Back to Basics: Treatment #1 Prednisone Patient Education Webinar Transcription

Amethyst: Welcome everyone to the Back to Basics Treatment Webinar series for our first call on Prednisone. This call is now being recorded. I'd like to thank you for being on the call with us today and to our sponsors, Genentech, Principia Biopharma, a Sanofi Company, argenx and Cabaletta Bio for making today's call possible. Information is a key factor in treating and living with any condition. However, every patient's situation is unique. The IPPF reminds you that any information found on the internet or during presentations should be discussed with your own doctor or health care team to determine if it applies to your specific situation. Let's get started and let me introduce you to our speaker for our webinar today. Dr. Donna Culton completed her medical degree at the University of North Carolina at Chapel Hill. While there, she also received her PdD in the Department of Microbiology and Immunology where she studied autoreactive B cell development and regulation. She continued her training at UNC and following her dermatology residency she completed a postdoctoral fellowship applying her knowledge of autoreactive B cell pathophysiology to pemphigus by studying B cells and autoantibodies from her patients. Her laboratory generated a novel murine model of pemphigus allowing for a better understanding of mucosal pemphigus vulgaris. In her current position as Associate Professor of Dermatology at the University of North Carolina at Chapel Hill, she serves as the director of the Clinical Immunofluorescence Laboratory at UNC and sees pemphigus and pemphigoid patients from North Carolina and neighboring states in her specialty autoimmune blistering disorder clinic. She has served as an investigator in clinical trials in pemphigus, has contributed to consensus statement publications as part of International Bullous Disease Group and supports outreach, education, and advocacy through her involvement with the International Pemphigus and Pemphigoid Foundation. Welcome Dr. Donna Culton. Before we begin, I want to go over a few housekeeping slides… (Reviews housekeeping slides).

Amethyst: It is now my pleasure to introduce Dr. Donna Culton to answer your questions about prednisone. Dr. Culton I'm gonna go ahead and make you the presenter.

Dr. Culton: So, I'm excited to be here with you all to speak about prednisone and corticosteroids in general. I reviewed all of the questions that had come in in advance and thought it might be easier to put all of this in a presentation format. So the first 15 to 20 minutes are going to be a presentation that really presents the information in an organized fashion and answers, I think, a lot of the questions that came in. And then we'll have plenty of time for other questions that may not have been addressed by these slides. I'm just gonna start with a little bit of a historical context. My biggest fear, I almost declined to give this talk, because as clinicians and that use prednisone and systemic steroids, we know how powerful they are and we know how amazing they are and we know how horrible they are. And my biggest fear was that giving this talk would scare every patient, and they would never want to take steroids again. So I

started with this historical context, which is that in the time before steroids were available, systemic steroids, pemphigus and pemphigoid were almost uniformly fatal diseases and. We live in a world now where prednisone is available and so most of the problems, the patient deaths, come from side effects of the medications and not from the disease itself. But fatalities have gone way down, right? So I want to just take a moment to remind everybody that prednisone and systemic corticosteroids are amazing and horrible medications that are saving your life. So every slide that we get to that talks about new potential side effects that maybe you weren't aware of, I just want you to go back and remember that without this medicine these diseases could kill you.

Dr. Culton: So with that, we're gonna get started, and I'd like to start with just an approach to treatment. So, when you roll in for your first visit with a specialist who understands the disease process, and is ready to get you started on some medications, and we all know that there's a delay to diagnosis and people suffer for a very long time before they finally get to someone who understands the disease and is ready to get going on treatment. So most of the time at that first visit, you're looking for something that's going to provide you some relief pretty quickly. So we almost always start with a medication that would be fast acting to bring you relief right away. As many of you know there's other medications out there, they are shown by the line in green here that are more slow acting. They may take 2 to 3 months before they fully kick in and you get any relief. So, a lot of times we'll overlap a medication that's fast acting and have a quick onset of action and bring you some relief quickly, but we'll also start another medication that's more slow to act and ultimately, over time, as the slow acting medication starts to build up in your body, the fast acting medication can be reduced. The fast acting medications that we have available really are only two, prednisone or other systemic steroids and IVIg. All the rest of the medications that we use to treat these diseases fall into the slow acting medication category. In fact, the other term that physicians use to describe these other medications, we sometimes say immunomodulator therapy or immunosuppressive therapy. But we also call them steroids sparing agents because the whole goal is that we know that prednisone has all of these side effects so we don't want you to be on it for a long term. We hope that the other medication we start will spare you from having to be on long term steroids.

Dr. Culton: So, when we look at this risk benefit ratio of all the medicines which is always what we're thinking about for every patient, risks and benefits, the benefit of prednisone and other systemic steroids is that they work quickly, they're very cheap and they're easy to take. The other option is IVIg, which does work quickly, but it's very expensive and difficult to arrange because it's IV therapy so it's not like you can go pick it up at the pharmacy. There's some really wonderful benefits of prednisone and other systemic steroids. Now the risks are great. And can be divided into both short term side effects and long term side effects and we're going to go into all of these in more detail. But if you are there, at your first visit and I think everybody probably remembers their first visit, there's a lot to talk about. So, you're talking about the disease. What is the disease because other people have never even heard of it?How does it work? The pathophysiology, what's going on inside your body. The prednisone and it's risk factors and then some other medication we're going to start potentially, such as Azathioprine or

Mycophenolate or Methotrexate or Rituximab, they talk about all of that stuff too. So, I just remind everybody that that first visit is very difficult. So you may after this talk think, gosh, I started on prednisone and my doctor didn't talk about any of these side effects or only a few of them, and it's just because I think there's so much to talk about at that first visit. Our main goal is to get you better and know that your doctor is thinking about all of these things. And so, again, remembering that it's really tricky to get all of this lined up, make you feel comfortable with the treatment plan all at once.

