

Back to Basics: All About Pemphigus- Patient Education Webinar Transcript

Amethyst: Welcome everyone to the “Back To Basics- All About Pemphigus” webinar, this call is now being recorded. I'd like to thank you all for being on the call with us this evening 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 healthcare team to determine if it applies to your specific situation.” Before we begin, I'd like to take a quick poll to see who we have on the call with us this evening and how long you've been diagnosed with pemphigus. So, if you can take the poll, and while you're doing that, I'd like to introduce you to our speaker for this evening.

Dr. Neil Korman is a Professor of Dermatology at Case Western Reserve University in Cleveland, Ohio and is the Director of the Dermatology Clinical Trials Unit in the Department of Dermatology at University Hospitals of Cleveland. In addition, he serves as the clinical director of the Murdough Family Center for Psoriasis. Dr. Korman earned his medical degree and doctorate in biomedical engineering both at Case Western Reserve University. His postdoctoral training included a medical internship and dermatology residency at University Hospitals of Cleveland and an immunodermatology fellowship at the National Institutes of Health in Bethesda, Maryland.

Dr. Korman holds subspecialty board certification in dermatological immunology/diagnostic and laboratory immunology. He is a member of the American Dermatologic Association, the Psoriasis Expert Resource Group of the American Academy of Dermatology, and an Emeritus Member of the Medical Advisory Board of the National Psoriasis Foundation. Dr. Korman is the founding Director of the Regional Center for Immunobullous Diseases and has published over 200 articles in peer-reviewed literature and since 1997, he has been the principal or co-principal investigator in more than 175 clinical trials.

Amethyst: I am going to close the poll now. Thank you all for taking that, and we're going to share the results here. And it looks like a good majority of you have had pemphigus for less than a year. So this is a great way for you guys to learn more about the disease. And then another good portion of you have had it for 10 plus years, and 1 to 3 years. So thank you all for taking that poll for us. And before we get to our questions, I'd like to go over a few housekeeping slides. (Reviews Housekeeping slides...). We've received many questions before the call, so we will try our best to answer as many questions as we can. Now, it is my pleasure to introduce Dr. Neil Korman to discuss all about pemphigus. I'm going to turn it over to you Dr. Korman.

Dr. Korman: So I've got a pile of slides here that we're going to try to get through and I suppose, Amethyst what do you think, can we take questions in the middle or are we going afterwards or what are we going to do here?

Amethyst: That is up to you, normally, we'd like to do them towards the end.

Dr. Korman: Let's try to do that. But, I'll leave it up to you. You're the MC. So, you get to make the call if there's some burning question that you think is important and relevant while I'm doing it, I'm okay with that too. So pemphigus, it's a hard disease to even pronounce, right? A lot of people struggle just to name that thing, right? So it's rare, a very important thing to say, autoimmune blistering disease of the skin and the mucous membranes. The mucous membranes are things like the mouth, the nose, the throat, even the genitals are mucous membranes. And the fact that it's rare makes it really tough for almost every non-dermatology physician that any of you have ever seen and most dermatologists unfortunately, to diagnose because they've never seen it. They can pronounce it as I said and many haven't even had to mention to them when they were in med school 5 or 10 or 20 or 30 years ago. Typically, it's a disease of what we call middle age. And I notice the older I get, the further out middle age gets pushed, but I said 40 to 60. Pemphigus is not an infection and it's not contagious. That's very, very important because a lot of people are worried about that. Pemphigus vulgaris, that sounds mean right? Vulgar, so vulgaris actually is a Latin word and it means common in Latin. So pemphigus vulgaris is a common form, the major form, and it's the one that probably 90%, or maybe even more people will have if they have it. They typically have sores in the mouth, oral lesions. That's the most common way that people will present with this but the scalp is another commonplace on the skin, the underarms, any of the folds. The underarms are a fold, under the breast is a fold, in the groin is a fold. Or if you're heavy, you can even have folds like your belly folds or God forbid, if you're really heavy, even folds and other places. So, those are the most common skin sites.

Dr. Korman: So, a great question that people always want to know. By the way, I don't know how many of you are old enough to remember the television show, I think it was called Art Linkletter and he had a show and he would talk to little kids and let them ask him questions. One of his lines was, "Kids ask the darndest things". Well, I think patients ask darndest things too. How do people develop pemphigus? That's a question I get asked all the time, why did I get this? So pemphigus is very rare. It's an antibody mediated autoimmune disease. What's an autoimmune disease? Well, normally your immune system is your friend and it helps you and it takes care of you, and it protects you. When you get a disease that's autoimmune, what's happening is, your immune system is messed. Your immune system is confused. It doesn't know why, but it goes awry, and it attacks you and attacks your own proteins. Why does it do that? I don't know, don't ask me, I'm just a doctor. What the heck do I know? That's the problem, people come to the doctor and they think we'd have all the answers. I want to tell you all right now, we do not have all the answers. This is one of my favorite lines actually, doctors

