

cream, homeopathic remedies and a low level light therapy device on my feet that helps tone the symptoms down, but does not eliminate them.

I have tried many dietary approaches and do many things related to the larger Lyme issue. The obvious downside of this approach is that it only takes the edge off the neuropathy but does not stop its advance and requires continuously remembering and making time to comply with therapies, even when traveling. More frustrating is that I don't feel I understand the cause of this symptom or the many others that I have that are attributable to end-stage Lyme disease.

Given the lack of knowledge that currently exists about neurological Lyme and the fact that I usually have unpleasant side effects to drugs, I doubt I would participate in clinical trials should a drug be developed for my condition. It would depend on the list of side effects. I would underscore most emphatically that more research is needed. Treatments with a clear rationale really can't be developed until

the impact of Lyme on the nervous system over time is fully understood. It has been reported that 300,000 people in the United States are diagnosed each year with Lyme and a significant percentage of them go on to develop the chronic form, often because they aren't treated soon enough.

I realize that the concept of chronic Lyme disease has not been totally accepted by some doctors. However, it's hard for me to come up with a rationale for all the medical issues I've had over my life without seeing Lyme as being involved or not causative. Knowing how slow the wheels of research grind, I don't really have much hope that treatments which might help me might appear during my lifetime. But I do hope that they will be developed in the next 20 to 30 years and help the coming larger group of people who will be presenting with foot neuropathy and other symptoms of end-stage Lyme. Thanks for the opportunity to give my input.

MS. GIAMBONE: Thank you so much, Jackie.

[Applause.]

MS. GIAMBONE: Okay. So, so similar to what I said for our topic one panelists, thank you so much to our topic two panelists for all the preparation you did. I know it's hard to put all these thoughts down and get the short amount of time to be able to express it all. But you did such a great job, so thank you for doing that, and thank you, Jackie, for joining us.

[Applause.]

MS. GIAMBONE: Okay. So I'd like to do another show of hands and ask you in the audience how many of you heard your own experience with treatments reflected in the comments shared by at least one of our panelists? Okay. So we have a few hands here. But it sounds like probably other experiences also then that were not shared. So we'll get to those in just a minute here.

Let's do our next polling question, so if you could get your clickers out. Okay.

Have you ever used any of the following drug therapies to help treat your neuropathic

pain, and you can check all that apply: A, anti-arrhythmic drugs; B, antidepressant drugs; C, anticonvulsant drugs; D, transdermal or topical patches; E, opioid pain medicines; F, prescription NSAIDs -- I'm sorry. I am going to butcher a lot of these words. So I'm going to say them as best as I can. -- G, over-the-counter products; H, other drug therapies not mentioned; or I, I'm not taking any drug therapies. So you can check all that apply. And those of you on the Web, please be sure to enter your thoughts in as well.

Okay, so what we have here, we have antidepressant drugs, anticonvulsant drugs, transdermal or topical patches, opioid pain medicines and then we have quite a few over-the-counter products, other drug therapies not mentioned. So we'll definitely be hearing from that and then also --- well, 23 percent of you that said I am not taking any drug therapies. So, so let's start with those of you that are taking some of these drug therapies. How many of you, by show of hands, take at least one of these things

daily? Okay, so one, two, three, four, five, six, seven -- we have about 14 hands raised. And then, how many of you take these drugs only when needed? Okay, so we have about three or four hands raised for that.

Graham, what are we seeing on the Web with the polling results?

MR. THOMPSON: We actually have very different results on the Web. We have 57 percent say they take antidepressants. Eighty percent say they take anticonvulsants, 41 percent transdermal or topical matches, 53 percent opioid pain medicines, 54 percent over- the-counter products and 41 percent say other drug therapies not mentioned.

LARGE-GROUP FACILITATED DISCUSSION ON TOPIC 2

MS. GIAMBONE: Okay. Thank you. So without focusing let's say on one drug in particular, can you -- would somebody like to share your experiences with what specific aspects of your neuropathic pain -- and I understand that

the pain comes -- you know, you have different sensations of pain and different severity of pain. But can you talk about what aspects of that pain does the drug address or not address well? So maybe if you could tell us what you're taking and then what -- you know, is it working, is it not working. What aspects of the pain is it addressing or not addressing?

MS. LANNON: Narcotics just -- I take narcotics just to make me fall asleep at night. That's it.

MS. GIAMBONE: Okay. Okay. And do you find that they help you stay asleep through the --

MS. LANNON: They don't help at all.

MS. GIAMBONE: They don't help? Okay. Okay.

MS LANNON: [Off mic.]

MS. GIAMBONE: Okay, okay. And --

MR. KLITZMAN: I rarely --

MS. GIAMBONE: Oh, sorry. I just want to say we do have a comment back there. So can we make sure we get to her too? Yeah, go ahead,

Steve.

MR. KLITZMAN: Yeah. I rarely have pain. But if I do, it just takes the edge off of it. You know, and just -- I forget about it basically after I take something.

MS. GIAMBONE: Okay. So it takes the edge off. Okay. Meghna, let's go to -- yeah.

MS. BENSON: Yes. I take a cocktail of meds.

MS. GIAMBONE: Okay.

MS. BENSON: I'm on Lyrica -- excuse me. I'm on Lyrica, baclofen, meloxicam and oxycodone. And it just -- on a scale of 1 to 10, usually mine is 11. And it just takes the edge off. I'm on -- I have chronic pain every day and I live with it. And it just takes the edge off so that I can barely get out of the bed.

MS. GIAMBONE: Okay.

MS. BENSON: But most of the time, I'm living in my bedroom.

MS. GIAMBONE: Okay. And your name?

MS. BENSON: My name is Mona Benson.

MS. GIAMBONE: Mona? Can you tell me what are the -- I know you said it takes the edge off.

MS. BENSON: Yes.

MS. GIAMBONE: What are the downsides that you're experiencing with the cocktail that you're taking?

MS. BENSON: What is the -- I'm sorry?

MS. GIAMBONE: What are some of the downsides that you --

MR. KLITZMAN: The side effects.

MS. BENSON: The side effects?

MS. GIAMBONE: The side effects.

MS. BENSON: I --

MR. KLITZMAN: Memory?

