

June 18, 2020- Treatments Patient Education Webinar

Becky: Hi, everybody. We're gonna get started here in just a minute with Dr. Korman to answer our questions. I'm just gonna launch a poll as we get started. If you wouldn't mind, just letting us know what treatments that you've been on. And then that gives us an idea of who's listening and what's going on in our community. So, we do see some answers going up. So if you're just joining us for the call if you could let us know what treatments that you've been prescribed for your pemphigus and pemphigoid we'd really appreciate it. Welcome, everyone, I do want you to know this call is being recorded. I'd like to thank you for being on the call with us today. And a big thank you to our sponsors, Genentech, Principia Biopharma, argenx and Cabaletta Bio for making today's call possible. Today's topic is a Q&A on treatments for pemphigus and pemphigoid with Dr. Neil Korman. So, if you haven't already, please respond to our poll, and I'm just going to introduce doctor Korman. Dr. Neil Korman is a Professor of Dermatology at Case Western University in Cleveland, Ohio. He's also the Director of the Dermatology Clinical Trials Unit in the Department of Dermatology at the University Hospitals of Cleveland. In addition, he serves as the Clinical Director of the Murdough Family Center for Psoriasis, a comprehensive psoriasis research, education, and treatment program. Dr. Korman holds a subspecialty board certification in dermatological immunology/diagnostic and laboratory immunology. Dr. Korman is also the founding director of the Regional Center for Immunobullous Diseases. So, I'm just going to close this poll real quick, and then I'm going to share my screen with everyone. So Doctor Korman, that was our brief introduction. How about if we just hop right into these questions and get going for our audience? So our first question, Tamir says, my husband was diagnosed with PV in 2017 and he is in a flare since July of 2019. And until now he didn't reach recovery. He is on pulse IV steroid every other week, cyclophosphamide every 14 days and Cellcept, three grams. But blisters still appear all over his body during the last two months. What triggers another flare up and when can remission can be reached?

Dr. Korman: Well first, I'd like to thank you all for joining. I'm looking at the list here of attendees and I see we're allowed a maximum of 501. And right now we have 71. So there's room for 430 more people. Call your friends with pemphigus and pemphigoid. We will get to them anyway, so sorry. Sorry to play with you all but I always like to have a little bit of levity is always a good thing. So Tamir, that's a great question. We don't always have good answers to why. Doctors are horrible at why, we're really good at what. We are horrible at why most of us don't answer the question why when we're asked. So I don't know why. I'll answer it for you. I don't know what causes a flare in pemphigus or pemphigoid or in any disease. I typically don't know the definitive answer but clearly your husband's got significant disease being treated pretty aggressively and if things are still active, things need to be changed. Other therapies are out there as choices and I would encourage you and he to talk to your doctor about what are

the other options. Given that he's on a pretty potent drug, like cyclophosphamide, that one may need to be stopped before another potent therapy would be introduced.

Becky: Great. Thank you. Patricia asks, Is there any connection to the treatment of blood pressure medications to pemphigoid? It was only after my husband was given an ACE inhibitor, that his symptoms worsened.

Dr. Korman: So, I just actually read a paper today in the latest dermatology medical journal about this. It was a study of what are the drugs that might cause bullous pemphigoid to flare. ACE inhibitors were not on the list. A bunch of other drugs are on the list. It's actually known that ACE inhibitors may cause pemphigus to flare. Pemphigus is a different disease than pemphigoid. About 60 years ago, the dermatologist by the name of a **07:11** separated pemphigus and pemphigoid. Until then, they were thought to be the same thing, which is why everything was called pemphigus for a long time. And then when this guy came along in the early 1950's he separated them. But there's no evidence, that pemphigoid is worsened by ACE inhibitors.

Becky: Great. So you had mentioned in the article that you read that some medicines do make it worse. What medicines would make it worse?

Dr. Korman: Sure, so the one that probably has the best data, are some of the medicines for diabetes. A group of drugs called the glitazone, and there's a whole different group of those, there's more than 1 to 3 or 4 of those, and they vary in terms of which ones different physicians use. But those are probably the largest group of drugs that I would talk about, that I am routinely concerned about.