are pretty good and most of us are pretty good at the what? And most of us are pretty horrible at why? And many of us won't tell you that we don't know, we will make stuff up. We'll say, oh, it's from stress. You've all heard that before. Why did I get this, well it's from stress. You have a lot of stress. I typically think, B.S., most of the time for that answer, I think that's a B.S. answer. So, genetic factors probably play a role in why some people get pemphigus. And that doesn't mean that if you have it then your kid's going to get it or if your parent had, that's not what genetic factors mean. Although, I think that's what a lot of non-medical people here think when I say genetic factors play a role. But we really don't really know why any particular person develops it at any given time. So, it's certainly not passed from generation to generation. I don't believe I've ever seen the one person who had another family member, particularly like a parent or a child, that had pemphigus. I suppose as possible, anything's possible, but I've been doing this 35 years and I've seen several hundred over 400, 500, or 600 people with this disease and I've never seen it in the same immediate family. Although it's very rare, it is more commonly found, although still rare, in those of Jewish background, Middle Eastern background, Indian background from India. There are rare reports of medicines and these are, particularly, the first medicine penicillin, it's a drug that almost nobody uses anymore. Captopril is a drug that is used to treat high blood pressure, so it's certainly used sometimes. There are rare reports that those medicines might cause pemphigus. And then this is a very, very unusual type of pemphigus that occurs in the jungles of Brazil so don't worry about that too much, not really relevant and it's thought to be due to something in the environment. That there's some kind of a fly, there's some kind of a virus on a fly that plays a role, but that's hot shot science. That's not really clinically relevant at all.

Dr. Korman: So how do you diagnose pemphigus? Well, it's got to be an experienced dermatologist and they have to suspect that disease based upon the presence of blisters or erosions. So blisters or fluid filled lesions and we will go over this in a minute and erosions are places where the blister breaks down and it leaves a sore and they're typically in the mouth, as I said earlier, or on the skin. So we do what's called a routine skin biopsy of involved skin and this will demonstrate the presence of a blister within the epidermis. So, epidermis, I'll show you in a second a real photo of what skin looks like. So within the top layer of the skin, the epidermis, and the separation of the skin cells from each other.

Dr. Korman: So here, on the left, this is a biopsy of normal skin. So this is the very top layer of your skin and then all of this from here to here, that's all the epidermis. Then from here, down is the dermis. So that's normal skin. And then over here on the right is skin that has a blister inside the epidermis. You see this purple stuff here and there's a little purple stuff down there, and then there's a lot of purple stuff up here and then there's a hole or a blister. The cells are kind of coming apart in that intra epidermal blister. This is just a higher power, greater magnification, looking at these cells over here. These cells are not sticking to each other, they're not attaching to each other and some of them are actually kind of starting to float free. So this is a higher power picture of the lower level, the dermis and these are some epidermal cells and this is the blister here. And if we could keep going up at the top here you would see some of the top of the epidermis but all of this clear area is where the blister is.

Dr. Korman: So that's what we call a routine biopsy and then the next kind of biopsy that's very important to diagnose pemphigus is called a direct immunofluorescence, or we call it for short DIF. So a biopsy for DIF is obtained from normal skin, not actually blistered skin but it's next to the blister or eroded skin. A DIF test is a specialized test, almost always performed only by dermatology. And a positive DIF biopsy, showing deposits of particular components is essentially almost always found in patients with pemphigus. So let me show you what one of these is. So what we do to do direct immunofluorescence is, we take this biopsy of, uninvolved skin of a patient who we think has pemphigus and then we add what are called antibodies. These antibodies are labeled with something so that we can then tell if there are any cells where there is any binding in the epidermis. So, here now is a biopsy for direct immunofluorescence. So, from here to here is epidermis. I'm going to talk about what's going on in epidermis. It looks like there's something going on there. And then from here down, the darker area is dermis. So what you see going on here is circles around each of the cells, these are the individual skin cells and each of them have staining around them, and this is called cell surface staining. This is a classic pattern that we see in patients who have pemphigus. And here's another one of these biopsies showing epidermis from here to here and then dermis. This dermis is lit up a little bit more. But again, look at each of these, it's like a basket weave or like a net. Each individual skin cell of the epidermis has binding, and this is binding of antibodies. These two pictures are diagnostic for a DIF finding of pemphigus, it's cell surface deposits for pemphigus.

Dr. Korman: There are also blood tests that we use to diagnose pemphigus. There is a test called the enzyme linked immunosorbent assay, we just call it ELISA, this is kind of the gold standard to diagnose the disease. So the ELISA can assay to different molecules, one called desmoglein 1 (DG 1) and one called desmoglein 3 (DG 3), and we can look for antibodies to desmoglein 1 or 3. So patients with pemphigus vulgaris are typically positive, either for desmoglein 3 alone, or both desmoglein 1 and 3. Then the other less common variant of pemphigus called pemphigus foliaceus, those patients are positive just for desmoglein 1 antibodies. All right, so I alluded to this before. Let's talk about the type of skin lesions that you see in pemphigus. A blister is a fluid filled lesion and it's the major type of lesion. Typically, these blisters are kind of soft and fragile. So they could easily break just like rubbing on them or whatever, you will break them. So the fluid in the blister is the same fluid that's in your blood but it doesn't have the red blood cells so it's typically clear or a little bit yellowish. Sometimes the blister might appear red or darker even than red because some red blood cells will get into it. But as I said, the blisters are very fragile and can break pretty easily. When they break, they leave a raw open area called an erosion and these can be quite painful. So therefore a lot of patients will say, should I break the blisters? I say, no, please don't break the blisters. Let them go through their normal course rather than break them because if you rush to break them you're going to have raw skin under there and you're going to be uncomfortable. It's going to hurt. The lesions of pemphigus do not leave a scar. They may sometimes leave discoloration depending on the color of the person's underlying color of the person's skin to begin with. So if the patient is a Caucasian, they usually won't leave much of a discoloration, but if somebody

has brown or black skin, they might have discoloration that might take longer to resolve and get back towards their normal color.