MS. BENSON: The worst part of it is it -- I lost my job. Basically I had to stop what I loved doing. I was a television news producer. I did that job for 28 years, most of it right here. Well, I'm sorry, in Philadelphia, P.A. I had to be very sharp. I mean, it was a -- it was a -- I worked the noon show, noon news and that was

always where it was always breaking news. I mean, it was one of those shows where every time right before you went on the air, something was always breaking and it was always something that you had to run in and scripts always changed, as soon as the anchors were going down, you know, to the news -- you know, to do the news. You had to tell them, okay, we're changing everything everybody.

Something is -- there's been a four-car pileup or somebody's just shot somebody or, you know, and you had to be sharp and you had to tell them in their ear while they're reading something else. You know, you had to be sharp and tell them while they're reading what you're changing. And I'm here taking -- I never told anybody for a year that I had been diagnosed with CIDP. Here I was taking Lyrica and oxycodone and I didn't tell anybody. And I was having memory gaps and it got to the point where I was -- at one point, I was taking at least two or three Lyrica and oxycodone before a show.

And at one point, I couldn't even

remember some of the things they were telling me and I'm supposed to be telling a news anchor in his ear and I can't even remember the stuff.

MS. GIAMBONE: Okay.

MS. BENSON: And I realized I couldn't do this job anymore. And that was one of the downsides, I guess.

MS. GIAMBONE: Absolutely. Absolutely.

MS. BENSON: Memory gaps, because --

MS. GIAMBONE: Thank you.

MS. BENSON: -- I couldn't -- I was having brain fogs.

MS. GIAMBONE: Okay. Thank you very much. And I know a few others had mentioned the brain fog also. So it sounds like it's definitely a significant downside. How about others? Can you talk about what medications you're taking and what specific aspects of the pain or the sensations that you feel that it addresses or does not address?

MS. WALDROP: Sure. I take gabapentin. I take a lot of gabapentin, 3,300 mg a day.

That's 11 pills. Without it, I couldn't function. With it, I can function. So all the symptoms that everybody's described are just a whole lot less with the medication. In terms of the side effects, I'm honestly not sure. Brain fog is there. But is it the fault of gabapentin or the chemo I had or the fact that I'll be 70 in August? I'm just not sure. But anyway, I wouldn't -- you know, I feel like wherever I go, I have that bottle or jar of my gabapentin pills. I just -- I'm tethered to it because it's miserable without it.

MS. GIAMBONE: So anybody else? Would you like to -- oh, sure. Let's -- we're going to hear from this gentleman right here first.

BOB: Okay. My name is Bob and I have Guillain-Barrsyndrome. And I take gabapentin, which works for me quite a bit of the time. But I try to exercise and I'm still learning that if I go very -- do too much, it's very easy for me to do too much and not feel the pain for maybe five days or so. And that's when the gabapentin

doesn't cut it anymore. And I really haven't changed anything at this point to address that. But that's what I find is when I do too much, the gabapentin is not enough.

MS. GIAMBONE: Okay.

UNIDENTIFIED AUDIENCE MEMBER: I had a question for --

MS. GIAMBONE: It was like your GPS is ready to get you out of here.

BOB: I thought it was off.

MS. GIAMBONE: No, that's okay. Don't worry.

UNIDENTIFIED AUDIENCE MEMBER: I had a question for the FDA panel. I know you approved the safety and the efficacy of the drugs. What about the long-term effects of drugs? I mean, do you periodically go back and evaluate or look at, you know, what are the long-term impacts of taking Lyrica or gabapentin for 20 years or 10 years or whatever, what does it do to you and do you change your certifications on the basis of long-term effects or --

DR. HERTZ: So the 20-year question is a tough one. What we do at the time of approval for drugs like this is we usually have data for about a year of exposure, some safety information. But once a product is approved, it is followed on a regular, continuous basis. Right now, we have a standard look after a newly approved drug meets certain criteria in terms of time and number of exposures. But what you'll see over time is that products that have been on the market, once we become aware of new information, we continually update the labels.

So for instance, when the association with suicidal thoughts was discovered for some of the antidepressants and the anticonvulsants and then it was explored to see if it was a class effect or a drug-specific effect, and then the products were all updated with that. So it's an ongoing, continual process. But we don't have a systematic way of evaluating that kind of really long-term exposure. I'm not sure that any country really has that. But we do consistently look for

signals. So for instance, some of you may be aware that we recently updated the labeling for all of the NSAIDs because we've been following the risk for cardiac events. And that's been a very challenging thing to explore over time. But it's something that we're continuously looking at. So for pretty much all of these drugs, we have ongoing surveillance.

MS. GIAMBONE: Thank you, Sharon. Okay, so let me look to my FDA panel to see if you have any questions at this point.

DR. HERTZ: If people will bear with me, I'd like to just go back and explore maybe a few more people's thoughts on if you were going to be reporting your -- it's the same question. I just would like to get a little bit more input, if people are so inclined. In terms of being able to rate your pain over time and how -- how you think it makes sense for us to ask you, how an investigator in a clinical study, or even your clinician, but clearly I'm interested in it also from the perspective of development of drugs, how

-- how to get at the painful aspects and are there any particular ways you think would be helpful in terms of instructions to people.

MS. GIAMBONE: It looks like we have several hands raised. Okay.

MR. MURPHY: Again, my name is Tim. It seems to me that pain is a very personal experience. And so, my thought is that when you're evaluating a patient, you need to get a baseline on an individual basis as to how do you describe it. What are the components? You can certainly use some of the common terms that are used. But I think they mean different things to different people. We all experience things differently. And then, from that baseline, we can -- and intensity -- and then, moving forward, you can rate the effectiveness of whatever we're measuring based on that initial evaluation. But I think it's going to be different for everybody.

MS. GIAMBONE: Thank you.

MS. LEVINE: I totally agree with the last speaker. I would say something like asking a

patient a baseline and then during a trial, something like does your pain allow you to -- how many hours a week does your pain allow you to work or how many hours a night do you lose sleep because of pain, rather than asking how do you rate your pain or something.

MS. GIAMBONE: Thank you. Adam?

MR. HALPER: I would I guess be the third person here to highlight that theme. I think for me, I keep what I would say is a quasi-pain journal and the reason I do that is, you know, I've experimented with some different medications and different alternative approaches to treating my neuropathy and I've found it's very useful to have -- I basically have a two-year set of notes that I can scroll back through and see, okay, well, this correlated with this improvement, et cetera.

What I have personally found is that the easiest way to measure improvement is functionality. So it's -- you know, for me, it's how far can I walk before it's time to sit down.