Becky: Great. Thank you. Our next question asks, if one is on prednisone, what is the maximum level per day we should be really worried about COVID-19 infections, more than others who are not on prednisone? Is 5 milligrams a day or 10 milligrams a day safer, or should we be concerned even at those levels?

Dr. Korman: Tough question. Great question but tough question. We don't have any definitive answers with COVID. As anyone who reads the newspapers carefully has learned over time, nobody knows the answers. So certainly prednisone is a drug that suppresses our immune systems. And so if you're on prednisone it can suppress your immune system and certainly the higher the dose the more it suppresses your immune system. But I cannot give you a specific answer that is the amount of prednisone that's safe. It needs to be individualized and depends upon what other factors are going on in the individual patient. How old they are, what other risk factors they have for COVID. Like if they have diabetes, or high blood pressure, heart, disease,

or lung disease. So, no simple answer. Most of the questions I'm going to get, I guess will be there is no simple answer, unfortunately, but I can at least give some flavor around them hopefully.

Becky: We appreciate it and our community does ask the tough questions. So we appreciate your giving as much information as you can, so we appreciate that. Our next question asks is there any evidence of using emu oil to prevent lesions?

Dr. Korman: Not that I'm aware of.

Becky: Okay, is there a potential shortage of Rituximab, IVIG, or any medications that are used to treat pemphigus or pemphigoid that might be caused from COVID-19.

Dr. Korman: No, I'm not aware of COVID-19 causing any particular shortages of the group of medicines, I haven't heard of Rituximab having shortages, but individual intravenous IVIG preparations often go into shortage. Often if somebody's on preparation A and they have to switch to preparation B because that particular preparation is no longer available. That's been a significant problem that I've experienced over the years.

Becky: Great. Thank you. Sandy asks, this is another COVID-19 question. With COVID-19, still looming. Is there any move to be able to get Rituximab infusions at infusion centers or even at home? And is there a safety concern of why they can't be given at home?

Dr. Korman: So Rituximab requires some knowledge about how to use it. And I always prefer to have my patients given Rituximab at a center where they've done it a lot. Sometimes patients say, well I want to go here because it's closer, and I say you're gonna go here, because they do it all the time. Even though it's a little closer. Because the potential side effects of Rituxan can be best managed by the nursing staff and the physicians there when they've seen it 200 or 500 or 1200 times, rather than having an order set and this is the third time doing it. So I would certainly prefer against doing Rituximab in the home because the person who is doing it is usually a nurse and infusion nurse is all alone. And it just would depend on his or her experience and how many times they've done it.

Becky: Great. Nancy has submitted a question through our text box and asked, is there a standard protocol for Rituxan? Is it two doses every two weeks apart, every six months or repeat again if there is a flare up?

Dr. Korman: So the question was, is it two doses to two times, two weeks apart? Or is it repeated every six months? But I didn't understand the last part about the flare?

Becky: And then repeat it every six months, if there's a flare up.

Dr. Korman: Okay, and what was the question for pemphigus or pemphigoid?

Becky: Nancy did not say.

Dr. Korman: So it will vary, depending on the disease state. There is actually some data that's come out in the last few years out of the University of Pennsylvania where they looked at for pemphigus, they looked at the two different ways to give Rituxan. The original way given for cancer lymphoma was four weeks in a row. And then the newer way for rheumatoid arthritis was two weeks apart. And that's the rheumatoid arthritis way, is the way that it got approved the year or year and a half ago by the FDA. But interestingly, the study out of the University of Pennsylvania found that it looked like it was better, that we got better results with the four weeks in a row dosing in pemphigus. All of what I said was only pemphigus. In terms of what to do at six months, I think a lot of people have different opinions about it, and I don't think we have consensus yet of how often. Certainly, if somebody's flaring I would certainly give them a repeat course at 6 months. But if the question is, if they're not flaring and what do you do? And I don't think anybody knows the right answer.

Becky: Okay Nancy said it was for pemphigus so thank you so much for answering that. Augustine asks, what is the prognosis of occasional blood filled blisters and the mouth versus PV? And why does PV relapse in spite of the antibody one and three being within normal limits?