Dr. Korman: All right so I alluded to the two most common types of pemphigus, pemphigus vulgaris, I said probably more than 90% and then pemphigus foliaceus is less common, maybe 10% or so. Then there's a bunch of even rarer types that we won't bother with today. So pemphigus vulgaris, the common or vulgar type, the majority present with sores in the mouth, I'd say probably two thirds of people. More than 90% of the patients will have a mouth sore at some point during their disease but much less commonly they have sores in other mucous membrane sites that I alluded to before like nose, throat, esophagus, genital, or rectal area. Common skin blisters or erosion sites are scalp, chest, back, skin folds, groin. So this is a picture of a woman, who doesn't have any upper teeth but she's got these super raw soft and hard palate erosions. This is somebody who had severe pemphigus that I took care of when I was in training at the NIH. I spent three years as a research fellow at the NIH, after a dermatology residency, doing research on pemphigus and pemphigoid, basic science research. But I also saw patients those three years and learned how to manage these diseases very well. That's where I really learned a lot. I learned some when I was a dermatology resident but the NIH at that time was very active in studying and learning about these diseases and that's why I went to study there and spent three years there. So here, this one's harder to see but this is the patient's head up there and this is their back with a large erosion and here's another erosion, and then maybe a couple of little blisters here. This is a big, what we call a crusted erosion. So that's somebody with a pretty severe disease on their body.

Dr. Korman: Pemphigus foliaceus, as I said, less common. The split in the skin is much higher up in the epidermis. The mucous membranes are not involved at all. Blisters are very rare, you typically just see crusted scaly patches on the face, scalp, chest, and back. Here's a few photos. So this is a patient with pretty severe pemphigus foliaceus with lots of redness, crusting, and erosions, but no blisters. Here is another guy, kind of the same area with scaly, red patches with maybe a little bit of crusting down here. Then this is his head showing more of that crusting as well.

Dr. Korman: So, what's the course of this condition and the prognosis? Back, before I was born in the 1950's before systemic steroids came around, when pemphigus was untreated it killed most people. Up to 90% of people died. Why did they die? Because pemphigus leaves, raw skin and raw skin is open and it makes patients prone to infection. So it's kind of like having a burn. That's why people died because we didn't have any way to treat them and they got secondary infections. Thank goodness, currently the mortality rate is very, very low, it's less than 5%. We think of this disease as probably a chronic disease. It's not something that we cure routinely and we'll get into that in a minute. So corticosteroids like prednisone, these were first used in the 1940's to treat rheumatoid arthritis, that's the first disease. Then in the 1950's,

they were used to treat skin diseases, including pemphigus and pemphigoid. They have many strong immunosuppressive and anti-inflammatory effects. They really have been the cornerstone for the last 50-60 years of treatment of the autoimmune blistering diseases, including pemphigus and pemphigoid as well. But corticosteroids just have a billion side effects. The good news is almost none of these occur early on and they can often be avoided or minimized by not treating for too long with steroids. Thinning of the bones, also something called the hypothalamic pituitary adrenal axis suppression. This is a part of your endocrine system that steroids can mess with. Myopathy, so people can get weak, their muscles cannot work. Osteonecrosis, so osteoporosis is when your bones get thin and they're more prone to break and osteonecrosis is actual destruction of bones. Cataracts and glaucoma, hypertension, diabetes, peptic ulcers all kinds of stuff. We want to get people off this, but it doesn't happen in a week or two. Pemphigus is a pretty severe disease so we definitely need to use corticosteroids but we need to respect them and we need to treat with them at the lowest dose and for the shortest amount of time. But, as I just alluded to, this can be challenging because pemphigus can be quite severe. So, what do we do, how do we try to avoid steroids side effects? Well, we do it by using steroid sparing agents. In the past, probably the two most frequently used agents, certainly by me and a lot of my colleagues who do a lot of this work, were Cellcept or a fancy name for Mycophenolate mofetil, just call it MMF, and Imuran or Azathioprine. If you were a patient of mine 5, 10, 15 years ago, we would be using prednisone and Cellcept or prednisone and Imuran. One or the other or maybe possibly sometimes even switching back and forth. But about three years ago Rituximab was approved for the treatment of pemphigus vulgaris. It's been around for a long time. It was FDA approved for lymphoma almost 25 years ago and it was FDA approved in 2006 for rheumatoid arthritis. So Rituximab is a steroid sparing agent. What is it? It's an antibody and it binds to a molecule called CD20. CD20 is a cell surface protein, a protein on the surface of lymphocytes. Lymphocytes are molecules in your blood that make antibodies. What's going on in pemphigus is you're making antibodies to these desmoglein proteins that I talked about. So, what Rituximab does is it leads to a depletion of both normal and abnormal or pathogenic or pemphigus B lymphocytes, so that those lymphocytes aren't there anymore, so they can't make those antibodies against desmoglein. Then we can get pemphigus under control when we treat it with Rituximab. So for the large majority of patients that I see with pemphigus, I typically start with oral prednisone while I'm waiting for insurance approval of Rituxan. Why is that an issue? Well Rituxan is a great treatment but it's not cheap so it typically is one of those therapies that you have to jump through hoops to get approved and depending on the time, it could take a few weeks. So a lot of patients who present with pemphigus, they have a pretty significant disease, and they need to be treated, they can't just sit around and twiddle our thumbs waiting for approval of Rituxan so I usually start them on some amount of prednisone. Then I'm waiting to get them approved for Rituxan. In this day and age, in 2021, 3 years after Rituxan was approved for the treatment of pemphigus vulgaris, I should say. But fortunately, I use it pretty much, almost always for all of these patients. For anyone with any variant of pemphigus I certainly try to get them approved for a Rituxan and most of the time I'm able to be successful. But as I alluded to, it's expensive so it's a process. It takes time to get them approved and most of us who are experienced in treating pemphigus consider this the treatment of choice in the year 2021. But, it's not known why some patients respond better than others. I would say that many to most of my patients