How long can I stand before it's time to sit down? And I think those might be a little bit more specific and measureable than, you know, rating your pain on a scale of 1 to 10. And I think Leslie is absolutely right. You know, you could also look at, you know, can -- you know, how long can you sleep without being woken up or you can certainly expand the criteria. But for me, it's really been, you know, just you could actually measure functionally -- you know, give people a Fitbit and they can get very specific right there. Yeah.

MS. GIAMBONE: Thank you, Adam. Let's go to Beth.

MS. LANNON: Is that on? I agree. I was going to say both of those things too. The other thing I would add to a questionnaire is what your mood is. You know, how are you doing today because that has a lot to do with how I will answer how painful I am, is how good a mood I'm in. So I think it's a rather complicated question and diary to keep. Like you, Adam, I kept one too

for years. I wanted to be able to into my doctor and say this is how I felt every single day, from morning to night. And I did always include those things like -- but today, you know, I was able to work. And so, even though I was in pain, I was feeling pretty good. You know, I assess my pain out of five because I've found my mood helps a lot.

MS. GIAMBONE: Thank you, Beth.

MS. LANNON: So it's a complicated -- you should ask people to write up samples of what they think a good pain scale is, like out on the Web or something.

MS. GIAMBONE: So it looks like we have -- oh, yeah. Go ahead.

DR. PATEL: I do have a question for you, Beth. I know you described mood, I guess. Could you give a little additional context to the mood? What do you mean by mood, I guess? Could you describe it a little further?

MS. LANNON: Oh, well I mean, I am a lot more painful when I am feeling alone and

depressed. You know, if there's a weekend I have absolutely nothing to do and nobody's invited me anywhere, nobody wants to come visit me, I would just say that I am in extreme pain. My pain is screaming and I don't want to live anymore. But if I go to work and I save a life, because I'm a veterinary technician, I'm feeling pretty good and that pain's not so bad anymore. Does that answer it?

DR. PATEL: Yeah, it does. And also, I have -- just getting back to the question that Sharon asked, I guess, you know, there are many aspects that I think Adam mentioned about, you know, cannot walk. You know, I used to be able to walk 10 miles, I guess. Now I can only walk a mile but with a lot of pain. What else is important that you think that we should include in questionnaire for clinical trials? You know, I know the numbness I heard was one of the questions. But again, you know, I'd like to hear other thoughts.

MS. GIAMBONE: Sure.

UNIDENTIFIED AUDIENCE MEMBER: One of the goofy things about this disease is that pain not be an absolute indicator of the progression of the disease. As mine has gotten worse over the years and the numbness has come up, where it used to really hurt and be oversensitive, now it's not. It doesn't hurt. I'll get, you know, the pitchfork through the foot thing at night. But the daily kind of pain may not be as intense. That may not be an indicator of improvement or anything.

MS. GIAMBONE: Okay. Thank you. And it looks like we have one more comment.

MR. YADLON: Two quick comments. Number one, a lot of these questions are on the Social Security Disability application that you may want to read because a lot of that is similar questioning about what you do and how long you do it, et cetera. And second, nobody's really mentioned water therapy. Anybody doing water therapy, pool therapy? Yeah. I think it's an excellent way of relieving and making you feel a

lot better mood-wise as well.

MS. GIAMBONE: Great. Thank you. And sorry, your name?

MR. YADLON: I'm sorry? Oh, my name is Jim.

MS. GIAMBONE: Jim. We have a question coming up with other therapies outside of the drug therapy. So I'm glad you brought that up, the water therapies. Now, I do want to ask a question. Several of you mentioned that you've tried different therapies and that's brought -- you know, you talked about a treatment journey, that it's brought you to your current set of treatments. And I'm curious how long do your -- how long do you try a treatment before you know that it's working or it's not working? And if you can talk a little bit about that treatment journey and how your treatments have evolved? Can you share some perspectives on that? Jim?

MR. YADLON: I'd say a lot of -- a lot of new pills or -- always say three or four weeks. You have to give it some time to work. Some work

right away. But most of them take some time.

MS. GIAMBONE: Okay. And I guess on that note, to ask you when you change -- you know, when you've had to change your therapies, is it primarily because they -- you know, the bothersome side effects or was it some sort of -- did it lose effectiveness? What were the reasons maybe why you changed? Tonya?

MS. CHARLESTON: I would say it was the side effects for changing because I would say my first two years or so, I did IVIG, tramadol and Lyrica. Somewhere around the third year mark, third -- or three-and-a-half-year mark, I was like, okay, no Lyrica, no tramadol because too much fogginess, too much. I can't do anything. I'm sleeping all the time. Let's try something else. So then we switched to plasmapheresis and another drug. Oh, and we got off the prednisone because that makes you swell, too much swelling. I didn't even recognize myself.

So about the fourth year, I would say weaning off all of the heavy stuff and then going

more to over-the-counter and just more or less recently, we've decided to try Celebrex because the doctor was saying that a lot of people with arthritis were using the Celebrex and they didn't have foggy mind or sleepiness and fatigue. And they were able to take the edge off the pain but still be functionable. So I've been trying that for about two months or so now. And it's a little bit better, you know, as far as taking the edge off. But I've not found a balance where there is no pain or like total relief at any point in time. So it's usually because of the side effects and I want to be active.

MS. GIAMBONE: Okay. Now, a few of you have mentioned that the treatments that you take help take the edge off. And so, can you describe what that means? What does it mean? And maybe that's closer to Adam's point about how can I walk a little bit longer or am I able to do an activity a little longer? Would somebody mind describing what you mean by that and sort of I guess how you -- how does that define whether the treatment is

working or not, if that makes sense? Yeah?

MR. GLENN: Okay. Hi, my name is Luther. That's a term I use all the time, and the way I define it is if I had not taken my medication today, I'd be in bed right now. So it's a -- for me, it's a term I use that would get me out of bed. But I'm always in pain. It's just the degree of pain that I'm in. And so, getting out of bed is a lot -- it's what I call taking the edge off.

MS. GIAMBONE: Okay. And Luther, can you elaborate a little on your treatment regimen and, you know, what is working for you or what's not working for you?

MR. GLENN: Well, I'm still living with a great deal of pain and I've been through all the gabapentin and the Lyrica and all of it still is the same to me. All it does is take the edge off for me. And I take Lyrica three times a day, Neurontin twice a day, naproxen twice a day. And all that together, it just takes the edge off. I'm sitting here and I'm still in a lot of pain.

But when I'm around people and doing other activities, it seems to help a lot. But mostly it's if I can get out of bed, I'm pretty much satisfied for right now.