Dr. Korman: So blood filled blisters in the mouth may not be PB at all. It may just be like you chewed on your lip, and you got a blood filled blister. And that's a known thing that anybody can get. Whereas PV is a different story. PV in the mouth usually doesn't form intact blisters.

Usually the tissue was very friable, easily broken and so people just have raw areas, they don't actually have blisters. Sorry. What was the second part?

Becky: Why does PB relapse in spite of antibodies one and three being within normal limits?

Dr. Korman: I don't know, nobody knows that one. But certainly, I see I've seen that as well. right, that you can still have disease in spite of having negative antibodies.

Becky: And it seems like in the opposite case it's true too. That, antibodies can be high, but patients don't have lesions. So we're all kind of color in our own coloring book that way, right?

Dr. Korman: The human body does what the human body does. That is my answer that a lot of patients don't like, but it's still true.

Becky: Absolutely. Our next question says, I'm currently taking doxycycline and I think I'm getting a sinus infection. Will the doxycycline take care of this infection or do I need a different antibiotic?

Dr. Korman: Tough question, probably your primary care doctor, or your ear, nose, and throat doctor would be a better person to make that assessment.

Becky: Great. Thank you. Our next question says, I'm currently in remission, but I hear about people talking about having transient lesions and flares. What is the difference between these two and when should I talk to my doctor about treatment?

Dr. Korman: So, if somebody is actually in remission, a lot of it is the definition of what's remission. So my definition of remission is that the person doesn't really have much disease at all and they have no antibodies and they are at that for quite awhile. But as we just said, they could still have you know a blister here and there. I usually explain to my patients, if you just have a random blister or random sore once in a while, no harm no foul. But if you all of a sudden start getting more, and more of them, then it's time to speak up. It's a fine line. There's no right answer. I try to teach my patients when I think it's appropriate to call me. Some people don't call me soon enough and some people call me every half an hour. So it's a matter of educating people what's normal for you, and what seems abnormal for you.

Becky: Great, thank you. And we've gotten quite a few questions in for this call that asks what you're you're talking about. Is it better to treat pemphigus or pemphigoid when I first notice lesions develop, or should I wait to see if they hang around for a little bit or if they get worse before contacting my doctor?

Dr. Korman: So I'm going to answer that question, assuming that the person who's asking already has a known diagnosis and then they are on therapy and they're doing okay. Then the question is, so am I flaring now, and how much am I flaring now? And again, that's about education between your doctor and you, about what is your normal and how bad is your flair? I don't want you to wait too long. What I try to do is educate my patients so if they call me three times in a row, for what I considered the same thing, which is, come on you are okay. I'm going to reassure you that it's okay. I'm hoping after three times that they'll get it and they'll tell me a month later that they were going to call but I taught them that they shouldn't call me and then it got better, just like I said it would, even though I didn't call you. Education.

Becky: So is there anything besides taking medication that I can do to prevent blistering? And I guess the question is probably assuming it's Western, traditional, medicine treatments. Are there any alternative therapies?

Dr. Korman: Oh, I see, okay alternative therapies. People ask me all the time, what do I think about this alternative therapy, and what do I think about that? And my answer always is, I don't know. Nobody knows, I have no problem with you trying things as long as they are not too far out there. I have my patient and I, together try to define what I think is too far out there, and then we take it from there. So if somebody says I want to do Tai Chi. Great, go for it. Somebody says, I want to start meditating. I say, great, go for it. And somebody says, I want to do chinese herbal medicine. I say, well, I really don't know anything about that and that one makes me a little more nervous. Then my answer is, I don't know, I'm not sure. I'm not sure I would advise it.

Becky: Great. Thank you. Marjory asks, I'm on 10 milligrams of Prednisone and 3 grams of Cellcept. Can I get the flu vaccine? Also, once a coronavirus vaccine is available, can I get that?