respond very nicely to Rituximab. Rituxan is the brand name I should be saying Rituximab which is the so-called generic name. But with the availability of Rituximab, I rarely use Cellcept or Imuran, which I used to use all the time as the steroid sparing agent prior to the FDA approval of Rituximab.

Dr. Korman: So how long does it take to show effect? Anywhere from 4 to 12 weeks and it varies. So usually patients are on some amount of prednisone and I will tailor how much prednisone to give them based upon how bad their disease is. And as they're improving, I will slowly taper their prednisone. Many to most of my patients who are getting Rituximab, can successfully be tapered off almost entirely or entirely their prednisone within about six months. I had a patient today whose status is post his second course of Rituximab and he's three months out and we have them down to five milligrams of prednisone every day and he was on 60 milligrams when I started him about four months ago. So he's done very, very nicely, but this is his second course of Rituximab meaning that after his first round, he got better and then about a year later it came back again. So many patients who go into remission after the first course of Rituximab, allowing them to get off prednisone, So how do you define remission? I define it as the absence of any clinical lesions of pemphigus while off therapy, such that people are not on any therapy at all. That's my definition of remission, but I use the word remission and not the "cure word", cure because an awful lot of patients relapse and I think it's very important to have proper expectations and lots of times patients don't have proper expectations, and no one should expect you to have them. But I should expect you to hear me when I try to teach you what your reasonable expectations are. You can be disappointed at what I'm telling you since it's not what you wanted to hear but you need to adjust your expectations to what I'm telling you, because guess what, I know just a little bit more about this than you do. So it's important to not use the word cure. So patients with more severe disease and those who have persistent, elevated, desmoglein 1 levels tend to have a higher risk of relapse after they get a course over Rituximab, meaning they may need another course, or they may need another course.

Dr. Korman: Other treatments, so intravenous immunoglobulin, IVIg is another steroids sparing agent that can be used and sometimes it's used along with Rituximab very nicely. There are other older oral medicines that are out there that are occasionally used such as Dapsone and Methotrexate, those are probably the main ones. Occasionally you'll see, or you'll hear about, or I will even do it, sometimes some patients will be treated with multiple different agents at the same time. Usually those are people that we're really attempting to gain better control of their disease and in an attempt to get them off prednisone more quickly. Or if they're developing some side effects from prednisone then I might add something else that I might have otherwise said, no you are okay, we don't need to. For pemphigus vulgaris patients, oral disease can be extremely stubborn. I will sometimes recommend patients go to the dentist and get what's called a dental tray made. What that is, it's essentially like when you guys or your kids had braces, and then after the braces came off, the dentist made a retainer. The retainer was to hold your teeth in place and the retainer sat on the teeth. Well, this dental tray is similar to a retainer, but it has a different purpose. It's not anything to do with the teeth. It's got to do with

the gums, an awful lot of pemphigus disease is on the gums. And so if the dentist makes a dental tray and it goes up above the teeth a little bit to the gums and on the higher on the upper gums and also goes below the teeth on the lower gums then it can sit there and we can use a medicine like a topical steroid and this dental tray will hold the topical steroids in place. Because otherwise just your saliva in your mouth tends to wash away the steroid. So if you put just a little steroids and rub it on your affected gum if you have pemphigus disease with blisters and erosions on dry areas, it just won't work. These dental trays can help make it work, and this can be very, very helpful for people with oral disease, especially particularly if it's on the gums.

Dr. Korman: So what about other approaches? So the role of natural or holistic approaches is unclear or not only in pemphigus but I would say in almost every disease. So when I address a question like this, you have to recognize how I'm addressing it. I'm addressing it as a physician and as a scientist. So how do I make decisions about what works and what doesn't work? Using evidence. Where does evidence come from? It comes from doing studies, doing research. So when my patients come to me and say, I started doing yoga and my stress level is down enormously. I started doing Tai Chi and I just feel so much better. You know, anything that minimizes your stress or maximizes your positive approach to a chronic disease, like pemphigus is totally fine with me. It's very different from you asking me, or you telling me as my patient that you started doing yoga and it's working. That's a very different scenario than saying, Dr. Korman, do you recommend yoga for all your patients who have pemphigus? The answer is, no, I don't because there's absolutely no data that demonstrates that this is a value. Do I think it could be helpful? Yeah, possibly, but I don't have any evidence that it is so again, as a physician and a scientist, I'm not likely to recommend this across the board. But it's pretty harmless except for the time that it takes to do it, or maybe the cost if you're going to a class and learning how to do it. What about food or diets? That's another very, very popular question out there that patients want to know about all the time. Same answer, unfortunately, there's no evidence that any particular diet is of value. It is, however, well known that patients who have bad oral disease or they have active oral disease with erosions and blisters in their mouth, should certainly avoid a firm food like chips, pretzels, stuff like that that's going to hit spots and make you bleed or hurt you. There's some evidence that, and I've certainly seen this with my patients, that things that are acidic like a tomato or oranges or orange juice, those will burn like hell again if you have raw areas. Spicy foods, the same thing. So these are more things not to take, not to eat rather than any particular diet that there's any evidence to support that will help pemphigus.