MS. GIAMBONE: Thank you, Luther. I saw a lot of heads nodding. And Meghna, you were saying? Cherie, you had a comment or Linda?

MS. PAGETT: You have a lot more experience than I. Go right ahead.

MS. SPINELLA: I was just going to add that dull -- it would dull the pain to some degree, to make it maybe a dull ache rather than a stabbing or shooting pain. Maybe the jolt that you -- or I feel when I have my herniated disc, if I turn a certain direction or I move too quickly, I get such a jolt that takes my breath away. So those opioids and the Lyrica is helping to try to take it down a notch and keep it so I can function.

MS. GIAMBONE: Okay. Thank you. Okay. An I think we have -- oh, Cherie? Yeah?

MS. PAGETT: I was going to say pretty

much the same thing. It's the sharpness that goes away. It's the, oh my God, I can't stand this, you know, I've got to have my teeth gritted to, okay, I can take a deep breath and I can bear this now.

MS. GIAMBONE: Okay.

MS. PAGETT: Or at night, it's the difference between going asleep and not.

MS. GIAMBONE: Okay. Thank you, Cherie. Graham, can you give us an update on what we're hearing on the Web, and then we'll move to our next polling question?

MR. THOMPSON: We've heard a wide range of treatments mentioned on the Web, from Neurontin, Lyrica, gabapentin, different compounding creams. In terms of non-drug therapies, meditation, audiovisual stimulation, things like hand controls for steering wheels so that your feet don't have to do as much and things like that. In terms of side effects, a lot of people have mentioned things like dizziness and constipation and other sorts of things.

MS. GIAMBONE: Thank you. Now, many of you indicated that there are other drug therapies not mentioned. Would somebody mind sharing what are some of those other drug therapies that you're using? Why don't we come to Lawrence here?

LAWRENCE: Thank you. First of all, I'd just like to say I am so impressed with your facility. You've certainly come a long way since you were on Wisconsin Avenue and impressed with the conference and the leap that you've made is so commendable to have us patients involved. Really, you all are to be commended tremendously, your time and effort.

[Applause.]

LAWRENCE: I have a very complex situation. I have a myeloproliferative disorder, polycythemia vera and I started -- my mother had neuropathy and I started to develop the neuropathy before I went on treatment. I'm going for the world's record on interferon, which is sort of -- not a real chemical therapeutic agent, but it's an agent which also can cause neuropathy. So with my

doctors, we can't figure out what aggravates what. And I think this happens with a number of us, that you really don't know. It's such a broad range of things.

What I -- what I have found, I discovered, first of all, tai chi has just done wonders. I think it's really, really amazing. I've noticed -- I go to the senior center tai chi class, that all of a sudden, my balance has gotten a lot better and my feet are numb too. And I've found when I drive, I have to keep my foot on the hump to make sure I don't go through the -- and hit the brake pedal and the gas pedal. And so, I've developed strategies.

And just in addition, what I feel about this disease is that I wish I didn't have it, or any of these. But I have had so many wonderful experiences and met so many wonderful people. The one thing I'm using now is called a rebuilder. It's sort of like nerve conduction in water. And I'm pretty sure temporarily it alters my perception of the pain. And after I use it for

about six hours, my feet feel great. My condition, my neuropathy is very intermittent and I've lost a lot of my small muscle -- my small nerve fibers. But I found that that was excellent.

And then, I would just like to say I'm hoping to hear about the use as a standard of nerve biopsy. I think that might be one, concrete tangible way, and also about the nerve regeneration medications. I think in other diseases, in certain carcinomas, they're making headway into looking at that after -- post a chemotherapeutic treatment. And then, the laser, there's a program where they're talking about rejuvenating nerve cells with a laser. So I don't know. That's my thoughts.

MS. GIAMBONE: Thank you, Lawrence. Thank you very much for -- yeah, and let's --

MR. SHROUT: The main thing that drove me up here today to participate in this was being in blind pig mode and stumbling on a gem, I think. There are a lot of supplements out there in snake

oil land. I stumbled across one about six months ago that has amazingly, surprisingly, unexpectedly impacted my neuropathy. It's going to tell the name so folks listening and in the room may be able to take advantage of this. I'm not trying to chauffer these guys.

But it's Elysium Health and the name of the product is Basis. There's five Nobel laureates on their panel. these guys are selling this as a mitochondrial cellular health supplement and they're doing it as a supplement because you get processed -- you guys know better than anybody. I took it because I thought maybe I'd get a little more energy out of this. I'm an old guy too. I'll be 70 soon. I thought, yeah, maybe a little more pep in the day. Two months later, much to my amazement, my feet that were numb aren't numb anymore and I think it is having a healing effect on my small fiber nerves as a positive impact on the neuropathy.

I would really love it if you guys could go ping these guys and poke at them and say, hey

dudes, go do some clinical trials. They promise they're going to do this. They promise they're going to do it in scientific mode. I'd love to see somebody on your side of the fence really work with these guys. Make them hold true to their word, and who knows, this could become a nerve regeneration medication totally unexpectedly. So that's why I'm here today. Thanks.

MS. GIAMBONE: Thank you. Thank you for that. Any other drug therapies not mentioned that you'd like to bring up? Sorry?

UNIDENTIFIED AUDIENCE MEMBER: IVIG.

MS. GIAMBONE: IVIG. Yeah. Okay. Thank you. All right. So let's move on to --

FDA panel, any questions before we move on to other therapies, non-drug therapies? Okay. All right. Let's go on to our next polling question. All right. So everybody get your clickers out again. Besides the therapies mentioned previously, what else are you doing to manage any symptoms you have experienced because of your neuropathic pain? And you can check all

that apply: A, surgical destruction of nerves; B, TENS; C, cannabinoids; D, dietary and herbal supplements; E, diet modifications and behavioral changes; F, complimentary or alternative therapies; G, physical or occupational therapy; H, other therapies not mentioned; I, I am not doing or taking any therapies to treat symptoms. And we've actually -- we've touched upon several of these and we've also heard aqua therapy. But let's see what else people are doing.

Okay. So again, a pretty wide range. We have touched on several of these. So I'm going to look to H, which is other therapies not mentioned. And so, I'd like to ask what are some of the other things that you're doing to manage the condition. Adam? And then, we'll come to you. Go ahead.