Dr. Culton: So we're going to now move into prednisone basics. Prednisone is not the only systemic corticosteroid but it's certainly, I think, the most commonly used because of its availability. And again, it's cost effective so I'll focus mostly on prednisone. The dose is typically based on weight and so for most autoimmune blistering disorders, the dose is 1 to 2 milligrams per kilogram per day. Now, most of us do not think in terms of kilograms and so there's a conversion factor that we use. But the average person, let's say a 60 kilogram adult, or 132 pounds. So, 60 milligrams is a pretty common starting dose. We have some patients that are a little bigger so we'll start them at 80 milligrams and certainly if their disease is very severe and we need to move up to two milligrams per kilogram per day, we can even go higher. But higher doses come with higher risk of side effects. In general, prednisone is a general immunosuppressive medication, anti-inflammatory. Other medicines such as Rituximab eliminate your B cells. Prednisone is just a general immunosuppressive medication. So it's harder to pinpoint exactly what it's doing. It affects B cells. It affects T cells. It affects your entire immune system in a very general way that reduces your immune system or suppresses your immune system. It’s an incredibly potent anti-inflammatory medication as well and the dosing is usually oral. We had a lot of questions such as, what are the other ways prednisone can be given? The beauty of the oral form of the medication is that you can adjust it day by day if needed. You have control over how much you're putting in your body every single day. Other options include a subcutaneous or intramuscular injection and that we sometimes use in dermatology for other diseases, not so much for pemphigus or pemphigoid and it's only because you don't have any control. You do the injection into the muscle and it’s like a big wapping dose at first that slowly reduces over three weeks but you don't have any control over how that is happening right. Once you put in that bolus, your body does the rest to reduce it. And so we just don't have control over it. You'll see you know again based on that first graph I showed you where prednisone starts high and then we bring it down and the other medications building up, if the other medication is going to take effect for 2 to 3 months, there's no sense and bringing your prednisone down over three weeks because as many of you have experienced, if you are just on prednisone and the disease gets better, you stop prednisone, the disease comes right back. So we really need to have control over the timing of the prednisone coming down. So that's one of the reasons we favor oral dosing. You can do IV dosing. Sometimes that is done if you're in a hospital setting. Many patients with pemphigus and pemphigoid, their initial presentation is so severe that they have to be hospitalized. So sometimes we'll do IV formulations for that. Then intralesional, there were a few questions about that. It's essentially the form of prednisone, steroids in the shot form. But instead of doing it into the muscle, you do it right into the skin lesion. And that, I think, can be helpful if you have

a few focal areas that are just being stubborn. As many of you know, if you have a body full of blisters or lesions, injecting into each one would be ridiculous, you couldn't possibly do it. So I will do that sometimes but it's typically, if there's one stubborn spot that just won't heal up, and really what that is doing is addressing the inflammation that's in the skin right at that spot. And so, when we talk about all of these side effects from prednisone we're really talking about systemic side effects, and that would only be with either the oral form, the intramuscular form or the IV form. So if your doctor offers you an intralesional injection, that should not have these same systemic side effects because really just going into the skin.

Prednisone: So more prednisone basics. Prednisone actually mimics a hormone in your body called cortisol. Cortisol is critical for life and it's made by an organ, your adrenal glands. The way your body makes it naturally is a big spike first thing in the morning. So if you were to measure your cortisol levels throughout the day, you would have a big spike of cortisol first thing in the morning. And I say it's your body's hormone, that's like you get up and go. Cortisol also spikes when you're stressed, so the fight or flight response, cortisol will spike then as well. Prednisone mimics cortisol and so when you start taking very high dose prednisone your adrenal glands think why should I make the cortisol? I'm getting it in a pill form. So your adrenal glands, I say they go to sleep. They quit making cortisol and your body really is relying on the prednisone. To mimic the natural cortisol spike, we usually recommend people take their entire dose of prednisone first thing in the morning so you get that same kind of spike. We'll talk more about insomnia later as one of the side effects of prednisone but that's one of the tips to reducing that. Don't take your prednisone at bedtime. That's not the way your body would normally have its cortisol peak. So take it first thing in the morning. There were some questions about what is a safe dose of prednisone? Ideally, there is no safe dose. But the dose that roughly mimics the amount of cortisol your body makes daily is 5 milligrams a day. So a lot of times when people get down to 5 milligrams a day, I kind of breathe a little easier and say, okay you're back down to what your body would be making normally. Then a lot of people ask, how can I come off prednisone? What's the safe way to come off of it? Many of you know if you're on prednisone for longer than two weeks, we need a taper. We taper the dose coming down slowly and that's because, as we talked about your adrenal glands fall asleep, they're not making cortisol anymore. And if you stop abruptly, you have no prednisone and you have no cortisol and that could be a life threatening situation, we call it adrenal crisis, or adrenal insufficiency. The prednisone taper is critically important. I have a lot of patients that will say, oh, I just ran out of my prednisone but I didn't think you wanted me to be taking it anymore because I didn't have a refill. If you get into that situation and you've been on prednisone for more than two weeks and you're about to run out, you definitely need to talk to your doctor. Be the squeaky wheel. Call the nurse line one thousand times, whatever you need to do because you really should not be stopping abruptly. And again, that's to give the adrenal glands a chance to wake up and be like, hey we're not getting as much prednisone from the outside so that slow taper allows the adrenal glands to wake up and start making cortisol again on their own. Now some people, their adrenal glands never wake up and I've had a few patients where that happens, so they have to maintain on the baseline prednisone of 5 milligrams a day. If you get into that situation, your doctor will be aware of it as you get down on your prednisone taper

and we usually partner up with endocrinology to really assess whether that's happening by blood work and then come up with a plan for your long term prednisone needs. It's pretty rare but it can happen and certainly something to be aware of.

Dr. Culton: So before we launch into all these side effects of prednisone, I'm just going to tell you overall approach and strategies to minimize risk. So always your doctors should be going for the lowest dose possible and the shortest duration possible. So the only wrong plan in my mind is prednisone forever. That's never the plan. We call that prednisone monotherapy. I've had a few patients be referred to me and they've been on prednisone for 20 years and nothing else. That should never be the plan. The plan should always be we're going to use prednisone temporarily, whether that means months to years but there should always be a plan that is getting some other medication to do the work so the prednisone can be reduced and hopefully stopped. For each person we identify their specific risk of each of the side effects and focus on them. After this talk, you'll be amazed or horrified at all the potential side effects from prednisone. Just know that the one that you should worry about the most is the one you are at highest risk for and that's different for every patient. Then always be considering preventative measures, so we'll talk about that.