Dr. Korman: Somebody wanted to know, how does pemphigus compare to pemphigoid? So both of these are autoimmune skin diseases. In pemphigus the patient develops antibodies against molecules on cells within the epidermis which is higher up. And then in pemphigoid, patients develop antibodies against molecules that are actually at the junction between the dermis and epidermis, the dermal-epidermal junction. So let me show you a picture here. So again, this is a photo of normal skin and here is epidermis from here all the way down to here. Then, right here I can attempt to draw a line, you see it kind of undulates, and this is what I call

the dermal-epidermal junction. And that's the place between where the epidermis ends and the dermis begins. Patients with pemphigus have antibodies and diseases that's in the epidermis. They have a blister that's in the epidermis. And patients with pemphigoid have antibodies and a blister between the epidermis and the dermis. So that's the difference under the microscope. So, 75 or so years ago, before oral steroids existed, the death rate from pemphigus, as I said, was up to 90%. The death rate from pemphigoid was only 5% to 10%. Why is that? Well, because of what I said before, that pemphigus left all these raw erosions in the skin and the raw erosions actually spread because the skin is not sticking together. And in the case of pemphigoid, the blisters that occur didn't they just didn't spread as much because the epidermis and the dermis, when that blister occurred there it kind of holds together better. So the skin doesn't separate in many other places. And this is the observation that pemphigoids natural history death rate is in the 5% to 10%. Typically, pemphigoid patients are older, 65 to 90 while pemphigus patients tend to be younger. The other thing about it is that pemphigoid typically will resolve within a few years, 3 to 5 years from diagnosis while pemphigus usually lasts longer and it can have periods of control and relapses and typically requires more aggressive therapies to get it under control.

Dr. Korman: So how do you find the doctor that might be able to help you? So you've started at the right place, you're on the International Pemphigus and Pemphigoid Foundation, one of their webinars. The best resource for helping you find a dermatologist who is experienced at taking care of patients is the IPPF. Now, many of you don't live in places where the number of people who are members of the IPPF practice. There's not a card carrying member of the IPPF or even a blistering disease expert in every major city let alone smaller places. And unfortunately, as I said, pemphigus is rare and only a minority of dermatologists are really comfortable caring for it. So, you need to ask the dermatologist how many pemphigus patients have they taken care of. Let's hope they give you an honest answer. If you see them hesitate, then I think you're getting the sense already. And if they say one, when I was a resident 18 years ago, that's maybe not your best choice. So, if you're unhappy with the physicians you're seeing, you could consider if it's feasible for you, traveling to go see somebody. I made this number up, Amethyst maybe you can answer whether I'm close to right or whether I'm off by a large extent. I said there are probably only a few dozen of us that are real experts. I might have undersold us. I think the fifth bullet point here is perhaps the most important one. I think it's really important that you consider your doctors fit for you. Does your Doctor listen to you? Do they give you enough time? Do they answer your questions? Do you feel comfortable with them? And if the answer to most of those questions inside that fifth bullet is, "I don't think so", then maybe it's time to think about finding somebody else. And actually, with the way medicine has changed as a function of the pandemic, you might be able to consider bullet number four and not have to travel to be able to have access to an expert by the web or a virtual visit. Sometimes, it's not enough to do that, but sometimes it can get you started. Or it can change your path a little bit if you feel like you're going around in circles and you don't have all the answers. So, I will agree to see people virtually. I'm actually doing a fair amount of virtual work these days because I'm older and I got the vaccine recently, but I was just being careful for myself and taking care of myself by minimizing my exposure to lots and lots of people.

Anyways, I think these points are very important when you think about how to find the best doctor that you think can help you. Okay I am done with my slides. I thank you for your attention. And now I am ready to attempt to answer the questions that might come my way. So, Amethyst let them roll.

Amethyst: Great. Thank you. That was amazing and you covered a lot of our questions that we received beforehand. So, thanks so much for that. Looking at the questions that had come in, Mensur asks, have you treated any younger patients with pemphigus vulgaris? They said that they are 23 and have been diagnosed via biopsy.

Dr. Korman: Sure. Yeah, absolutely. I have treated people down into the teenage years. Not a lot, it's less common that younger people get it. And certainly, you would want to think about the pros and cons of various therapies in somebody who is younger and has a longer life ahead of them. But, as I said, this is a serious disease so you have to do a balancing act of what I call risk versus benefit. But, yes, I have taken care of people 23 years and younger.

Amethyst: Great. Thank you. Augustine wants to know what's your experience using Rituxan and IVIg as a combined therapy? I know you discussed a little bit about sometimes you use multiple treatments. Is that something you do frequently?