MR. HALPER: Yeah. So I'd list -- and I'm sort of discovering these through trial and error as I go. But I'd say there are five in the supplementary/alternative realm that I've personally found to be helpful. The first is

Epsom salt baths. Epsom salt is magnesium sulfate. You need to use a lot of it. But I personally found that, at least in the short-term, it can really take the edge off of the burning pain and to say that is to say I can go into a bath with a lot of pain and walk out feeling fine. So that's something I would highly encourage people to at least experiment with because it's not exactly high risk.

A second, I know other folks in the room have probably tried this, I've personally found massage of my legs to be very effective as a short-term remedy. The third point I would make, particularly for folks who have functional limitations like I do, is just experimentation with different types of footwear. So I've found, for example, that if the surface I'm walking on is softer, it makes an extraordinary difference, so different types of orthotics, different types of orthopedic footwear at least in my situation can really change the game.

A fourth is -- and this would tie in

with physical therapy, but different types of stretches I think in my case have really made a difference and particularly what I would call dynamic stretching, which is, for those who aren't familiar, instead of a fixed stretch, it's you're actually moving as you stretch. So it's sort of like a leg swing and those types of things where you're actually getting the blood flowing. I've found those to be pretty effective. And then, finally, I would second Louis and I would say that I'm a firm believer in both the physical and psychological benefits of meditation practice. And I was fortunate in that I had a practice before I even developed neuropathy. But you know, I can't say strongly enough how valuable it can be if you're dealing with something like this.

MS. GIAMBONE: Adam, a quick follow-up question for you. So when you talk about the Epsom salt baths and the massage --

MR. HALPER: Yeah.

MS. GIAMBONE: And you mentioned it gives you relief. How long is your relief?

MR. HALPER: Yeah. I think that's hard to quantify. You know, certainly -- I mean, I think the most useful situation is, you know, there are just some days, for whatever reason, I'm experiencing burning pain. And so, if I take that bath at night, more often than not I'm able to just go to sleep, no problem. Is it possible that there's some carryover effect to the following days? Absolutely. And my intuition is that there might be. But it becomes a little harder to quantify.

MS. GIAMBONE: Thank you. Any other comments? Yeah, let's --

MS. WALDROP: Yeah. I'd just like to third what Louis said about the importance of exercise. I think any kind of movement has been extraordinarily helpful for me. I too think that the dynamic stretches -- tai chi has helped. I work on my balance all the time. I mean, really all the time. And I think this psychological benefit you get as well as physical, functional improvement just can't be overestimated. But I

also had a question and that is whether anybody in the group here has tried reflexology, where they really concentrate on your feet? And did it help?

MS. GIAMBONE: So we're hearing --

UNIDENTIFIED AUDIENCE MEMBER: [Off mic.]

MS. GIAMBONE: Okay. So it felt great while they were doing it. Okay, and we'll take one more comment.

JEREMY: My name's Jeremy. I don't know whether this is placebo effect or not, but I've had very good luck with yoga. I've been -- I can work a lot further since I started yoga. But I have been doing it for a couple of years.

MS. GIAMBONE: Great. Thank you, Jeremy. I'm going to ask you a few questions. I'm going to read a few statements out loud and we'll do a show of hands and then I promise I'll come to you. I promise. Okay. So since we are talking about -- you know, we talked about prescription drug therapies. We've talked about some non-prescription drug therapies or non-drug therapies. So how many of you would say that your

first focus for treatment is a non-drug approach such as making changes to your lifestyle or pacing your activities or -- okay. So we have four hands raised for that.

How many of you would say collectively your non-drug therapies or lifestyle changes give you as much or more overall benefit than your medications? So how many of you would say that your non-drug therapies or changes that you've made give you as much or more benefit than your drug therapies? Two, three, two-and-a-half. Okay. And then how many of you would say that your non-drug therapies are important but that they can't match the benefit of your medications? Four, five, six, seven, eight, nine, ten, eleven twelve -- 12 hands raised, 13 hands raised. Okay. Great. Thank you. That really helps put a lot of perspective around this.

Graham, are we hearing anything on the Web?

MR. THOMPSON: Mostly consistent with what we're hearing in the room.

MS. GIAMBONE: Okay. Great. Let's do -- let's do another show of hands as we're approaching, believe it or not, the closing of our afternoon session shortly. So thinking about all of your therapies together, how many of you feel that you're managing your pain as best as you can? Okay. We have about 16 hands raised for that. And this sort of goes into our discussion on ideal treatment. So let's talk a little bit about ideal treatments before we move into our scenario. So you know, we talked about specific aspects of your neuropathic pain and we even talked a little bit about sort of, you know, is there a particular sensation that's worse than the other sensation and so forth. So you know, for those of you that said your condition is not well-managed -- you know, many of you said your condition is not well-managed. What are the aspects of an ideal treatment that you look for? Leslie?

MS. LEVINE: This is something that's not on the list, that at least most of the 60 people in my neuropathy support group feel, that

their pain is more manageable if you're -- if you're in something like a support group where you're with people who understand that neuropathy, while it's invisible, produces real pain and know what people are going through. It's very helpful to have peers.

MS. GIAMBONE: Thank you, Leslie. And we -- yes, Linda?

MS. SPINELLA: I think ideal treatment includes a good night's sleep. I think sleep is very underrated, should be very important, whether it comes from the drugs or whatever. You feel much better if you've had a good night's sleep. When you don't, that's it. I would like to see a drug that covers more, so I don't have to take a whole list of drugs to cover certain aspects of my pain or, you know, other side effects, take a drug to cover that side effect or something like that. If there is a broader -- like Lyrica is a broad drug that covers a lot. So, but I would like to see something like that.

MS. GIAMBONE: Linda, just to follow up

to your question -- or to what you just said, thinking about your current treatment regimen, what aspect of your neuropathic pain symptoms or the way your symptoms manifest does your treatment regimen not address at all? I mean, you mentioned that you'd like something to help you sleep through the night. So is that -- in your current treatment regimen, are you not able to have --

MS. SPINELLA: Yes. I get that from a muscle relaxer. I get that every night. Along with everybody else, I also have the tingling that the Lyrica -- they say that I have scar tissue from the surgeries that I've had. So that's why I'm getting the Lyrica. And that should help with the tingling. So far, I haven't found any relief from that, although it's helped with the pain.

MS. GIAMBONE: Okay.

MS. SPINELLA: So I understand what everybody is saying about the numbness and the tingling.

MS. GIAMBONE: Okay. Okay. Thank you, Linda. Cherie?

