

May 31st, 2022 Patient Education Webinar- PTSD and Pemphigus/Pemphigoid

Becky: Welcome, everyone. My name is Becky Strong and I'm the Outreach Director at the IPPF. Thank you for joining us today. The month of May is Mental Health Awareness month so we've invited Dr. Erin Wei to discuss PTSD and pemphigus and pemphigoid for today's Patient Education webinar. This call is now being recorded. I'd like to thank you for being on the call with us today and a big thank you to our sponsors, Genentech, argenx, and Cabaletta Bio for making today's call possible. "Information is a key factor and living with any disease or condition, however, every patient situation is unique. The IPPF reminds you that any information found on the internet, or during any presentation, like the one today should be discussed with your own doctor or health care team to determine if it applies to your specific situation." So, we have a poll for you today before we begin. We want to know whether or not your physician has discussed mental health with you, and recommended you to seek psychological support after being diagnosed with pemphigus or pemphigoid. And while you're taking the time to answer that poll, let me introduce you to our speaker for today.

Becky: Dr. Erin Wei is a graduate of Massachusetts Institute of Technology (MIT) where she majored in chemistry with a minor in biology. She received her MD from Harvard Medical School, graduating with honors. While at Harvard Medical school, she was the recipient of the competitive Doris Duke Fellowship for Clinical Research. She completed her residency and served as chief resident at the University of Miami Department of Dermatology and Cutaneous Surgery at Jackson Memorial Hospital. Since 2016, she served on faculty at Brigham and Women's Hospital-Harvard Medical School, where she directed the Brigham and Women's Health Care Center at Westwood and served as the Director of the Bullous Disease Clinic. She is currently an assistant professor at Harvard Medical School. She is the recipient of the 2017-2018 Research Grant from the IPPF. For her excellence in patient care she was the recipient of the Brigham Way recognition and BWH Certificate of Excellence for Patient Satisfaction. Additionally, she currently serves as an associate editor at VisualDx. She regularly serves as reviewer for top tier journals including the Journal of the American Academy of Dermatology, British Journal of Dermatology and The Journal of the American Medical Association Dermatology. She will be joining University of Nebraska Medical Center in the Fall of 2022 as the Director of Clinical Trials and co-Director of the Bullous Disease Clinic.

Becky: Thank you for taking the poll. It looks like for many of you, about 78%, mental health wasn't discussed, and only about 22% said, Yes, that it was. So, we thank you for being honest, and sharing that information with us. So, before we begin, I'd like to go over a few housekeeping items... (Reviews Housekeeping Slides). Now, it is my pleasure to hand it over to Dr. Wei to discuss her research on Post-traumatic Stress Disorder and pemphigus and pemphigoid.

Dr. Wei: Thank you so much Becky, for the introduction. It's a pleasure to be here to discuss PTSD in autoimmune bullous disease, one of my passions. Can everybody see my slides? Let me just pull that up. While I'm giving this talk, unfortunately, I cannot see the polling questions or see your faces so I apologize, but I will take questions at the end, and I incorporated some of the questions in my talk, as well that were submitted prior to the talk. And I apologize this talk had to be rescheduled. I had lost my voice during the previous date. My name is Erin Wei Barrett, and I am currently at Brigham and Women's Hospital, Harvard Medical School where I have directed the bullous disease program since 2016. I think many of my patients are here as well, which I'm really happy to see. I have no conflict of interests that's relevant to the topic discussed today. However, I want to mention that this study was actually generously funded by the IPPF.

Dr. Wei: So let's start with the definition, what is PTSD? So broadly speaking, Post Traumatic Stress Disorder, or PTSD is a condition in which a person has difficulty recovering after an experience that threatens their psychological or physical integrity. These individuals continue to experience negative thoughts and feelings related to the experience long after the experience has ended. It was first described in combat veterans as early as in ancient Greece, interestingly. Symptoms of PTSD include but are not limited to, intrusive thoughts about the trauma, avoidance of talking about the subject. So, in our case the patient may even decline to seek further medical care. Trouble sleeping, or staying asleep, changes in mood, and loss of interest in things you once enjoyed.

Dr. Wei: Non-combat, PTSD has been observed in both life altering and life-threatening medical diagnosis, or events such as after a cancer diagnosis or an asthma attack, or after a defibrillator discharge. And cancer related PTSD of all these diagnoses had been the most well studied. Interestingly, cancer related PTSD is similar to but usually less severe than combat related PTSD, but it can occur anytime during the disease diagnosis and treatment. It is characterized by repeated frightening thoughts, being distracted or overexcited, trouble sleeping or feeling detached from one's reality.