Dr. Korman: I don't do it that frequently. So, I alluded to the fact that Rituxan can take some time to get approved because it's not an inexpensive therapy. IVIg makes Rituxan look like a bargain. Rituxan is maybe \$50,000, \$60,000, or \$70,000 a course. A course typically being 2 infusions, two weeks apart. Occasionally 4 infusions, four weeks in a row. And IVIg might be \$200,000, \$300,000, or \$400,000 a year. So, I don't do a ton of the two of them together because of the finances because it can sometimes take 2-3 months to get IVIg approved in my experience. And a lot of this will vary depending on where you're located and how insurance coverage is and such. I have a patient that I had on IVIg not for pemphigus actually but for a different serious skin disease and it was helping him enormously and all of a sudden the year changed and his new insurance said, no you can't have it and here we are in April still fighting to try to get them back on it. So, I have used the two of them together. I don't use the two of them together a ton because of the difficulty of getting it covered routinely.

Amethyst: Great. Thank you. Along the same lines, Ed said that he recently had a flare up and his new dermatologist has increased his Cellcept from 2,000 milligrams to 3,000 milligrams per day and also added 20 milligrams of prednisone and 100 milligrams of Dapsone per day. He's also scheduled for 8 IVIg infusions and 4 infusions of Rituximab. His flare mostly subsided, but it's curious if you feel that all of these new meds, which have been used in the past individually, if using them all at once is normal procedure?

Dr. Korman: Totally, totally reasonable. I don't always throw the kitchen sink at somebody if they're not doing perfectly. I might add them one at a time but I have no problem with all of those therapies together. And I've done the same thing before so it sounds perfectly reasonable.

Amethyst: Great, thank you. We've got a lot of questions coming in so we're going to try to get through these here. Tarla says she's diabetics, so her doctor only prescribed Cellcept, 1500 milligrams twice a day, but she still is getting erosions in her mouth. What would be perhaps your next recommendation?

Dr. Korman: Yeah. That's a common problem that many physicians who are not as comfortable with this disease will say, oh, you're a diabetic, you can't take prednisone. I think that a lot of things are not black and white, they're shades of gray. So, I think that usually I can't get almost anybody under control without some prednisone. The answer is, it's a balancing act and it needs to be done with the assistance of their internist or their endocrinologist or somebody who's comfortable with managing diabetes and comfortable managing it if we have to give somebody prednisone. It's not what I would say is an absolute contraindication to take prednisone if you're a diabetic. Yes, it makes things more challenging but it's not an absolute contraindication. I don't know the story here, right? I don't know if it's really a good idea for this particular person. Maybe a different approach would be to say how about Rituxan because maybe we can get it under control with Rituxan and maybe we could still avoid prednisone. It's hard to give real specific advice in this kind of scenario. Those are some of my thoughts though.

Amethyst: Thank you, Keisha says that she has had PV for 14 years and takes Dapsone three times a day. The side effects seem to be getting worse with muscle aches and benign tumors. She asked, if there is a better medication that you think she should take?

Dr. Korman: Kind of the same answer as the last one, you know, it's hard to get specific advice about a specific person but if somebody is starting to develop side effects from any medicine that I have them on, that maybe it was working before, yeah, it's time to think about another medicine. I named them all. I named Cellcept, Imuran, Dapsone, Methotrexate, IVIg, Rituximab, prednisone, I named them all. So I don't know which is the right one for this particular person at this particular juncture, but I would support the idea that it's time to consider a new approach if the Dapsone is causing these side effects.

Amethyst: That's great, good recommendation. If it doesn't seem to be working or making things worse, discuss with their doctor, maybe a different treatment option.

Dr. Korman: Or as I said on one of my last slides, maybe if your doctor is being stubborn and doesn't want to hear what you have to say, maybe it's worth considering is that the right doctor for your right? Same answer to the question from somebody whose doctor won't prescribe prednisone because they're a diabetic. Maybe the patient doesn't want to take prednisone, that's okay too. But if the patient says, I went to this webinar and somebody said that they could use prednisone with a diabetic, and they mentioned that to their treating physician, and that treating physician says, oh nonsense, and the patient still is interested in it. Maybe the answer is, if they have other options, maybe there's another dermatologist to see that could potentially have a different approach and be a little more what I would say, open minded.

Amethyst: That's great, very good advice. I'm not sure if you did cover this or not, but why does it seem that pemphigus begins to form more frequently in the mouth than on other parts of the skin or body?

Dr. Korman: I don't think we actually really understand that. I think it may be that there's higher concentrations of desmoglein in the mouth so when you get these antibodies, they will more readily tear up the oral mucous membranes. That's about the only understanding that I have that might explain it, but I think, probably we don't really know. I told you, we were really good at what, but not so good at why. So you threw a why at me.

Amethyst: Great, thank you. Terana asks, is it usual to lose taste from pemphigus and what can be done about that?

Dr. Korman: No, that's not a usual one at all. That's a little out of the realm of a dermatologist. If that were my patient, I'd be sending them probably to an ear, nose and throat doctor and see if they have any suggestions. This is not a side effect I've ever seen and I wouldn't necessarily attribute it to pemphigus, necessarily. There's also this little disease that's going around in the world these days is called COVID. COVID causes a loss of taste and smell so maybe this person that's attributing their loss of taste and smell to pemphigus in fact had COVID, was asymptomatic and didn't know it and that's why they don't have their taste and smell.

Amethyst: Great, thank you. This person wants to know what's your experience with blood-filled blisters in the mouth? Is there any particular treatment that you would do for that or is that more that dentist?