Dr. Culton: So the way I have organized the talk is each slide is going to talk about the risks, additional risk factors that might apply to you that should be taken into consideration and then possible prevention measures. So we'll start with diabetes, and I put diabetes plus because I threw high blood pressure in here as well. The risk we know is that prednisone can raise your blood sugars. So if you are already diabetic, prednisone will put your blood sugars higher even if you maintain the same diet that you had been on with excellent control with your same diet and medication for years. We throw prednisone in the mix and your blood sugars are gonna go higher. Some patients who don't have diabetes but may have a predisposition towards it, either a family history or pre-diabetes, some people have that, prednisone can unmask it. You can see elevated blood sugars in somebody who did not have that before and prednisone can certainly increase your blood pressure as well. So if you have a history of high blood pressure, you want to let your doctor know. And additional risk factors, as I said, is really just the history of either of these things. History of diabetes, or you have diabetes or you have hypertension, we need to be thinking about those things. Then prevention wise, it’s really coordination with your primary care physician. You can be your own best advocate, but you also want a doctor who's willing to talk to your primary care physician. If you don't have a primary doctor, you need to get one because the dermatologist can handle a lot, but they are not going to be prescribing your insulin. So we really need to have a team built around you to help manage these. And really your primary doctor is going to be the go to person for managing blood sugars and blood pressure. And it is difficult, I will tell you that because as you all know, prednisone doses may start high and then they go low and then you're flaring so they go high again. So for your blood sugars, it's not like they're going to start you on another blood sugar medicine that you're going to be on forever because prednisone hopefully shouldn't be forever. So it really requires a two-way communication, well three-way, you, your primary care physician and your dermatologist. I will say, just in the last week I had a patient who had a history of diabetes, well

controlled and we started prednisone. Gave a heads up that it was probably going to raise blood sugars and he messaged me that he had to go to the ER for a blood sugar of over 500. He also admitted that he had a cinnamon roll in addition to his meal that he was having. It's a scary thing when that happens, and of course, the ER doctors think, we need to get you down off that prednisone rapidly and I agreed, but safely. So we had to taper. You can do a fast taper or a slow taper, but a taper had to happen. He couldn't just stop at cold turkey. Again, lots of communication around diabetes. A blood sugar over 500 is scary in any situation but let's say your blood sugar is just riding a little bit higher than it normally does. What I try to remind people is that the real risk of high blood sugars that ride a little high come with a long duration of that. The changes from diabetes of your kidneys and the neuropathy and the retinal problems come when your blood sugars run high for years and years. So if it's riding a little high and we know prednisone is our temporary bridge to the other medication kicking in, it's okay to ride a little high. We don't need perfect blood sugar control as long as it's not in the scary levels. So again, a big discussion with all your doctors is what is needed there.

Dr. Culton: Infections. So we warn people about this all the time, there is a risk of increased infection when you're on prednisone because it suppresses your immune system. Additional risk factors would be if you have a history of other infectious diseases such as hepatitis, HIV, tuberculosis. And if you're on multiple immunosuppressive medications, which again, I just told you, we start prednisone then we start something else right behind it. Almost all of you, when you're on prednisone you are on something else. So higher risk of infection if you're on multiple medications that suppress your immune system at the same time. Then prevention, really is everything we're doing right now for COVID. Staying away from sick people, washing your hands frequently. There is a very small risk of a certain type of pneumonia and some physicians would recommend if you're over a certain dose of prednisone, you should be on an antibiotic to prevent that particular type of pneumonia. There's been a lot of debate among the doctors who treat pemphigus and pemphigoid about the risk benefit ratio, because that type of pneumonia is very rare, even in pemphigus patients on all of these medications. Less than 1%, 0.5%, probably even less than that. In all my years, 15 years of treating pemphigus and pemphigoid patients, I think I've had one patient to get that type of pneumonia. The medication that we use to prevent it and has its own risks, including a terrible skin reaction where all your skin dies, called Stevens Johnson Syndrome. So everything that we give you to prevent something else, could have its own side effects. So we're trying to think, what is the risk of that terrible Stevens Johnson Syndrome happening versus the risk of this pneumonia happening? Many physicians feel that it's best just to warn you if you start to feel sick, reach out to me, but do not recommend antibiotics to prevent that type of pneumonia. I just throw this out there because probably some of you were on medications to prevent that, and some are not, and there is no right or wrong answer. But it's a conversation with your physician, and it's a risk vs. benefit thing that you have to talk about there. Then I put COVID-19 on here. I know there's a ton of questions about COVID-19. The risk of COVID-19 tends to go up if you're on more than 10 milligrams of prednisone a day, which again, many of you are on higher doses of prednisone. Right now, a lot of people are asking, should I come down on my prednisone? Again, a very difficult conversation, but for you to have with your physician. If you are being

safe and staying at home and you have that option to really self isolate and reduce your risk of getting COVID, most of us feel like you should not be coming down on your medication. I tell people, the worst thing that happens is you have a horrible flare of your pemphigus or pemphigoid because you came down on your prednisone and then you end up in the hospital, which is the last place you want to be during a pandemic. It really is about what you can control to avoid getting COVID but the data suggests that your risk of a worse infection or getting the infection more easily, would be if you're on higher than 10 milligrams a day.

Dr. Culton: Okay, we're gonna move to bone health. The risks are bone thinning. A little bone thinning is osteopenia, a lot of bone thinning is osteoporosis. The real risk is that you're going to get fractures, compression fractures of the spine are one of the most horrible things and they almost don't happen any other way. You might fall and break an arm because you have regular osteopenia, but compression fractures of the spine are a unique thing that is often due to long term prednisone use. I've had a few patients who have had these compression fractures of the spine, and they're very painful. Another thing we worry about is a vascular necrosis which is bone death. That often happens around the hip. I have unfortunately had patients that have had that side effect as well, which often requires a hip replacement. Additional risk factors, osteoporosis is more likely in thin elderly white women and people who are quite sedentary. You want to build your bone health if you can by staying active, cardiovascular and kind of high impact activities are good. Then prevention wise, a lot of us will recommend calcium and vitamin D for bone health. Yearly bone scans, DEXA scans to see how your bones are looking. Then if the bones are continuing to become thinner, there is a type of medication called bisphosphonates that can help improve bone health as well. Bisphosphonates have their own issues and side effects. There's osteonecrosis of the jaw, which is death of the bones that make up your jaw that have been related to bisphosphonate. So I again, think about my patients, and I think, you already have a mouthful of blisters, maybe the last thing you need now, is your jaw bone dying. These are all of the risks and benefits that you and your physicians should be weighing out if you do already have osteoporosis.