MS. PAGETT: I think one of the reasons I've said that my pain is managed but perhaps not well-managed is I don't know how much longer I'm going to live or live with this pain, whether it's going to be another 10 years of 15. So I've not maxed out on the meds I'm taking. Yeah, I could go to every night and take up to the 3,600 or whatever it is of the gabapentin and I could take a couple of OxyContin. But I'm afraid what that's going to do, not only short-term but long-term and where am I going to turn in 10 years when the pain is more intense. And so, I hold back until I can't take it anymore basically.

MS. GIAMBONE: Sure.

MS. PAGETT: Last night, before I went to bed, I knew it was important that I slept. So I did take some oxy -- whatever it was. I don't even remember what it was. But I did take some so I could sleep.

MS. GIAMBONE: So Cherie, following up to what you just said then, what would you look for in an ideal treatment?

MS. PAGETT: Something that would not have the side effects, I mean, because when I -- if I do take 3,600 mg of gabapentin, I'm not much good the next day or wouldn't have the potential addictive problems that the opioid products do. So it's sort of a scary field out there and I would just like something that I could take and wouldn't have to worry so much about the consequences.

MS. GIAMBONE: Sure. Thank you. Yes, Linda, let's hear from you and then we'll go -- I'll go back to the other --

MS. SPINELLA: Sorry. One more thing. As Cherie already said, you know, I'm only 47. I am worried about what'll happen to me in 10 years, 15 years, 20 years. And with the mention of Lyrica, if I am on this for long-term, what are the long-term side effects. That would be in the ideal treatment too, that you're going to have a drug that doesn't have something so damaging as dementia or some other long-term effect on your brain.

MS. GIAMBONE: Thank you, Linda. Meghna, yes? Yeah, Steve?

MR. KLITZMAN: Yeah, going back to one of my earlier comments, ideally I would love to see a drug that did reduce or eliminate the numbness and regenerated the nerves. But realistically, I'm not sure there's enough research, you know, basic research going on now to do that. And then, let me just follow up on this woman's comment about the support groups. I lead the only support group in Maryland, Virginia or D.C. We have 150 members, a wide range of neuropathies. We meet once a month in Annandale, Virginia. We have speakers that come in that help us, you know, professional neurologists and podiatrists and physical therapists and nutritionists.

But the main benefit we get from it is we help each other psychologically, emotionally. We can speak to each other's pain. We sort of understand what we're dealing with. We have nine people who are here today who are in the group,

including Cherie and Beth, and six or seven others of us. And I have a flyer here about the group and there's also one on the table outside. So if anybody's interesting in joining a support group in this area, D.C., Maryland or Virginia, you know, speak to me. There's unfortunately not enough of them in the country.

We did a -- we did a study in the state of Virginia a few years ago and we had Governor McDonnell at that time sign a proclamation and we put it through the Department of Health in Virginia. And we estimated that there were 500,000 people just in the state of Virginia that had a form of neuropathy, 500,000, based on the number that the neuropathy association came up with, that there are about 45 million Americans that have diabetes and about half of them have neuropathy. So they estimated maybe 20, 25 million Americans have neuropathy. And so, just in the state of Virginia, 500,000. And we're the only support group in the entire D.C. Metro area.

So there's probably thousands, if not

hundreds of thousands of people around the country that really could use the benefit of a support group and certainly could benefit from medication and treatment and other alternatives. And unfortunately -- this isn't the forum for it -- there's a tremendous amount of underfunding to study neuropathy. At the NIH, a $5 billion budget, they spend about $150 million a year on neuropathy compared to Alzheimer's and epilepsy and stroke and other neurological diseases. Neuropathy is an orphan disease. It doesn't get very much attention and yet it affects millions of people. And it seems to be increasing in recent years. Younger and younger people are coming down with it.

I mean, I'm 71. But we have people in our group that are in their 20s and 30s and that's really sad for me that, you know, they're that young and getting this disease. And there's really not enough basic research going on as to why, what is causing the disease, why does it progress. Just calling it -- just saying it's

caused by diabetes -- it's dealing sort of with the surface symptoms of it. But there's very little money being spent on basic underlying research as to what is causing neuropathy and why does it persist in this society.

And you know, people say, you know, assuming there's no cure -- well, why should there be no cure? There should be a cure for it and why isn't more attention being given to it? There should be more attention. If members of Congress had neuropathy, you know, maybe we'd get more funding for it. I don't know. They don't want to admit that they have it, I guess. But I'm sure there are probably dozens of members of Congress that have peripheral neuropathy. But they haven't spoken about it, so --

MS. GIAMBONE: Thank you, Steve. Thank you. Okay. So I know we have a few people waiting on the phone. Let's -- I'm going to tee up the phone here and we'll get to them in just a minute here. Let's go to our scenario question, which is coming up next. Okay. So we're going to

do a short scenario. And what this is, is I'm going to read you just a very short blurb. It really doesn't contain a lot of information and I know that information is very important. But after I read this, I want you to just tell us the first thoughts that come to mind. It could be a question. It could be a comment. It could be a decision. Whatever it may be is perfectly fine. But we just want to hear from you.

So imagine that a new medication to treat neuropathic pain associated with peripheral neuropathy has recently been approved by FDA. Your doctor believes that you may be a good candidate for this medication. In the clinical trials that were conducted, one-half of adults treated for 12 weeks had a 50 percent reduction in their pain. Common side effects of this medication include nausea, fatigue and weight gain. Rare but serious side effects of this medication include nerve damage and liver damage. The medication is unlikely to be addictive or to be used for abuse, such as to get high.

So hearing this very, very short piece of information, what are the first thoughts that come to mind when hearing this scenario? And what kind of questions would you ask your doctor about this new treatment for neuropathic pain? There's -- again, it could be a question. It could be a comment. Anything is okay. Lawrence?

LAWRENCE: I think that's a great scenario. I think what would be important is I'd want to know what the protocols are. I would like this medication. But I would want to know what the protocols are when I started, what do I do before, what do I do during and what do I do and how long after to look for the nerve damage, the liver damage. Are they going to follow me by enzymes? What's been the experience? That would be my point.

MS. GIAMBONE: Okay. Thank you, Lawrence. Others? Adam?

MR. HALPER: Yeah. I think Lawrence made some excellent points there. The only point that I would add is I'd be curious to know the

statistical likelihood of the serious side effects. Rare is an awfully vague term. So that'd be the big one for me.

MS. GIAMBONE: Thank you. You wanted to -- yeah, sure.