Dr. Wei: So why did I decide to focus on autoimmune bullous disease? This is because a diagnosis of AIBD can be life altering and changing one's self perception of well-being. You may have experienced this when you were first diagnosed as well. Among patients who respond to treatment, the sometimes unpredictable, relapsing, and remitting nature of the diseases can result in long term uncertainty, anxiety, and fear. I think these aspects of AIBD may cause symptoms similar to PTSD. So I wanted to look at this.

Dr. Wei: In my own clinic, many AIBD patients' biggest concerns are sudden relapse and needing repeating treatment. Many patients come into my clinic scrutinizing every new skin lesion, itchy eyes, and mouth sore during their remission and they are fearful that this is a sign of a recurrent disease and I see this every day. So, I think there is a practice gap in evaluating

the psychological morbidity, and in fact, there's nothing in the literature on this topic in AIBD patients. So thus, we performed a study that aimed to evaluate the prevalence of PTSD among patients with AIBD.

Dr. Wei: Many of you are familiar with some of the most common diagnoses here which include pemphigus and pemphigoid. The most common is pemphigus vulgaris in the U.S. and then pemphigus foliaceus is the second and then we And then see a lot of bullous pemphigoid patients and mucous membrane pemphigoid patients. And this is one of the questions submitted, about what diagnosis we're actually talking about, but we included some of the other AIBDs as well in the study.

Dr. Wei: How was the study performed? We performed a single center, IRB approved cross-sectional study in my outpatient clinic at Brigham and Women's Hospital. What we used was what's called PCL-5 , which is a 20 item self-reported measure that evaluates the presence and severity of PTSD symptoms. We gave this to 50 random consecutive AIBD patients in my clinic. I'll talk a little bit, and I'll show you what this actually looks like. Items on the PCL-5 actually correspond to the diagnostic criteria for PTSD and a score above 33 is considered diagnostic. However, a score of between 31 and 33 may indicate that the patient may have some sub therapeutic symptoms of PTSD.

Dr. Wei: A little more about PCL-5, so it is intended to assess the patient's symptoms in the last month only. Participants basically will rank these 20 questions 0 to 4 in terms of severity and we add these scores together. 0= not at all, 1= a little bit, 2= moderately, 3= quite a bit, and 4=extremely. As I mentioned, a score of 31 to 33, although not considered diagnostic, is still considered suggestive of PTSD symptoms, but we only counted those who were 33 or above.

Dr. Wei: So let's look at some of the questions to give you an idea. So questions are grouped to assess different symptoms of PTSD. Questions 1 to 5 assess the symptoms of intrusion. For instance, one of the questions asks, in the past month have you had repeated, disturbing and unwanted memories of the stressful experience? Another question in this category is, in the past month, have you been feeling very upset when something reminded you of this stressful experience?

Dr. Wei: Question 6 and 7 assess for avoidance. So, for instance, it would ask, in the past month, have you been avoiding memories or thoughts or feelings related to the stressful experience? Have you been avoiding external reminders of the extra stressful experience? For example, the place, such as the hospital or people, or things that remind you of the infusion or things like that.

Dr. Wei: Questions 8 through 14 assess for alterations in mood and cognition. For instance, questions asked, in the past month, have you had any strong, negative feelings such as fear or anger, guilt or shame? Have you lost interest in activities you used to enjoy? Have you been feeling distant or cut off from other people? And have you had trouble experiencing positive feelings?

Dr. Wei: Finally, the last five questions assess for alterations in arousal and reactivity. And they ask questions such as in the past month, have you been feeling jumpy or easily startled? Having difficulty concentrating? Are having trouble falling or staying asleep?

Dr. Wei: What did we find after giving this survey to our patients? So first, let me tell you a little bit about the patients we randomly surveyed. About half of the randomly selected patients have pemphigus, a quarter have bullous pemphigoid and the other quarter had mucous membrane pemphigoid and the remainder had a mix of other diagnoses. We had more female than male participants in the random selection. And interestingly, 86% of people, not surprisingly, I guess, were undergoing treatment at a time that they were surveyed, and 14% were in remission, defined as having no new lesions and off all medications for the last two months, and they were just seeing me for routine follow up when we surveyed them.

Dr. Wei: Here's what we found. Of all the PCL-5 questions I showed you, the strongest and the highest scoring questions were those of intrusion. People were having these repetitive thoughts, as you recall these questions asked in the last month, have you had any disturbing or unwanted memories of the experience? Have you been feeling upset when thinking about it? And have you had a strong physical reaction when thinking about your diagnosis and the experience of treatment? This is not surprising. A close second were the questions on disturbance of cognition and mood, shown here in this table. These are questions that were basically asking, in the last month have you lost interests and things you used to enjoy? Have you had trouble having positive feelings? For instance, being unable to feel happiness or loving feelings for people close to you. Not surprising, this is also a category where our patients scored high on. Overall, the most important finding of our study is that 1 out of 6 individuals, or about 16% of our participants, had a score of 33 or above on the PCL-5 meeting diagnostic criteria for PTSD in the last month. It shows here with the blue arrows, bullous pemphigoid interestingly, had the highest percentage of individuals meeting criteria, followed by pemphigus and mucous membrane pemphigoid.