Dr. Culton: Gastrointestinal side effects, the risks are reflux which can get worse and more seriously would be gastric ulcers. Additional risk factors, there's a lot here. If you're using any of the non-steroidal anti-inflammatories as well, such as the classic one ibuprofen. High dose ibuprofen, smoking, a history of H pylori infection, alcohol use, a history of gastric ulcers. Bisphosphonates can raise your risk of gastric ulcers and being over 65. So here you start to see that the treatment to prevent one side effect might give you another side effect. So it's very complicated. And then prevention wise, to prevent against GI side effects, we typically recommend proton pump inhibitors. I tend to recommend it more for my patients that might already have a history of gastric ulcers. Many people are already on these medications because some of them are over the counter. But they have their own side effects too. I think within the last five years there was a study that said, they may increase the risk of dementia. So risk and benefits, we always go back to risk and benefits.

Dr. Culton: Eye issues, the risks are cataracts and glaucoma. Glaucoma is increased pressure in the eye that you may not feel. Additional risk factors would be if you already have a history of cataracts or glaucoma before even starting prednisone, you should consider. Prevention is baseline eye exams and yearly eye exams, which many people are getting. Again, hopefully, you are not on prednisone for years and years but some people end up in just that situation because the other medications have not been as helpful. So if you are in that category, then having yearly eye exams is recommended. Someone asked a really good question which is, if you get cataracts and you've had cataract surgery and you're on prednisone, can you get cataracts again? I actually had to look that up because I wasn't sure but it seems that you can. And so I think if you are in that situation where you've already had cataracts or had cataract surgery, you definitely want to be having eye exams with your ophthalmologists.

Dr. Culton: Mood and cognition, this probably is the biggest one that people bring up to me at their visits. The risks and what we look for, irritability and insomnia. Then things that are more severe, like true mania or even psychosis. So I've had that happen to patients where they start seeing things that aren't there, talking crazy out of their head. Their spouse is like, there is something serious here. Then, probably more common is brain fog. Thinking you can't think straight or that your brain is just not clicking along like you used to. Additional risk factors that might predispose you to one of these would be a history of anxiety, depression, underlying mental health disorder such as you have a history of depression or bipolar disorder. Certainly, that should be taken into consideration and then if you are older. Truthfully, the sad truth around this one is that there's no real prevention strategy here, it’s just close monitoring. So if I'm starting high dose steroids in patients who are in their eighties, I say, you shouldn't be living alone. We need somebody around you that can monitor. If you have a history of depression, make sure that you have your team of support around you, your personal support team such as family members, friends who can check on you to make sure that you're doing okay.

Dr. Culton: Then other things that really didn't fall into any of those categories, but can definitely happen are muscle weakness, we call that prednisone induced myopathy. Acne and folliculitis, those are the effects we see on the skin. Skin tearing, I didn't put that, but a lot of patients will have skin tearing with very thin skin that tears very easily. Weight gain and water retention. So prednisone increases the appetite. I have patients that cannot pass the fridge without opening it and getting something to eat when I'm on prednisone. But even if you've never opened the fridge and if you never put another extra thing in your mouth, then you will have some water retention. So the weight gain is not only increased food intake, but it's also water retention that happens. Then I put hair loss because there were some questions. So certainly, I think prednisone can lead to some hair thinning that in some patients is more severe than in others.

Dr. Culton: So I am just going to spend a little time talking about vaccines. The risk is really, prednisone like all other immunosuppressive medications may limit your ability to fully respond to vaccines. The key number there is if you're on a prednisone dose over 20 milligrams for over

two weeks, which I would venture to say most people at the beginning of their treatment would fall into that category. So additional risk factors would be, again, if you're on other immunosuppressive medications. So prevention is, I think, silly a little bit, but it's, get all your vaccines before you start the prednisone. Well, that's easier said than done, right? Because when you come in for that first visit you are like, I want to feel better now. Often patients are not able to or willing to wait a month to get vaccines and then start the prednisone later. The timing is 2 to 3 weeks after your vaccines, you can start prednisone. So essentially, you would have to go see your primary care physician to get all your vaccines and then start the prednisone after that. Then there are situations where you are already on the prednisone and the vaccine is due, what do you do then? Really, people on higher doses of 20 milligrams of prednisone should not take live vaccines but protein based vaccines or the new M-RNA based vaccines are safe for you to take. It's just your body may not respond to them fully. They won't cause you to get the disease, but you may not make as much of a protective immune response as you would have otherwise. So specifically related to the COVID-19 vaccine because I know there's a lot of questions around that, as you know, patients on immunosuppressive medications were excluded from the clinical trials. So we really don't have a lot of data. The data suggests that again, it's safe for you because it's not a live vaccine, but we don't know how you're going to respond. And again, it probably depends not only on your prednisone dose but on the dose of whatever other medications you are on. They are all unique and we have no idea is the bottom line. I've put here, if possible, if you could reduce your prednisone dose to less than 20 milligrams a day, that would be ideal. You would have to do that before you get your first dose of the vaccine and then again, maintain that until a couple of weeks after your second dose of the vaccine. So, it's a pretty long time. Again, in my opinion, the worst thing would be if you did not do that safely like you just dropped straight down from a very high dose to 20 and your adrenal glands are not doing well that could be bad news or if you have a horrible flare up of your disease, that would be bad too. So, do this in combination with your physician. Do not take this into your own hands. But if you feel like your disease is actually doing pretty good and you would like to try to taper down, that's definitely something that should be considered and talked about. Then, I put this last part in there, and I'm just going to spend a little time talking about this. Right now, the CDC is not recommending that if you are immunosuppressed and you get the vaccine that you then get antibodies drawn after the vaccine to see if you made antibodies. How do we determine then if a vaccine has been effective is hopefully if you don't get COVID after you get the vaccine. But a surrogate marker is, did you develop antibodies? So, right now, the CDC is not recommending that patients have antibodies drawn. And I respect the CDC a lot, but I also remember when they didn't recommend masks at the beginning of COVID. I think that we can also just be thoughtful about this. So many physicians who treat patients and have patients on immunosuppressive therapies are considering drawing antibodies after you get the second dose of the vaccine to see if you made antibodies. Now, the tricky part of this is you can just roll up to CVS and get the antibody tests they have there because most of the antibody tests available right now test against a part of the virus that you would only have antibodies for if you had actually had COVID. It's called the nucleic capsid test, and that's the one that's widely available that you would go get if you thought you had COVID and you just wanted to see, did you have it? Maybe you have antibodies to this nucleic capsid if you had COVID. But for the vaccine, it's to the spike protein. If you're going to potentially have these antibody tests