KATHLEEN: My name is Kathleen. And I'd be interested to know how many people were in this study and if there had been any longer term studies, because 12 weeks isn't very long to see if there's any long-term effects.

MS. GIAMBONE: Okay. Thank you very much. Any other thoughts before we -- I'll turn to the FDA panel. Any other questions? Okay. Great. Okay. So why don't we take some phone calls? I know we've had some people patiently waiting. Operator, would you mind dialing in with the first caller?

OPERATOR: Yes. The first caller on the comment is Bruce Stewart. Your line is now open.

MR. STEWART: Hello. Thank you for taking my call. I'd just like to say -- you know, I lived in Florida and due to the DEA's aggressive

approach to, you know, policing opioids, I was unable to fill my prescription and I basically was run out of the state of Florida because each pharmacy was left to their own devices as far as, you know, not serving their clients and even long-term clients such as myself. I'm out in Nevada and there are ceilings at the Las Vegas pain clinic that I go to, to where -- I take OxyContin 10 mg. I am likely to take a higher dose but, you know, I declined it because, like one of the women said before, I'm kind of afraid, where do I turn, you know, 10 or 15 or 20 years from now. I'm 55.

And I just wanted to say that they're only allowed to dispense four pills a day, regardless of the medication. You know, I think if you have a patent -- I take tramadol. I take Cymbalta and I take the Oxy. And this medicine is only rated to last, you know, four to five hours. But we're expected to make it stretch over a 24-hour period, which his pretty distressing because, you know, if you do a simple multiplier, you know, it's four hours a piece, you know, four pills and

that's 16 hours. I mean, what do you do with the rest of the day? And that's one of the dilemmas that I've had and a lot of people have had with the DEA crackdown.

And I just would like to see opioids -- a conversation about opioids open up because, you know, I don't get high off of it. I'm in severe pain. I have sensory neuropathy in my feet and it just affects the pain and it makes it, you know -- makes me able to go about my daily business.

MS. GIAMBONE: Thank you so much. Thank you. Graham, we'll take one more caller. So Operator, one more caller, please.

OPERATOR: The next comment in the queue is from Janet Metapol [ph]. Your line is now open.

JANET: Hello?

MS. GIAMBONE: Yeah, we can hear you, Janet.

JANET: Hi. Yes. I have neuropathy --

MS. GIAMBONE: So now we can't hear you, Janet. So can you --

JANET: Hello?

MS. GIAMBONE: Yeah. Can you maybe speak a little bit louder into the phone?

JANET: Okay. I'm sorry about that. Okay. Yes. I was diagnosed with -- [off mic] -- but I've been suffering from it for a few years back and forth. I was suffering from it. It was called -- [off mic] -- I traveled from different states to find out what was -- what I had. And finally, here in Florida, they -- the doctors, the neurologists told me it was neuropathy. But it was hard to find out what it was because I didn't have diabetes. So it was harder for the neurologists to find out what it was.

MS. GIAMBONE: And Janet, can you tell us very quickly what you would look for in an ideal treatment?

JANET: Ideal treatment? Right now, I am doing therapy at home. I am thinking about doing -- I can't really walk that much. I am -- I am taking medication because I am taking Trivantin, which is Neurontin, 3,600 mg. I'm

taking Topamax. I'm taking Topamax, Lyrica and I'm taking --

MS. GIAMBONE: Okay.

JANET: -- I'm taking Cymbalta. I'm taking -- what is the other medication -- I am taking a whole bunch of other medications that I can't really remember right now.

MS. GIAMBONE: That's okay. Thank you so much, Janet. Thank you for sharing those comments. We appreciate it. Okay. So I'm going to stop in just a minute here. I just want to thank everybody for all of your comments. Again, I know we didn't get to everything. But please go to the public docket. Please enter your comments there. They're very, very important and that's a way to continue the discussion. At this point -- and again, thank you all for being here. It was so important to us and wonderful to hear everything that you've had to say. So I'm going to turn it over to my colleague, Meghna, for the open public comment period now. Meghna?

OPEN PUBLIC COMMENT

MS. CHALASANI: Yeah. Hi, everyone. I want to thank you all again for coming today and staying with us until Friday, at 5 p.m. And thank you so much for sharing all your wonderful stories with us. They've been very insightful and informative. We're now going to be moving on to the open public comment session. And for those of you that are not aware, the purpose of this session is to allow an opportunity for those who have not had a chance to speak on issues that are not related necessarily to our two main discussion topics.

This is also an opportunity for participants who are not patients or patients' representatives to comment as well. Please keep in mind that we will not be responding to your comments. But they will be transcribed and be a part of the public record. Since we would like to be transparent, we would encourage you to note any financial interests that you have that are related to your comment. If you do not have such interests, you may state that for the record as

well. And if you prefer not to provide this information, you may still provide your comments.

We have collected six folks who are interested in providing their comments and we have about 10 minutes. So if we could have about two minutes per speaker, that would be great. And I am going to be a little strict with time as well. If you start approaching the two- minute time limit, I will ask you to start wrapping up. So first, we have James Yadlon. I apologize if I'm mispronouncing anyone's name. If we could get a mic to James, please?

MR. YADLON: First of all, I want to thank the FDA for doing this. This is an incredible afternoon, very educational.

[Applause.]

MR. YADLON: Second, the panel, the ladies and gentlemen on the panel, with your courage and your incredible stories are just mind-boggling and I commend you and wish you the very best in the future. I'm on the board of directors of the GBS Foundation and I had GBS 42 years ago.

I was totally paralyzed. For the last 42 years, I've had very sore feet. And they hurt. But what I'd like to take a minute or so to do is read a couple of the comments from our members who sent -- who I solicited -- I said please put in one sentence a description of your pain. So I'm going to read a couple. You just stop me when you want to stop me.

It feels like I put my feet into scalding water and dealing with the after-effects of that burn 24/7, while simultaneously having them in a washing machine with the vibration coming up from the soles of my feet, up through to my calves. It is like walking on a board barefoot full of 16-pennynails, 24/7. The only thing I can say is it feels like a toothache in my arms and legs. That's the only way I can describe my pain. Without pain management -- these are all from different people, by the way. These are all individual ones.

Without pain management, I would be unable to get out of bed. The pain feels like

lightning bolts, severe sunburn and numbness all at once and in levels. When I'm asking about my pain, my answer is simple. My legs feel like telephone poles filled with razor blades. If that doesn't get the message across, nothing will. My nerve pain is like being constantly rolled on a bed of red-hot nails, burning, prickling, stinging, stabbing. The mere touch of my child's hand on mine can feel like a 12,000-volt electric shock. I don't know if you want to let me do a couple more --

MS. CHALASANI: How about two more?