Dr. Wei: Overall, just to put that into perspective. What does that mean, 1 out of 6 people? So, according to this study, this is actually a similar prevalence to that after a cancer diagnosis, which is really, really powerful and shocking because people think of cancer as a really serious diagnosis where people don't really think of autoimmune diseases as serious. But we found that, actually, the prevalence of PTSD similar. Given these results, we believe that, perhaps the

sudden and dramatic nature of AIBD, and having the images I showed you, and the unpredictable remission and relapse, really contribute to the development of PTSD in patients.

Dr. Wei: So the next question is, is PTSD preventable and treatable? This also came from a lot of questions from the audience. I'll talk a little bit about how to prevent and how to treat. Factors found to lower your chances of PTSD, this has been really looked at in cancer patients. It has not been looked at in autoimmune disease, but basically they found three things that really help decrease the chance of PTSD from developing. One, is having good social support. Two, having clear medical information about prognosis and treatment. And three, having an open relationship and good communication with healthcare providers. Obviously, it doesn't always prevent PTSD, but it can lower your chances.

Dr. Wei: Many of you are aware, there are certain medicines we can give people to prevent PTSD in traumatic events. Propranolol, which is a beta-blocker, is often used to treat blood pressure and it's been found that, when given immediately after a traumatic event, it may reduce the consolidation of emotional memories and prevent PTSD from developing. This is most well studied in kind violent crimes and things like that, they give victims Propranolol and it would decrease the chance of PTSD.

Dr. Wei: What about once PTSD develops, is it treatable? And the answer is yes. This was a question posed as well by some of the audience. Some treatment methods include crisis intervention techniques, relaxation techniques such as cognitive behavioral therapy, meditation, support groups are helpful, and medications for anxiety and depression if the symptoms of PTSD are severe. It has to be co-managed obviously with a psychiatrist or psychologist. And time, PTSD has been consistently shown to improve with time as well from the event.

Dr. Wei: Very briefly, I'm not a psychiatrist or psychologist, but I want to talk about CBT. What is Cognitive Behavioral Therapy? This is the type of therapy, and many of you may be familiar with that have been particularly effective in PTSD. It's a psycho-social intervention that focuses on changing unhelpful thoughts, beliefs, and attitudes and patterns of behavior and is supposed to improve emotional regulation and help patients create strategies to solve problems instead of escalating into negative emotions. Many of the most popular effective CBT techniques are applied to what's called cognitive distortions, I listed some here. What are cognitive distortions? These are basically inaccurate thoughts that reinforce negative thoughts and emotions and propagate PTSD or any other negative psychiatric condition. Some of the more common cognitive distortions, I'll just give you some examples. I think we're all guilty of some of these feelings such as filtering which is focusing on the negative and ignoring all the positive. Another one is catastrophizing, when you just basically think about the worst-case scenario and minimize the evidence to suggest nothing positive.

Dr. Wei: Here are some other ones, which I won't go into. Some of the essential CBT techniques and tools are shown here. For instance, cognitive restructuring is one of them; journaling; exposure techniques. In terms of cognitive restructuring for instance, instead of a patient believing that you will go through the same experience again as your initial diagnosis, however positive or negative it may be, perhaps restructure your thinking and think about what is the real evidence you may have a relapse. And even if I relapse, is it going to be as severe as my initial presentation? Usually not? Also, it's going to be caught earlier and because I'm being monitored, the treatment will not likely be as intensive. So, these are some helpful thought techniques to kind of help patients cope.

Dr. Wei: One thing I want to point out is there are limitations of the study I'm presenting. Recruitment in clinic, we basically only posed these questions to individuals who came to my clinic, and they may lead to selection bias that either include patients who are really worried about their condition, and therefore a higher risk for PTSD, or conversely we may have missed patients who are healthcare avoidant. I believe that future study is needed to evaluate risk factors of PTSD in autoimmune diseases including AIBD and figure out what is the overall burden in the larger population. Given the potential significant impact of PTSD on patients, I think early intervention and management in those who show signs should be critical to every physician who sees these patients, and we should refer the patient to the right professionals for treatment.