done after your second dose of the vaccine, the timing would be probably 3 to 4 weeks after your second dose and it should be an antibody measurement that is testing against spike protein antibodies. Lots of doctors are thinking, we need to know this information for our patients. So there's lots of studies going on right now looking for these antibodies after immunosuppressed patients have had the COVID vaccine. I would say, just ask your physician if there's any studies they know of and then also, it can be done as a standard of care. I'll provide some information to the IPPF so if that's something that you're really interested in and your doctors like, “I don't know which antibody test to order,” we can put that information out there for the IPPF as well. The last thing to talk about though is, let's say your antibody test comes back negative, what can be done? Right now, there's nothing. There's no guidance on what happens if you got your COVID vaccine and you didn't make antibodies. That can be really frustrating. I just say that because then I think there's people out there who are doers and they're like, “okay I didn’t make antibodies should I get a booster shot?” We don't have any information about that right now. So that's what hopefully some of these studies will provide the information needed to be able to know what to do next. But right now there's nothing to offer you, except to say, just continue to wear your mask and be safe, which, of course we're recommending anyway. Then, there's a whole other side of the immune system. We talked about the T cells. The M-RNDA vaccines give B cell and T cell response. So even if you don't make antibodies and you don't have the B cells, you still may have a T cell response that's protecting you and that's just harder to measure. So even if you don't have antibodies doesn't mean that you don't have any protection at all. So I say all that because it is a test that can be done but the interpretation and what to do with the results afterwards are very tricky. Okay, that was longer than I meant talk about that. So I'm getting towards the end here. So learning more there is a new scale that's been developed called the Glucocorticoid Toxicity Index or the GTI and it is a combination of patient questionnaire and doctor questionnaire that really is meant to capture the side effects from steroids and this is being rolled out across the world really right now. There's a study looking to validate the GTI as a way to capture the side effects of prednisone. So that's exciting that we're paying more attention and really trying to go after capturing these side effects and how they impact patients. You might say, what side effects should I be most worried about? And I say your personal risk factors. So, we talked about the baseline things we're worried about but then if you have these other risk factors, that's really what puts you at higher risk so that's something to think about and talk with your doctor about. I would also say how common and how serious these risks are. We talked about a special type of pneumonia that some people get and it's so rare. It can be very serious, but if it's so rare, is that something you should be worried about? Maybe, maybe not, depending on your personal risk factors. My husband is an emergency medicine physician, so when I was preparing this talk, I asked him, what do you worry most about? What do you see in the ER? And certainly, knowing that one of my patients had just been in the ER with high blood sugars, that was one, but he was really concerned about gastric ulcers. I said, in all my years, I have never had a patient have a gastric ulcer from prednisone. So maybe I'm just lucky. But that was his thing that was at the top of the list. Other people, it's going to be their bone health or their eyes. I think it really is a “you” kind of thing about, what are your risk factors that you bring to the table, plus, what prednisone is going to be doing. Then always, how do we know if things are working? If you're getting fewer or no new lesions. Is prednisone doing its job? That's what we

look for. But I have some patients that just do not respond to prednisone. You can throw all the prednisone in the world at them but it's not doing anything. So, why should we be subjecting them to these risks? And in that case, we taper down. It's rare, but it happens. We call it steroid sparing again, can we taper the prednisone and the disease stays quiet? That's how we know if the other medications are working well.

Dr. Culton: When to switch treatments? I always say, the treatment should not be worse than the disease. So, I've had several patients that come in, and they're pemphigus is looking awesome, or maybe not totally perfect, but so much better. And they're like, I can't sleep, I'm irritable, my blood sugars are through the roof or shaky and jittery and I would rather have my pemphigus be more active than have these side effects. That's something that you need to advocate for yourself. And really, it's a personal decision. Some people say, no, I feel these things and they're awful, but like I can handle them a little bit longer because I don't want the pemphigus or pemphigoid to come back. But if you're on the other side where you're like, I cannot handle this. You tell your doctor and come up with a plan to taper. So that is the end. And I am sorry I took a lot of the time talking but I thought it was a useful way, again to share all this information. And now I'm gonna let Amethyst ask some of the questions that I'm sure people have.

Amethyst: Great. Thank you. That was a lot of great information and we had many questions that came in before the call, but we did have a lot of questions coming in fast and furious throughout. So I'm just going to get started here with a couple of questions about being on low dose prednisone. TJ said that she's been tapering by 0.5 every 2 weeks and right now she's at 2.5 milligrams, does it make sense to take a prednisone dose less than 5 milligrams?

Dr. Culton: So that is tricky. In general, less than five milligrams is, I would say homeopathic dosing, it's like barely anything at all. But I have had some patients that I say, that the last five milligrams is like the glue that's holding it all together and you stop it, and it all comes back. That happens rarely, but it happens. In my opinion, the only time to come down lower than 5 milligrams is if you're at the tail end and you need to taper off completely, you can go down to 2.5 for a few weeks. If no new blisters or lesions are coming you can stop, or you can do an every other day taper to get yourself off that last little bit. Really, at that point, you're trying to make sure your adrenal glands are woken up. After the 5 milligrams, that's what you're doing there. So people who have adrenal insufficiency, we actually do go down by like 1 milligram however long because even 1 milligram difference could be the difference between them going into this adrenal crisis.