Dr. Korman: So the answer with vaccines and immunosuppression. So medicines like prednisone and cellcept suppress the immune system. And so, then, the question with a vaccine is, is it safe to get a vaccine A, and B, will the vaccine work? So, when you're on immunosuppressive medicine, such as prednisone and Cellcept they definitely suppress your immune system. So if you got a live vaccine, it's unsafe. Absolutely no way in heck, don't ever get a live vaccine while you're on drugs like prednisone and Cellcept. Fortunately, there's very

few vaccines that traditionally in the US, that most of us are going to be getting that are live vaccine. So a couple of years ago, the shingles vaccine was a live vaccine and that was a no-no. Don't get that. Now, we have a brand new shingles vaccine that's a killed vaccine. It's called Shingrix and it's totally safe to get a killed vaccine while you are on drugs like prednisone and Cellcept. What people don't know and it hasn't been studied, is, we know it's safe. but will it work? Will it work as well? We don't know the answer to that. The other vaccine that's out there that can be a live vaccine is the flu vaccine. The enormous majority of people are offered the killed flu vaccine, which is the shot in the arm. But there has been in certain years, there has been a inhaled flu vaccine, which is typically a live vaccine. And that's a no-no. Do not ever accept a live flu vaccine. If you're traveling to exotic places such as Africa, things like yellow fever is a live vaccine. Weird stuff, out there, stuff. If you're traveling and you're a pemphigus or pemphigoid patient and you're on immunosuppressive drugs, absolutely go to a traveler's clinic and make sure you're clear about what vaccines you're getting, and whether they live or, killed. I can't answer the Corona vaccine, because we don't know what kind of vaccine we're going to have there, but the same thing holds. Live, no way. Killed should be totally fine.

Becky: Great, thank you so much. Our next question is from Maxine and she asks, how do I know if I'm experiencing side effects of Rituximab or PV? In particular, what my internist could be nerve related.

Dr. Korman: Side effects, well anything can be a side effect and nerve related and I'm not entirely sure what that means. I think it might mean you're a nervous person, and you're overreacting and you're worrying about stuff. I'm going to just re-assure you and calm you down, don't worry, everything's okay. It's nothing to worry about. But, typically Rituxan side effects are things that happen when you're getting the infusion. Your blood pressure might go up. You might get short of breath. Things that are important that need to be managed, like I talked about earlier, that need to be managed by experienced people who give Rituxan infusions. Sometimes for a day or two after Rituxan and people can kind of feel wiped out and crappy and kinda tired, but usually, that's not long term side effects. It's rare, but Rituxan does suppress the immune system so you can be at increased risk for an infection. So if you're having fevers and chills and other signs of an infection, that you feel crappy, you need to talk to your doctor, that could be side effects.

Becky: Great. Our next question asks, can you describe what is going on in my body month to month, following 2 Rituxan infusions? How will I know when my body resumes making B cells and when my immunity is restored? It seems especially relevant because of COVID-19.

Dr. Korman: Well, first of all, I want to share that we're really getting close to 100 people on this call. That's very exciting to me! 86, we're up to 86, go, baby. You cannot know when your B

cells are being made, again. Sorry, that's a good question. Some doctors will check blood levels of B cells of certain markers and such, but I don't see a whole lot of advantage to that. You'll know when you start getting better, that your Rituxan is working. And, yes, in the time of COVID we're concerned about it. It's a balancing act. I have not, not given anybody Rituxan in the last three months who had severe disease and needed it.

Becky: Great, thank you. Mark. says that, I've noticed I get a lot of joint pain when I come down off of high-dose prednisone. Is there anything that can be done to avoid this and is it something that I should be concerned about?

Dr. Korman: That fits into the category of what I call nuisance, side effects of prednisone. There's all the terrible side effects of prednisone such as diabetes, high blood pressure, broken bones, all those terrible things that happen over the long term, typically, not out over the short-term. But there's a lot of nuisance side effects that we doctors call nuisance side effects and you patients call, these are horrible and they're ruining my life. We call them nuisance in the sense that they're typically not dangerous compared to diabetes or high blood pressure, or broken bones. And the answer is, there's not a whole lot to do about it. You kind of have to deal with it, unfortunately. We try to hold your hand and get you through it and manage it but there is not a whole lot to do about it, if you're lucky enough to have something like that.