MR. YADLON: Two more. All right. I think you've got the idea. One more. I live with pain, burning, hot, cold, numb, tingly feet 24/7, 365, trying to concentrate and live life.

MS. CHALASANI: Thank you, James. And I know Soujanya and other folks have mentioned this, but please submit your comments to the public docket so that they'll be a part of the public record and this summary report as well. Next, we have Tim Murphy.

MR. MURPHY: I'll pass.

MS. CHALASANI: Okay. Thanks, Tim. Gary? Gary Shrout?

MR. SHROUT: I'll be quite quick because I've had plenty of chance to comment. But I didn't know signing up, so I signed up. One, I'd encourage you to look for the cure. Yeah, you've got to treat pain. Totally agree with you. You know, folks that are that bad off, you've got to treat them. But please look for the cure and I think there's some things coming out -- and again, what I said before, what drove me up here, please each out to the Elysium Health guys. I've got a couple of articles I'm going to leave with you all, Scientific American and Fast Company Magazine. It's where I found out about them. Help them -- keep them honest.

I have no financial association with them. I'm a completely surprised, caught off-guard customer that wound up being positively affected. My life is an uncontrolled multivariate experiment. Is this going to help others? I have

no idea. But it sure helped me. And if you guys can help it to help others and things like that and get the cost down, that's awesome. And thank you. I'm impressed. This is an impressive function. Thank you for taking time and you're telling us thanks for staying here until 5 o'clock on a Friday. You guys work here. You've been here all week. Thank you very much.

[Applause.]

MS. CHALASANI: Thank you, Gary. Next, we have Pam Schlemon.

MS. SCHLEMON: Thanks. Hi. I'm Pam Schlemon. I'm the president of the Foundation for Peripheral Neuropathy, and I do want to echo what everybody said here today. Thank you. I applaud you for selecting peripheral neuropathy as part of the patient-focused drug development initiative. I think we all know the impact that peripheral neuropathy has, not only with the patients here, but there are families, the economy, the healthcare economy. So I do want to say thank you.

The foundation focuses its efforts on education, funding research. We have a peripheral neuropathy research registry that's going to address hopefully some of the very things that everybody has been talking about today. What are the underlying mechanisms that are causing peripheral neuropathy and then most importantly trying to identify and deliver new therapies specifically for peripheral neuropathy that will help these patients because, as we know today, we've heard a lot today that much of the drugs that people are taking are not very effective? And I also want to let you know that we did a survey as well. We had over a thousand responders. We have put some of them, about 590 of the -- what I want to say is we did an analysis of the 590 responders and that information and the results of that survey is on the public docket. So again, thank you very much.

MS. CHALASANI: Thank you, Pam. Next, we have Larry Silverburg.

DR. SILVERBURG: I will be quick. As a

family physician, retired for 43 years, a professor of family medicine teaching, teaching medical ethics of professionalism at a college medical school in Philadelphia, what I would like to say is as patients, you have a right to expect your doctor to communicate with you and to be kind, to be gentle. There is no inconsistency between being highly intelligent and also being very nice. A lot of times, doctors, even today, do not handle their patients and listen to their patients. We were talking -- Dr. Hertz and I were talking about the patient narrative. It's a very difficult narrative.

And so, I just want to say you should be expecting of your doctors to be kind, to be open-minded. It's okay if you make a mistake with them or they make a mistake with you. If you can't work with your physician, find another physician. But also, work with them. Tell them what bothers you. They are human. They may not have the time. They're under a lot of pressure. Things in healthcare are changing. Learn to communicate and

be prepared with your doctors. And thank you again.

MS. CHALASANI: Thank you, Larry. And last, we have Leslie Levine.

MS. LEVINE: I will also be very brief. It was estimated that there are over a hundred types and causes of neuropathy. And it's really a challenge to approve a new drug for neuropathy for anything other than diabetic neuropathy because clinical trials, by their nature, need a homogenous population of subjects that is of a certain size. And most forms of neuropathy are rare.

As a person who's being treated with IVIG, which is only approved for three types of neuropathy -- and mine isn't one of them -- it can be a very -- a real struggle for people with neuropathy since the drug choices are so limited and so many are not on-label. Insurance companies are very reluctant to pay for expensive drugs off-label. So I know this is not something that the FDA has a whole lot of control over, but I just

wanted to voice the issue that when things come up for -- that might be expanded in their label, that it would be great if you can do what you can to enlarge the indications. Thank you.

MS. CHALASANI: Thank you, Leslie. Exactly 10 minutes. I didn't even need to bother anyone today. Now, I would like to call Dr. Sharon Hertz to the stand for closing remarks.

CLOSING REMARKS

DR. HERTZ: Well, this was our second patient-focused drug development experience. And I am glad that we have as an agency embarked on this because this has been another extremely valuable experience. It's always interesting to get responses that you don't expect, which is of course the value because I don't need to hear what I already know. We need to hear what we don't know. And I think that we've gotten some very good information from everyone here in terms of not just the personal experience, but what's important and some areas of need. And so, I appreciate that and I thank you all for taking the

time out of your busy lives, in spite of your pain, to come and participate. We appreciate it.

We will go over the discussions from today and we will go over the docket submissions very carefully, trying to get as much information as we can to help move forward the development of products to treat painful neuropathies as much as possible. If you have any comments, please send them to the docket. Down the road, if you have comments, you can always find us here at FDA and we're always interested to hear what you're thinking. Thank you [Applause.]

[WHEREUPON, the foregoing adjourned at 4:57 p.m.]

CERTIFICATE OF NOTARY PUBLIC

I, ERICK MCNAIR, the officer before whom the foregoing proceeding was taken, do hereby certify that the proceedings were recorded by me and thereafter reduced to typewriting under my direction; that said proceedings are a true and accurate record to the best of my knowledge, skills, and ability; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

Erick McNair

ERICK MCNAIR

Notary Public in and for the

STATE OF MARYLAND

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I, BENJAMIN GRAHAM, hereby certify that I am not the Court Reporter who reported the following proceeding and that I have typed the transcript of this proceeding using the Court Reporter's notes and recordings. The foregoing/attached transcript is a true, correct, and complete transcription of said proceeding.

06/20/2016

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