Amethyst: Great, thank you. Mo also said that he's been on 5 milligrams for over three months. His skin is good, but his antibody tests show that he's not negative. Does he need to

stay on 5 milligrams for long term? And if so, what are the long term effects of being on 5 milligrams of prednisone?

Dr. Culton: Yeah, this is a tricky one. So, one question would be, is he on other medications? Is there a secondary medicine in addition to prednisone? I do have patients that get exactly to that point 5 milligrams and if they go less than 5 milligrams, their skin starts getting active again or their mouth but as long as they stay on 5 milligrams everything's fine. As doctors, we're always trying to get you off that last little bit but if the thing that we're going to offer you in the place of 5 milligrams of prednisone is riskier, then maybe you choose to stay on the prednisone. So, if we're about to offer you say cyclophosphamide that can have all these terrible side effects and you're like, the risks of each of those if I'm weighing them out, the risk of 5 milligrams of prednisone is less than the risks of this other medicine then you might choose to stay on 5 milligrams. I do tell patients that it's not ideal for you to stay on 5 milligrams of prednisone a day, but it's also not ideal that you have this horrible disease. As long as you understand the risks and you feel like you're able to make an informed decision for yourself, then, I think again, that's something you have to answer that question, but ideally we get you off at the 5 milligrams, but if the ways to get you off a riskier than maybe we just stay.

Amethyst: Great, thank you and to piggyback on that real quick and I think you mostly answered this but Barry said that he's been on 5 milligrams of prednisone for 25 years but he's in remission. So, what are your thoughts of staying on that?

Dr. Culton: That's a, that's a scary thing. If you're in remission, I would take a deep breath and hold your dermatologist's hand or whoever your doctor is and try to make a plan to come off of it. Because again, you don't know unless you try, if you come off of it, maybe you really are in a remission where you don't need medication. I say that, not knowing the other details about the case. Because, I have a patient who has adrenal insufficiency, and she has to stay on 5milligrams a day, or bad things can happen. So I don't know if that's the reason why the 5 milligram is being maintained, but I do think if otherwise, there's a remission, it is possible to try to come off of that last little bit.

Amethyst: Great, thank you. Real quick, going back to the antibody tests, Eric just wrote in and just said, what is the antibody test, if you could explain that?

Dr. Culton: You mean the antibody test against COVID to see if you responded to the vaccine, maybe?

Dr. Culton: Oh, I don't know, he did not say. Eric, if you want to write back into the chat box real quick. Are you talking about the antibody test for COVID?

Dr. Cutlon: Because, we do the titers for pemphigus often. The antibody test for COVID, again, there's two types of antibody tests available. There's one to the nucleic capsid protein and you would only have that antibody if you actually had COVID. Then there's antibodies to the spike protein and that you would have those antibodies if you'd had COVID but you also have those antibodies if you had the vaccine. Let's say you're a normal person, you're not on any immunosuppressive medications and you get your COVID vaccine, you make antibodies to this spike protein and they're supposed to be protective. We don't know how long they stay in your body. These are just some of the caveats to this testing that we have, not every test is a perfect test or answers the exact question we're asking. But in general, you want an antibody to the spike protein. And the ideal timing is 3 to 4 weeks after your second shot. And if it's negative, we're like that's a bummer, but there's not anything we're really going to do. If it's positive, we give a little cheer.

Amethyst: Great. Thank you, Sorry, Eric just wrote and he said he was referring to the titer test. He said that he had a biopsy, but I don't think he's had the titer test.

Dr. Culton: Pemphigus and pemphigoid are antibody mediated diseases, so oftentimes we will check the antibody levels in the blood. We do that at various times during your disease course. Often at diagnosis, will have that test done to see what you're starting with antibody level wise. The other time is, if you are completely clear of lesions and we're about to stop your medications, sometimes we will draw that test because there is a correlation, studies have shown all this, if you have still antibodies in your blood, there's an increased chance that you would flare after stopping the medications. Whereas if you are totally clear and you don't have antibodies in your blood, that's a better sign that you can stop the medications and not have a big flare up.

Amethyst: Awesome, thank you. Erska wrote in and she says that she has two ulcers that have been persistent for a few months behind two of her molars. She's tried dexamethasone rinse so far, but would a steroid injection be applicable in her case?

Dr. Culton: That's a great question. That place particularly, I kinda made a little face when you said that, because it's a really hard place and for a lot of people that's like their most stubborn spot, right behind those molars. I do think it's one of the last areas to clear up for a lot of people. Dexamethasone rinse is a great option to get way back there but you certainly could consider intralesional injections there. Intralesional injections are not for the faint of heart. It's a shot into the most sensitive ulcer area anyway, but I have plenty of patients that do it and it

can be really helpful. So you can try it and if you don't get a good response or if it hurts like crazy, you can say I will never do that again as well. I think it's worth testing out just to see how it goes. Historically, we would always say it works better for pemphigoid lesions than for pemphigus lesions, but I think there's more data coming out that it could at least be considered for pemphigus as well.

Amethyst: Great, thank you. And she just wrote in as well and that would be directly into the ulcer, correct?

Dr. Culton: It's like right around the edges. It's not into the center of the sore spot but kind of around the edges. Some doctors are quite comfortable doing this in the mouth. I do injections in the mouth often and I do biopsies in the mouth. You need good lighting. You need good retraction, there's things that you need to be able to do that safely. So if your doctors like, yeah, I really think we need to do that. I add one patient who I had been following for years and her most stubborn spot is actually on the palate pharyngeal arch, it's right before the tonsils. It's a really hard area and very sensitive. It's right near your uvula, which is part of your gag reflex, and I was like, I'm not sticking the needle spot. So, we sent her to ENT and they were able to do the intralesional injections there and it was very helpful for her. So if your doctor doesn't feel comfortable, maybe partnering with another physician who does feel comfortable would be an option.

Amethyst: Great. Thank you. Madeline just wrote in too about those intralesional injections. Do you have to have multiple injections? Or will one clear it up? Or is there a frequency that you do those?