Dr. Korman: So assuming that blood-filled blisters in the mouth are actually blisters of pemphigus then it needs to be treated like pemphigus. So when somebody goes to the doctor and they have sores in their mouth, the first thing that even an experienced dermatologist might

think of would not be pemphigus because I told you, this is a rare disease. So what would they think? They would think of things like canker sores, or what they call aphthous ulcers, usually those are ulcers and not blisters with fluid in them but they have blood in them. But there are times when canker sores can do that, too. So there's no specific treatment because a blister has blood in it necessarily. And the main reason it might have some blood in it is perhaps because there's been some trauma. It's been banged or whatever. But not every blister that has blood in it is pemphigus and if it is, if it's somebody who has pemphigus and they are flaring and they have blood filled blisters in their mouth and they're flaring with that then well, the answer is, they need some more therapy above and beyond what they're currently on because it's not doing a good enough job.

Amethyst: Great. Thank you. I know we discussed a little bit about Rituximab. What are the side effects of Rituximab?

Dr. Korman: So Rituximab is an antibody and it wipes out your B cells, your B lymphocytes. And so it can increase the risk of infection. That's the short term, intermediate side effects of it. The most acute side effects, acute meaning things that happen right away is while you're at the infusion center where they're giving you the IV dose of Rituxan that takes 2 or 3 hours, a small subset of people might have things like flushing. Their blood pressure might go up a little or go down a little, they might get dizzy or light headed. These are all things that can be managed very, very nicely in the infusion center where people are getting Rituxan and they're typically not a big deal. The main issue is potentially increased risk of infection.

Amethyst: Great, Thank you. Speaking of infections and risk of potential other side effects, we have a lot of patients asking obviously about COVID and the COVID vaccine. Should patients vaccinate against COVID if they received Rituxan more than one year ago?

Dr. Korman: So, a patient had their Rituxan a year ago and the question is, should they get the COVID vaccine now?

Amethyst: Yes.

Dr. Korman: Absolutely, 100%. So, I'll answer a slightly different question which is, you have active pemphigus and you need to be treated with Rituxan and you're worried about getting COVID or taking the COVID vaccine. The answer is, typically, we don't actually know. I've addressed this question at my hospital with the experts, infectious disease experts, and there was actually just something published about this. The recommendation is, if you've just recently got a course of Rituxan and you need to be vaccinated, you probably ought to wait 2 to 4 weeks from when you finished your most recent Rituxan before you take the COVID vaccine. I have yet to meet a live human being that I have recommended, or than anybody else's properly

and appropriately recommended, not to take the COVID vaccine. Every single person needs to take the COVID vaccine. We need a 100% vaccination rate. I don't think we're ever getting there, but everybody needs it. Yeah, people with pemphigus who are on some drugs that suppress your immune system, like Rituxan, you'll want to wait a few weeks. I think pretty much all the other medicines that we have our patients on, whether that be prednisone or Cellcept or Imuran, I think people can get vaccinated while they're on it. What we don't entirely know is, might those people who are vaccinated with the COVID vaccine, that are those that have pemphigus and are on immunosuppressive drugs, might the COVID vaccine not work as well? And the answer is, we don't know. But should they get the COVID vaccine? Absolutely. They should get it.

Amethyst: Great. Thank you. Alex said they had treatment with Rituximab and they think that it might have affected some vaccinations that they had in their youth. They didn't specify what vaccines, but is that something they should look at? Or is that even a possibility? Have you heard anything about that?

Dr. Korman: So, this patient got Rituxan and now, the question is that they're no longer immune to a previous potential infection that they were vaccinated for when they were younger. Did I get that right?

Amethyst: Correct.

Dr. Korman: The answer is I don't think anybody knows. I think that this is like one of these medical question marks with not an answer. So, I think it's something that I've heard bandied about. I don't think there's any data on it. I think it's one of these things that people worry about with a drug like Rituximab but I don't know the answer if, if it's actually real. And if it's real, is it for any particular vaccines? Is it no more relevant for the flu vaccine or tetanus or polio? I don't know, I don't know the answer.

Amethyst: Guess more research needs to be done, right?

Dr. Korman: I love when people ask hard questions, that's the best kind of question. Ones that nobody knows the answer to that just demonstrates, like I said before, we do not know all the answers. Just because we're doctors doesn't mean we know all the answers. Yes, maybe we know a little more than the patients who have the conditions, but we don't know at all.

Amethyst: Great, well, thank you. Next question here is, what are the highest levels of desmoglein 1 and 3 that you've seen? And is it possible that even if they are showing no antibodies that they still can have disease activity?

Dr. Korman: So as far as the highest levels, I've seen them in the hundreds, So, a level of DG 1 and 3, it's something like over 15 to 25 is positive, but I've seen them in the several hundreds for both of them. It doesn't correlate directly. It's not like if you have a DG 1 of 400, that you have worse disease than the person next to you that has a DG 1 antibody of 300. It's really much more relevant for what your antibody titer is doing over time. Like, it used to be super high and now I'm getting better, and it's lower. That's really more where the correlation is. Then, the second question, sorry I lost, tell me again.

Amethyst: Is it possible that a patient can have zero and still have symptoms?