Dr. Wei: Next, I'm going to go over some, in the last couple of minutes, audience questions, and then in the end, I'll take additional questions. I try to incorporate a lot of the questions that were submitted into the talk. But, if you don't see your question, feel free to ask me at the end.

Dr. Wei: One really good question from the audience is, how long does PTSD take to develop an autoimmune patients? That's a really good question. So, based on studies in other diseases, PTSD can actually develop any time during disease onset, treatment, or remission. Even if a person seems fine after they've gone into remission, it can actually occur at any time.

Dr. Wei: Another really interesting question is, does stress cause pemphigus or pemphigoid? We don't really have a good answer for this because stress itself is really difficult to measure and quantify. While we don't believe stress actually causes the disease itself, because you have to have the genetic factors for it, stress can certainly contribute to a flare of not just autoimmune bullous diseases, but many dermatological and even non dermatological diagnosis and it causes patients to feel worse in general, so stress management is key.

Dr. Wei: Another really interesting question I got was, is there a link between PTSD and Alzheimer's? So interestingly, both chronic stress and PTSD can increase dementia later in life and many studies have shown that there's a higher prevalence of neurological disease including dementia in patients with bullous pemphigoid. Although I don't have a direct answer to

this, I would have to guess, yes, there is a link. We know from combat veterans that have PTSD. there is an increase in dementia later in life. And we know from studies in bullous pemphigoid there's an increase. So I would say, yes or most likely, I don't know the exact answer because people have never looked at this, but it's an interesting question. I may take a look as well in the population I treat, but I would imagine people who develop PTSD in our population do have a higher chance of dementia. But this is kind of a long term study that we have to basically follow patients for many years.

Dr. Wei: The next question is, what are some of the real risk factors for PTSD in autoimmune disease? So most of what we know is from people who develop cancer and I'll present some of those. What we know is, PTSD can develop in anyone. So demographic characteristics such as age, gender, education level, have not been reliable in predicting who will develop PTSD with cancer. So it really can impact anybody. Some risk factors, so disease related variables, include severity, type or number of treatments can contribute, and preexisting psychiatric diagnosis if someone has already depression, anxiety, or PTSD it may be a risk factor. Some protective factors, which I've mentioned in my talk, are social support, stress management techniques, good coping mechanisms, and good patient provider-communication, which is something I can control. I tried to be a good communicator with my patients.

Dr. Wei: Another question is, does time from initial diagnosis to treatment affect the risk of PTSD? I thought it was a great question. We didn't look at this in our cohort but in general, it's a good question to look at the future. From the cancer literature, the answer seems to be no, but they come from very small studies. I imagine that uncertainty and also basically, the longer you wait from diagnosis to treatment and more severe the disease sometimes. I think it may contribute in our population, but we have to take a look.

Dr. Wei: So, what's the next step one of the audience asks? To expand the study and spark conversation. I think webinars such as this really spread information on the prevalence of PTSD for both patients and physicians. And I do believe a larger study is needed to look at what is the overall burden and what are the real risk factors. And I think more funding should be available and dedicated to mental health for patients with autoimmune diseases like it is for cancer. Most importantly, if you feel like you're experiencing symptoms of PTSD, don't be afraid to ask for help through your healthcare provider, because it is a real disease. With that, I conclude my talk. I would like to thank the IPPF for this opportunity and their generous support for this really important work for our patients. I'd like to thank Brigham and Women's Hospital and Harvard Medical School, shown on the left and the right picture there, my department, for on and off the past decade of my life. Many of you know, I will be leaving Boston and moving to the midwest in the fall for family reasons. I'm thrilled for the new opportunities I have with this group here, showing in the middle at University of Nebraska Medical Center. And I'm hoping to continue doing work in therapeutics for all diseases, and especially my passion which is autoimmune bullous disease. I hope to continue to see patients who are affected as well. Thank you and with that, I conclude and I'll take any additional questions.

Becky: Thank you Dr. Wei, that was a lot of information packed into a very short amount of time and I really appreciate you sharing with us. One of the questions that came in and I think you touched on it, is post traumatic stress disorder with patients with autoimmune blistering diseases, did they affect men and women equally in your study?

Dr. Wei: That's a great question. I think we don't have the answer to that. Unfortunately, in our population, I think either coincidentally or just women are more likely to talk about things. Most of the people we surveyed, I think it was about more than two thirds of the patients were women, and only a third were men. I think there's couple of factors that contribute to those numbers. Like I said, even though these diseases tend to affect men and women equally, I think men and women may just express their emotions in different ways. I think men may fall into more of the avoidance category. We had a lot of people who did not want to take the survey, so I imagine it's a pretty accurate representation of the patients I was seeing at that time. I think it may just be a coincidence that we had a higher female prevalence, but there are certain conditions, such as depression or anxiety that may be more common in certain populations and there'll be some giant gender predilection. History of PTSD tends to be probably more common in men, just given more the violence related PTSD. But I don't know the answers to that. I think it needs to be looked at. I think when we evaluated it, there's a coincidence because overwhelmingly my patients at that time were female for some reason?