Dr. Culton: So in general, in dermatology, these injections will only last about four weeks. So you do one injection and then like if we were going to keep doing injections on something, we would do it every four weeks until the thing is settled down. I do find for a lot of patients if we can just get that ulcer cleared up, maybe it takes 1 or 2 injections and then you're done. I wouldn't ever imagine that you would do it repeatedly for months on end. If that's the case you're in, we probably need to be looking at a different systemic medicine. But, I will sometimes offer it to see if we get that one last spot to clear up. And we might do it 1 or 2 times before we give up on it.

Amethyst: Great, thank you. Eric wrote in before the call and asked, is there a specific protocol that you follow for first line treatment? When a patient comes in, is prednisone the first drug you prescribe? And then after that, do you have a specific step that you work through?

Dr. Culton: In general, yes. I would say most every doctor who treats pemphigus and pemphigoid use prednisone first line. We all wish we had something better but we just do not. So it is, for better or for worse, the mainstay of first line treatment. But we're all right away trying to think, what's the next thing we're going to do? For a long time, we didn't have Rituximab,so we were using Azathioprine or Mycophenolate. Then Rituximab came along, and initially, and now I'm making myself seem old, but initially when it first came out, we were reserving it for the patients who had failed everything else. And over time, and with more studies, now most of us are using it first line. That was where we were right before COVID and then COVID came and so it really shook things up again, because, as you know Rituximab I would say is my first line treatment. To be that green line, the steroids sparing agent to help you get off the prednisone and most of us who treat these disorders feel that same way. But with COVID, when you have Rituximab it wipes out your B cells. That happens immediately and the Rituximab leaves your body pretty quickly, but the effects of it, the B cells don't come back for at least six months. So you are automatically immunosuppressant now for six months and there's nothing we can do to make your B cells come back faster. We know that it probably is longer than six months. They start coming back at six months, but certainly they're not back to their normal levels. So when COVID came, we thought, well maybe we shouldn't be giving Rituximab right now because you can't turn it off. The other pills you stop taking and they'll get out of your system faster, but with the Rituximab you can't undo it once it's done. So, we kind of reverted back to some of our old ways. Now, I still have patients saying, no, I want the Rituximab. I know how to keep myself safe, I'm not going to leave my house. So, it really was a very one-on-one conversation with each patient about where they were with all of this, because we still feel like Rituximab still has the highest chance of inducing a remission, a durable remission. And the faster you start it, the better. Meaning, earlier in the course of disease. So COVID shook everything up and then we kind of fell into a new normal. Then when the vaccines came out, we had to go back again. Do you want your Rituximab now? Do you want to get your vaccine and then get your Rituximab? If someone says they had Rituximab in December, we would recommend you don't get any vaccines because they wouldn't be effective, not because they're harmful. You wouldn't get a vaccine until six months later, and some patients are choosing to wait six months and then get their COVID vaccine, and other people are saying, no, I want it now. I fully acknowledge that, I don't have any B cells to respond, but maybe my T cells will be responding. There's a study right now at UNC for patients who are in that second category, that say, I want my Rituximab and I also want my vaccine. Then we will collect their blood and look in the lab to see about their B cell and T cell responses. Again, I use UNC as an example, but these studies have to be happening at other academic institutions, because we're all asking the same question.

Amethyst: Definitely. We get a lot of questions about that, so that’s great. You talked a little bit about the risk/benefit and things like that. Are there any people who should absolutely not take prednisone?

Dr. Culton: In general there are no absolute contraindications. I have patients who say they have an allergy to prednisone. It's interesting because we give prednisone to people who have

severe allergic reactions. So when people say, allergy, I really tried to get what they are talking about because maybe they got psychotic and that's somebody who I would probably not give prednisone ever again. That's scary, you don't want to do that. Or somebody who has what we call brittle diabetes, which is type one diabetes where their blood sugars are just so erratic and you can send them into diabetic ketoacidosis. Even a little bit of prednisone, those patients I probably would not use prednisone on. But almost anybody else it really is kind of that risk benefit ratio. And you just want to make sure that if something bad is happening to you you can get in touch with your doctor pretty quickly. And they're going to take you seriously, and listen to what you're saying, and help you talk through it. It was interesting, because when putting this together and looking at side effects of some of the other medications that we sometimes recommend, like the proton pump inhibitors for GI prophylaxis. They can cause nausea and vomiting, headaches, all this other stuff that often gets attributed to prednisone. So I think sometimes all these medications people are getting prescribed at the same time is actually hard to know what the side effects are from. In general, I would say for somebody who has horrible diabetes, sometimes we just can't avoid prednisone in them. There's no absolute contraindications, but your doctor has to know you pretty well, and know what you've been through and what your risk factors you bring to the table are.

Amethyst: Great, Thank you, Deb wrote, and she said that she has pemphigus gestationis. Is she able to use prednisone and corticosteroids during pregnancy and while breastfeeding?

Dr. Culton: Yeah, that's a great question. So, prednisone for all its horribleness that I just described is actually the safest medication to be taking during pregnancy. All of the other medications are considered to be too high risk to take during pregnancy. Now, there's some that are better than others. In Rheumatology, patients who have severe, systemic lupus, Azathioprine is preferred over Mycophenolate. There's some medications you absolutely should not take while you're pregnant Methotrexate and Cyclophosphamide, but prednisone is actually pretty safe. So it doesn't mean it's without risk. And there is a risk for having a baby that has a larger size coming out. And certainly, having blood sugar issues when the baby's first born. There are risks of it, but it's still considered the safest medication during pregnancy. I've had several patients with pemphigoid gestationis and prednisone is the goto medication. That's a unique form of pemphigoid and you hope postpartum sometimes people have a flare, but ultimately you're not with pemphigoid for life. So again, some of these risk factors, the risks are bad but it's short-term. Hopefully during the pregnancy and then afterwards you won't have to be on prednisone for longer. It is definitely a special form of pemphigoid that requires coordination with your OBGYN as well. But yes, safe during pregnancy and breastfeeding, but again, making sure all the doctors know what's happening.

Amethyst: Great, thank you. We had a few questions come in about topical steroids and I know we're at the top of the hour.

Dr. Culton: I'm not in a big rush.

Amethyst: Great, thank you! So Paul asks, is it dangerous to use Clobetasol everyday on your face and temple area. They're worried about skin thinning.