Dr. Korman: So, I suppose anything's possible. I don't usually answer questions, such as, is this possible or do I think it's a likely scenario? And the answer is, no, I don't think it's a likely scenario. Have I ever seen it? I don't routinely measure a lot of DG levels, actually. I know a lot of my colleagues and a lot of experts, measure them a lot. I don't measure them a lot. I think it's much more important to know how the patient is doing clinically. So looking at a patient's chart over a five year period, I don't have 5 or 10 levels of desmoglein 1 or desmoglein 3 antibodies that I'm following for my patients. I'm following how they are doing clinically. Do you have any sores? Do you have any blisters? Do you have erosions? Do you have signs of the disease still being active or is it just continuing to get better and better and better? So, is it possible? In my world, I think it is possible because I don't measure a lot of DG levels on a given person over a function of time, but I know some physicians who do a lot of this will do that and they will say, well your antibody level is zero so you're fine. But I still have some activity, what do I do? So I think the answer is yes, it's possible. I think it's relatively uncommon, but it's definitely possible.

Amethyst: Great, thank you. Rosetta asked, Is there anyone looking at the correlation of blood type and the incidence of pemphigus or pemphigoid?

Dr. Korman: Blood type like A, B, O. I don't think so but I'm not positive.

Amethyst: Great, thank you. Let's do 1 or 2 more questions if you don't mind. Ruth asked and I know you don't like to use this word, she wants to know if you can use the word cure if she's not been on medication since 2004.

Dr. Korman: I'd say she's in prolonged remission. That's what I would tell her. I mean, 17 years is a long time and certainly, I don't expect her to get the disease again. I think it's important to

set proper expectations and if Ruth comes away from tonight, saying this doctor said, I'm cured after 17 years. He says, And a lot of patients hang on every word of their doctor. As I've gotten older, I go to a fair amount of doctors, too many doctors, actually, and I noticed that I do it. So, I forgive you for doing it, because even though I'm a doctor, I do it too. I come home, and my wife says, so, what did they say? And I go, oh, I should have written it down. I get frustrated with my patients that they don't always know everything that's going on at the next visit. I think it's normal human behavior. So back to Ruth's question, 17 years without any disease off of all meds, I'm going to assume that is what she means. She had no clinical lesions and she hasn't taken any meds in 17 years and she wants to know, is she cured? And I would say, Ruth, you are in prolonged remission and I expect you'll likely stay there. But I won't, I won't give her the "C".

Amethyst: Great. Thank you. Is there an average time typically for remission based on the different medications that you've seen?

Dr. Korman: No, everybody is different. Everybody has their own story and certainly what I find a lot of times, even though I take care of a lot of people with this disease, or these diseases, when people get all better, they disappear. They don't come in and see me every year to say, I'm doing great. How are you doing? I'm doing great. I still don't have any disease, I'll see you next year. I mean, a few people will do that, but many people will just say, I'm done, I don't need to see him anymore. So, the answer is, I don't always know the answer. I don't know what's going on with every single person that I've ever seen who's had pemphigus. I don't keep track of them all and guess what, they don't keep track of me. They're perfectly happy to be done with me. Right?

Amethyst: Right, we see that too at the foundation.

Dr. Korman: Yep, it's normal human behavior. It makes perfect sense. Unless you have somebody who's, what I would say is tightly wound, and they just like they have to stay on it. But most people are not like that. Most people are like, yay, this is over and I don't want to think about it anymore. This was one of the worst things that happened to me. So I mean, some crazy people like Amethyst, you join because of family members and some other crazy who have the disease are very involved in the foundation, but an awful lot of people want to run like hell and the opposite direction from anything relating to this disease as they get better, and that's understandable because it's not a good time in people's lives. So once it's behind me, I want it to stay behind me.

Amethyst: Very true. Great, Well thank you so much Dr. Korman for sticking around a few minutes extra with us and explaining everything so well. We got a lot of comments saying that it

was a great presentation and everything was so easy for everybody to understand, and you did an amazing job, so thank you again for being on here with us today.

Dr. Korman: My pleasure. Thank you all for joining. Good luck with your journey. Don't be shy and don't let doctors push you around, you got to push your doctors around. You have to become experts, and that's what you're doing by being members of the foundation because sometimes you're going to hold their hand and they're not gonna like it. And if they don't like it and you're not getting along with them, then it's time to maybe consider moving on.

Amethyst: Great, thank you, very good advice. Well before we go, everyone, I just have a few quick announcements. Our next webinar will be the Back To Basics: All about Pemphigoid, on Monday May 10th with Dr. Ron Feldman, Assistant Professor of Dermatology and Director of the Autoimmune Blistering Disease Clinic at Emory University in Atlanta, Georgia. Registration will open soon. If you have bullous pemphigoid you are invited to participate in an interview as part of a research study to better understand the challenges of diagnosis, treatment, and everyday life of living with bullous pemphigoid. Contact Magnolia Innovation at ilymanscott@magnoliainnovation.com or call 914-414-6767 for more information. 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, the sooner they can find better treatments, earlier diagnosis, and one day – A CURE! Lastly, If you have a question that didn't get answered on the call, or have additional questions please contact one of the IPPF's Peer Health Coaches on our website by visiting: www.pemphigus.org/peer-health-coaches/ or you can call (916)922-1298, and we would be more than happy to help. This call recording will be sent out with the survey following this call. Thank you all so much for joining us and thank you Dr. Korman. We greatly appreciate it.

Dr. Korman: Thank you, guys. Have a good night.

Amethyst: Have a great night, everyone. Thank you so much.