Becky: Great. Thank you. We have a lot of caregivers on the phone with us as well and I know a lot of this is inside all of our own heads, but is there any advice that you have for caregivers? Any signs or symptoms that we should be looking for that our loved ones might be experiencing to kind of nudge them to get some mental help?

Dr. Wei: There are a lot of great points that you just brought up there. So I think there are also some elements of PTSD in caregivers. I think that's something we should really look at. That's not been looked at enough in the medical literature because I think a lot of family members are affected by things such as family members who have terminally ill loved ones. I think that's something that they need to be cognizant of, self care in caregivers. I think for caregivers, one thing to monitor is the patient acting like themselves? Are they still enjoying the things they used to enjoy and things like that? And if they aren't, you should really seek out help through their dermatologist and really seek out that referral to a professional. Dermatologists are not psychiatrists, but we can refer you to the right people. I think those are really important things. Caregivers caring for themselves because they probably experienced some elements of PTSD as well. Husband, wives, kids who are the primary responsible party for caring for the patients, and just really monitoring for symptoms of PTSD in these patients. If their symptoms continue, even after they're in remission, if they are hypervigilant of their symptoms, if they are avoiding healthcare, if their personalities are really different, they don't enjoy the things they used to, they should absolutely seek out help. Another really great resource is through their primary care doctors, as well. And there's a lot of online counseling platforms as well that many insurances will cover. Those are all really good resources.

Becky: That's a good one, to contact your insurance to see what online resources are available. We seem to be all webinars and virtual meetings, so having the ability to do that from your home in a safe environment may be very helpful to somebody, as well. Jennifer asked, you mentioned medications that help with PTSD, however, we've been told that most SSRI medications affect red blood cells and therefore aren't advisable. Do you have any specific medications that can be generally used safely in the pemphigus and pemphigoid community?

Dr. Wei: I am not a psychiatrist. So, I would definitely not be the one prescribing and also giving any medical advice on what's appropriate for the symptoms but it would definitely depend on what the predominant symptoms are. If you have more hyperarousal than they probably give you something that helps more with sleep and things like that. So although some of the SSRI's can affect your red blood cell count it's just one of the side effects. You just have to weigh your risk benefit ratio, how severe your symptoms are. Not everybody will experience the side effects. Unfortunately if you are somebody who experiences these, they might change it to a different category, but there's so many medicines that are available now. Just for the SSRI's alone, there's different generations and there's definitely other antidepressants that could be beneficial. But I would definitely work with the professional who's used to prescribing them. There is a solution for you, even if you do develop the rare side effects. Yeah. So don't be afraid to seek out care because there are other medicines.

Becky: So I'm going to ask you a question from my personal experience. When I was diagnosed with PV and going through my initial treatments, I had high blood pressure and I was having trouble sleeping and I couldn't decide which was causing, which, or if they were two completely separate issues. And I felt like my practitioner almost thought that I was seeking medications at that time. Do you have any advice for bringing up, looking for some help? I know you mentioned talking to providers, but how can we do that so we're not being judged and looking like we're looking for sleeping medication, or for uppers or downers or whatever the perception is.

Dr. Wei: I think it's really important to educate our dermatologists, and also primary care doctors about these phenomena that we see that are real. We do see a lot of patients develop these symptoms after, it is a trend. So, you're not alone in that. I think many people here will tell you as well, that they have similar difficulty sleeping or anxiety and high blood pressure and things like that. We also give patients a lot of medicines that cause these issues. When you are on high dose steroids for instance, we know it causes personality changes and anxiety, we know it causes high blood pressure, we know it causes insomnia. I've seen patients who are perfectly calm and just never had any psychiatric or anxiety or insomnia prior, but once I give them high dose prednisone they completely change. There are steroid receptors in a lot of your neurons and in other places and they can impact your response to stress and things like that. So it's really important for us to educate both patients and other doctors to educate providers on these real organic symptoms. So I think these kinds of webinars are really important. The other thing is I stress this to my patients, not just for bullous pemphigoid or PV patients I see,