Dr. Culton: Yeah, it's a good question. So the standard party line in dermatology is you should not use Clobetasol that is on your face and I kind of giggled a little bit when I heard that question because my husband has a completely separate condition, not pemphigus or pemphigoid but when he found Clobetasol, he calls it the good stuff, he uses it on his face. I can tell because we have the ointment and it is a little shiny, and I tell him, you put on your face, again, didn't you? Anyway, we do worry that it's a little too strong for daily use on the face. So I would say temporarily, maybe for a week or two, that's something that can be super helpful. But ideally if you're having to use it every day for longer than that, we probably need to be thinking about a different medication. Now you might say, well, if the other medication is a systemic medicine that suppresses my immune system and has all this other stuff that can happen, do I care about a little skin thinning? Maybe you don't. Again, it's a personal decision that you're thinking about, but skin thinning can definitely happen. Skin tears we worry about it a lot. I think it's a little bit of a contextual question. Ideally you don't use it on your face every day for longer than two weeks, but again it's about that risk benefit. So if the next treatment option is something way worse, maybe you keep going with it. And try to minimize it. We always say the Clobetasol is not meant to be like to keep the spots away. It's like that game at the county fair, whack-a-mole, where the thing pops up and you take the thing and smash it down. That's how Clobetasol is supposed to be used. It should never be used to keep new spots from coming.

Amethyst: Awesome. Janet asks, does applying topical steroids 2 to 3 times a day on 30 to 40 lesions, also carry prednisone side effects?

Dr. Culton: That's a great question. So topical steroids, we didn't really talk too much about here, but there was a study done out of Europe, where they compared systemic steroids, so prednisone by mouth versus topical steroids, and this was in pemphigoid and they said full body application, definitely greater, I don't tend to think about so many is like number of lesions, but body surface area. So if it's pretty much over 50% of your body surface area you're putting Clobetasol on several times a day, you can get systemic absorption. Mostly thinking in Europe they have like hospitals that can do these topical steroids or there are family members and patients who are willing to do it. In the US, I can't imagine any of my patients slathering up in Clobetasol which is ridiculously expensive, getting enough, and doing that several times a day. And it's only probably working by systemic absorption so why not just take it and a pill form? But their data suggested that the topical steroids were safer than the pill form. So you are getting systemic absorption but it's probably not to the same degree, as if you were taking it by mouth. Now, if you're talking 40 spots, one that's all I work for you, so good job to keep up with

that, but I don't think it's going to be the same level of absorption. Now, three times a day, we usually say 2 to 3 times a day is the max, you should be doing any topical steroids. Again, you might ask, is there another treatment option that would allow you not to have to do that? One, for the burden of having to do it, but for safety because of absorption of it.

Ametyst: Great. Thank you. Jennifer wrote in and she said that she has pemphigoid but she's not taking any other medications other than topical. Should she worry about taking the vaccine? She's under the impression that the immunosuppressant medications make someone high risks for COVID but she's not quite sure what category she falls into.

Dr. Culton: There's been a lot of great discussions and calls among a lot of the experts that treat these disorders and the general feeling is that just having one of these diseases in and of itself does not put you at higher risk, it's the medications we use. And it's mostly the systemic medication. So topical steroids should not put you at higher risk for getting the disease. So again, I am recommending all my patients get the vaccine. Some of them are gung ho and so excited and can't wait. Others are a little leery and want to think about it. Again any vaccine as a personal decision. But I do think it would be safe for her to get the vaccine if you're just on topicals. One, you're not really at higher risk but two, the vaccine should be fully effective.

Amethyst: Great. thank you. Well, thank you so much for hanging on with us for a few extra minutes today. Everything was so educational. I know, I learned a lot today. That was definitely a very quick hour, so thank you so much. And then I'd also like to give everybody a huge thank you for joining us today and a thank you to our sponsors Genentech, Principia Biopharma, a Sanofi Company, argenx and Cabaletta Bio for making today's call possible. Before we go, I do have a few quick announcements. We have a lot going on in our community within the next few weeks and I'd like to share that with you. Our next webinar in the treatment series will be on Wednesday March 3rd to discuss IVIG with Dr. Kyle Amber, Assistant Professor of Dermatology from Rush University Medical Center in Chicago. Registration will open tomorrow.

Monday kicked off Rare Across America, an event that the IPPF is participating in to spread awareness of pemphigus and pemphigoid and advocate for legislation that helps the rare disease community. The IPPF will be participating in Rare Across America at the end this month. This week is selfie week and we want to see our strong community! Take a picture of yourself and post it to social media with the hashtags #RareAcrossAmerica202, #healourskin, and #EveryVoiceMatters.

Are you interested in helping accelerate research? The IPPF is participating in GlobalSkin's Global Research on the Impact of Dermatological Diseases project. GlobalSkin is calling on adult dermatology patients representing all diseases/conditions to participate in the study. By

participating in, you will be helping to design a new and credible measurement tool that fully explains the impacts and challenges that people living with dermatological conditions experience. Studies like this are a great way to help advance medicine and treatment for pemphigus and pemphigoid patients. If you are interested in participating in the survey, please contact Marc Yale, at marc@pemphiugs.org and I will send you the link to participate in the study.

The IPPF has been looking towards the future and how we can continue to help you and our community. We need your help to grow our community of Healing Heroes. 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.

If you have not registered for the IPPF's natural history study we encourage you to do so. The IPPF Natural History study is a patient registry sponsored by the National Organization for Rare Disorders (NORD) and the US Food and Drug Administration (FDA). You can register today at www.pemphigus.iamrare.org. This online data system collects, stores, and retrieves patient data for analysis in research studies. The more data we can collect, the better the information we can give to researchers, and our doctors like Dr. Culton, the sooner they can find better treatments, earlier diagnosis, and one day hopefully a cure!

Lastly, If you have a question that didn't get answered on the call, or have additional questions please e-mail Becky Strong, at becky@pemphigus.org, or call (916) 922-1298 x:105, and we would be more than happy to help.This call recording will be sent out and also posted on our website following this call and also a survey as well.Thank you so much for joining us today, Dr. Culton. I hope everyone has a wonderful rest of your afternoon.

Dr. Culton: Thanks for having me.

Amethyst: Have a good day everyone. Bye.