but I tell everyone, sometimes you have to change doctors. Sometimes you have to find somebody who you really can jive with. It's hard but sometimes it's really important to find somebody who matches your needs. I think, sometimes there's not that many options, but I think that's really important. I don't get offended, I want my patients to find somebody they can really trust because it is a long term relationship. Another really good resource to talk to your primary care doctors because they're the ones who followed you as a patient long term. They know you at baselines. A lot of dermatologists meet you for the first time when you get this diagnosis and we don't really know what the baseline is. So it's really important for patients to talk to people who know them and so I think primary care is a great resource especially if they know you well. They know you year after year. Many of my patients in that acute stage, we don't really jive well because I don't know what their baseline is. They feel like I'm not communicating well with them. I've had one patient in the last five years that we could not communicate well for whatever reason. She didn't feel comfortable with me, then slowly over time we communicated better, and then she understood the process. We all have our own perspective, right? I always felt very comfortable in our relationship, but from her perspective, it was like, I didn't listen to her, etcetera, I kinda talked over her. But it was good feedback for me as well. When she told me this, we have a really good long-term relationship now, but when she told me this, I was like, Oh, I really need to think about how to treat some of these patients because I'm giving them a lot of information. Am I rushing it? Also, I didn't know her at a baseline. I didn't know her prior to her very stressful diagnosis. So it's difficult from both aspects. I can see it from both sides, but I think it is really important to educate our providers on these types of things our patients experience, which are really important because not having a restful night sleep doesn't help with anything. And we're giving them medicines that interfere with their sleep and their mood. So, we really need to be really cognizant that there's a real organic thing that happens. Then the other thing is, reaching out to people that you really have long term relationships with and building that long-term relationship, perhaps, with your doctor. That really is helpful. But I know there's no perfect solution, though. I'm really sorry you had to go through something like that. That doesn't sound good. I think we all can learn from that, right? So, to really give each other the time and the benefit of the doubt. But, yeah there's no perfect answer for that, but I think it's all too common, though. I don't think it's a unique experience that you had. I think a lot of people have had similar experiences, as well.

Becky: And I appreciate you giving your insight and sharing conversations that you've had with your patients, as well, and kind of giving each other the benefit of the doubt. We have a question come in, you mentioned Propranolol during your presentation, are there any reasons why a patient should not be able to take Propranolol or is there any pre-testing that needs to be done in order to get that medication?

Dr. Wei: We make sure their heart rate is normal. We make sure they have no normal blood pressure. So I've prescribed it for various things. People who give lectures will take it sometimes. I've taken it before big lectures, it really does kind of decrease the acute state of anxiety and that spike in your endorphins. So the idea is you give it to somebody who just experienced a really traumatic event. It will help calm them a little bit, it has a little bit of an

anti-anxiety effect because once your heart rate becomes faster your whole sympathetic system gets really revved up. The biggest thing is that you can tolerate it. As somebody who has taken it in the past, I have low blood pressure to begin with, so you really have to make sure that someone is appropriate and you start with a very low dose and they don't have any heart rhythm issues because you don't want to slow down someone's heart rate when they have other issues. So, that may be a question if you have heart disease to talk to your cardiologist or primary care about before you start taking it. But it generally is very well tolerated. If you're pregnant or nursing obviously, you cannot take it, unless it is medically, really, really necessary such as blood pressure is very high or whatnot because it can, I believe it is relatively contraindicated. And obviously, you can be allergic to any medicine that you take if you've never taken beta blockers before. Generally, the most important thing is, I always check if I give anyone medicines that affect their blood pressure, which I do in various conditions, I always make sure their blood pressure is in the normal range and that they don't have a heart rate issue. If they have a history of cardiac problems, I wanna make sure I talk to their cardiologists or primary care and if they're on other medicines that slow down their heart rate, or lower their blood pressure, I want to make sure I talk to the prescriber and just make sure they know that we're adding this additional medicine. I can't say I've given it for PTSD, the Propranolol but we definitely have given it for other similar conditions like, speaking anxiety or public speaking anxiety and flushing from rosacea. Mostly give it for those. So people tend to get really red when they speak so we tend to give them a little bit of beta blocker or some other medicines that lower their blood pressure because that's from you raising your heart rate and your blood pressure.

Becky: Great. Great information. Thank you. There was a question that you had mentioned that we patients can fall in and out of remission and need to go back on treatment. Was there any statistic or any correlation you found in your research that found the number of times that a patient fell out of remission. Did they have an increased incidence of PTSD?

Dr. Wei: That's a really good point. I think that's really important to look at. I don't have the answer to that. We didn't really look at that specifically. My hunch would be to say yes but at the same time, I feel like there's some kind of desensitization with that. I think patients are really always fearful of that first relapse but then when they have their first relapse, they realize it's actually not as bad as their initial diagnosis usually because usually they know exactly what's happening. They come in earlier or other doctors are continuously monitoring them, they know which therapy really helped them. Then usually they don't have to go on these high doses of steroids or be admitted to a hospital like they did the first time they had this diagnosis. So I think there's both. I can see both sides, if you have repeated relapses, I can see how that could be anxiety producing for some people. But I would hope, at least in my own patients, that having these relapses caught early and treated in a streamlined way is helpful in alleviating their anxiety because we know what you have and we have. I always tell my patients, in five years the treatment for this may be very different. There are so many things that are in clinical trials now and then there may be a cure. And we have good therapies for now. I tend to see that my patients have had milder remissions each time and they get longer and longer

remissions, because we're just getting better at treating it. And eventually, I hope there'll be a cure. So I think that's both folds but that's a great question. I think it needs to be studied. We need to look at two groups of people who've had no relapses and people who have multiple relapses. I imagine people with multiple relapses will have a higher percentage of PTSD. But I don't know. Yeah, that's a great question.

Becky: One other question. You had mentioned that we do have this cycle of cognitive distortions. Are there any tips or tricks that you share with your patients that help them to break that cycle earlier than later?

Dr. Wei: I give them all the information upfront. I give them the statistics, I think that's really helpful for people in having. If they bring up certain fears, I address it but if they don't, I give them the common things. Like these are your chances of relapse, and when do people tend to relapse. What percentage of people do not have any relapse in that time. And what we are going to do to monitor you for relapse, whether it's through blood work, whether it's to clinical monitoring and what we're going to do once you relapse. So just being very clear to people. I have patients with real PTSD, they scrutinize every single spot. For some of those patients, re-assuring them is not enough. I have to make sure there's organic and real things I measure to show them that they're not relapsing. A lot of times we have to biopsy to see if they're relapsing. We trend their antibodies in some diseases like pemphigus to see if they're coming back up and those are real things that people can look at and be like, okay I'm stable or I'm still negative. I've been surprised many times, patients know their bodies really well. I've been surprised that some people come in and I really didn't think clinically they're relapsing but they are. So it's just really good to kind of not be fearful of it I tell my patients, but be cognizant of it, that it can't happen. Try not to catastrophize and overly think of the negative because your experience will be very different the second time. It won't be like the first time, where nobody knew what was happening to you, and you had to go to multiple physicians, etcetera, etcetera. And usually it's not as severe. That's a great question. Other things that we talk about, just having good support I think is really important for a lot of patients. I have to look at all the different cognitive distortions that people do, but we're all guilty of it, right? We all kinda think sometimes the worst-case scenario, where we go like black and white, either this is going to be horrible or this is going to be good. Really life is in-between most of the time. I think it's really hard for people when they have a condition that could do this, I think that's really hard for people. But it's definitely helpful, for me at least, for patients that are more into the hard measures, I think it's really important to have concrete things they can look for and concrete things that we can measure and to have routine follow ups. I think those are really helpful things for people and have a plan for when they relapse. I think those are really helpful. I do think that having a chronic condition can have little peaks and valleys, and that it is stressful in and of itself. So you have to seek out help if you need it, if you feel like it's overwhelming psychologically then you have to seek your help. But if you are somebody who can use these techniques, there's many books on CBT. I'm definitely not an expert in it, but they're workbooks for it. I think, if you can use these techniques and really kind of restructure how you think about it, I think it is very powerful and very helpful. There is a phenomenon I see, it's not well written

about, that stress can trigger these really transient flares that tend to go away. We don't tend to worry about them as much if they just go away on their own, like if you get a sore for a couple of days and then it goes away. But I do believe that stress can contribute like I said in the one quick question. So any type of stress management will help patients in the long run to their overall health and to their autoimmune disease.

Becky: Great, Thank you. Martha is asking, what exposure techniques are recommended for the relief of PTSD?

Dr. Wei: So it depends on the event. Again, I'm not a psychiatrist. So basically for instance, if certain things remind you of the diagnosis, I think it's really important to not avoid it. So for instance, some people are really afraid of blood draws or really afraid of the infusions. So there's different techniques. I'm not going to pretend I'm an expert in it, but basically you have the same exposure and then a psychiatrist will use different techniques to calm your whole system so you don't get that huge adrenaline surge and like palpitations and blood pressure. So, I've heard of techniques in which you look at a pendulum. I've heard of a technique while you're being exposed to your trigger. I've heard of techniques of focusing on something very different during the exposure. But, basically, the idea is the more you're exposed to that stimulus, if you do it in a calm way, that helps you the next time so you won't need that distraction to be exposed. But again, I'm not an expert in it but those are some very basic to my understanding of how people do exposure therapy. I think there is probably some role of medications like things like Propranolol and anti-anxiety medicines in those exposures as well. I think the more common and the more important way that we can do this is using your own mind to calm yourself during those exposures.

Becky: Great. A lot of great information, and we really appreciate all that you've shared with us.

Dr. Wei: Thank you all for coming, before we answer the last question. I really appreciate it. This is an important topic.

Becky: Absolutely, and we appreciate you taking the time to research us and to highlight all of the information for our community. The last question was, you had mentioned that in your study of patients with PTSD had a higher tendency to have bullous pemphigoid. The question is, why do you think that is? Was it just the number of patients in your office? Or was there another reason you think?

Dr. Wei: This was a small study to begin with. So we found that patients with bullous pemphigoid had a higher percentage with PTSD. I really think it has to do with the fact that it

affects a much older population with a lot more comorbidities, so it's a sicker population. People with PV or pemphigus tend to be much younger, they tend to be middle aged. They tend to have a lot more social support whereas, people with bullous pemphigoid a lot of times are in their 80's and 90's and tend to be more isolated, with not as good social support. It tends to be harder for them to come to the doctors that have that good, kind of back and forth with their physicians. They don't have a lot of support. If you've ever talked to somebody with bullous pemphigoid, they have this diffuse, intense itching. That can be really mind numbing, anxiety provoking, and disrupts your sleep and every day, every moment. It's like having bugs bite you all the time. I'm super allergic to mosquitoes and when I have a lot of mosquito bites, it really disturbs your entire mood and everything. So I think many factors contribute. I suspect in our paper we talked about, I think it's because it's a population with a lot of comorbidities, with lack of social support typically because they are towards the end of their lives a lot of times. Not everybody, obviously, we see young people with a lot of social support with bullous pemphigoid. But we do see a lot of older people, because it increases with age. And the fact that this disease, when it's severe we have a tertiary referral, so we see the more severe cases. It's basically incredibly debilitating. Not to say that PV is not. PV is also incredibly debilitating, but in a very different way. When you have BP it's constant and it's really one of the worst symptoms I think you can have in any disease, is this nagging itch that you have. But I do think that we have to be especially careful with people who socially don't have that support, who are older, who have other health conditions, and who have really bad bullous pemphigoid. That's the population we should really be very cognizant that we're providing them support when they need it. But yes, that's a great question! We don't know why. But that's kind of how I would conjecture as to why that is.

Becky: We appreciate it so much. Thank you. That was a super quick hour packed full of a lot of great information. Thank you for taking the time out for us.

Dr. Wei: Thank you to the people that came. I'm really happy that you came. I know some of my patients came so thank you all.

Becky: Thank you all for being with us today. And a big thank you to our sponsors, Genentech, argenx and Cabaletta Bio for making today's call possible. Before we go, I do have a few announcements. Our next IPPF Patient Education Webinar on June 7th with Dr. Jun Lu to discuss "Nutrition with Pemphigus and Pemphigoid". You can register online and submit your questions to me, becky@pemphigus.org.

Also, the IPPF is beginning to plan this year's Patient Education Conference and working now to put together the agenda. This is an exciting opportunity for all of us to join in **Uniting Our Global Community** by bringing together patients, physicians, researchers, and community

stakeholders to help all those affected by pemphigus and pemphigoid. Stay tuned for more information on the Annual Patient Education Conference.

Do you wish there was a better understanding of our diseases by doctors and researchers? Do you wish there were more FDA-approved treatments and better treatments available? Well here's your chance to get involved and make these goals a reality - Join the IPPF Natural History Study today! The Natural History Study is a patient registry sponsored by the National Organization for Rare Disorders (NORD) and the US Food and Drug Administration (FDA). Your information is private, the IPPF Natural History Study follows strict government guidelines to assure patient information is protected. Your participation and the data will be used by the IPPF to help advance research, better understand the patient journey, find better treatments, and hopefully one day a cure. By sharing your journey and answering some questions, you directly have an effect on the future of all people affected by pemphigus and pemphigoid. So get involved today! You can find the Natural History Study by visiting www.pemphigus.iamrare.org

If you are interested in continuing to help support the IPPF and allow us to continue to provide free programs and services like today's webinar, you can become a healing hero. Healing Heroes fund the future of the IPPF community by making sustaining, monthly gifts to support our mission of improving the quality of life for all those affected by pemphigus and pemphigoid. No amount is too small, even a \$5 or \$10 monthly donation goes a long way and continues to allow us to provide for the greater good of our community.

The IPPF has a number of upcoming virtual support groups across the country. If you are interested in attending a meeting, please check the IPPF's Event Page to register for a meeting. Also, we are always looking to expand our support network. If you are interested in starting a support group in your region please contact me at becky@pemphigus.org. It's easier than it sounds to start a support group and you can help connect others in your area with other patients.

This call recording will be sent out with the survey following this call. Thank you all for joining us.