Becky: Great. We got a question via our text box and it says that dexamethasone was recently cited as being able to treat COVID-19. Is it a similar dose used in COVID-19 that we would be taking in pemphigus or pemphigoid?

Dr. Korman: I have seen the data on dexamethasone for COVID, but I must confess I didn't look specifically at what that dosing is. But it's a totally different story, obviously. This is dexamethasone given to people who are super sick in the ICU and have bad, bad lung disease that they're using dexamethasone and it has shown some significant improvement in lung function and shortening these people's bad course. But I don't know the answer to the dose and how you compare those.

Becky: Okay, Liz says that I'm still on treatment with Cellcept for my PV but we'd like to consider getting pregnant. Are there any safer treatments for me, or my baby? Should I get pregnant? And how do the treatments for PV interfere with a woman's fertility?

Dr. Korman: So Cellcept is definitely not a drug that a woman would want to be on if she was trying to get pregnant because it's known to potentially have birth defects. When we say things like potentially have birth defects, we don't know, is that a 1 in 50 chance or 1 in 5,000 chance.

We just know it's a bad idea. I'm quite confident it is not 1 in 50, that was just me talking. It's not that high for sure, but I don't think we know how common it is. That's the problem. In terms of safer therapies for a woman who wants to have a baby, generally, if you have active pemphigus because it's not that common, most of my patients with active pemphigus are not also thinking about having babies at the same time. In the sense of you got to fix A before you start thinking about B. Maybe that's too strong. Probably as the dermatologist managing that patient, I would encourage that woman to say can we hold off a little bit? Let's try to get better and then let's talk about it again. A drug like IVIg, for example, is probably the safest therapy to use if a woman were pregnant and then had active pemphigus but generally IVIG alone doesn't work all by itself. Generally other therapies along with IVIg.

Becky: Great. So, my next question says I am off of all steroids, but I'm still on Cellcept. I tapered down from 2000 milligrams a day to 750 milligrams a day and so far I'm staying lesion free. The question is: Should my goal be to taper off Cellcept completely or should I plan on staying on the drug permanently? I'm under the care of a dermatologist but she's not an expert on this subject and I'm not sure what she thinks about tapering off and staying in total remission.

Dr. Korman: I think that's a great question. So my style and what I do in this scenario is if a patient like that is doing well on 750 and remains lesion free, I would very, very slowly continue to taper. So maybe after 3, 4, or 5 months on 750, I'd take her down to 500, and then I'd wait and see if you're still in remission at 500. Then after several months I might take you down to 250 and if you're still lesion free at 250, what I would do at that point is I would actually test your blood for antibodies for desmoglein 1 and 3 antibodies. And if your blood were negative, I would say it looks like not only are you in clinical remission, but you are in an immunologic remission and I would recommend coming off the therapy. That's been my typical approach over the years. I don't see any reason to do anything differently at this point. But certainly, not everybody does it that way and some people say a small dose of Cellcept has me under control so I just want to stay on a small dose of Cellcept and not take the risk. I certainly have people who remain on 250 or 500 once a day in spite of my telling them, I think we'd be better off if we taper off. And they say, well, I don't want to. My style as a physician is I like the patient and I to have an agreement, and I like us to both be on the same page and I can recommend something, and the patient can say, no thank you. And I'll say okay as long as it's a reasonable idea. Lots of people have crazy ideas, and then I say, no, you're crazy, your idea is crazy, I will not listen to you. That's a bad idea. Here are the reasons why.

Becky: Great. Thank you. Sheila says that she's been treated with 2000 milligrams once a day of Cellcept for bullous pemphigoid for over two years. For the past six months she's been doing much better and has reducing her Cellcept slowly and is now down to 250 milligrams. Is a dose this low even doing anything? Also, her second question is, she's experiencing severe itching

on her feet and palms, especially at night. Is the itching of her skin without blisters related to the reduction of her Cellcept and will the itching ever go away?

Dr. Korman: That's a great question. Sheila, I have no idea. I would say that the itching of palms and soles in pemphigoid is certainly not a common story. There is a variant in pemphigoid that could present with itching in the palms and soles. So the answer is it might be related to her pemphigoid but it might be totally unrelated to her pemphigoid. Tough question for somebody like me to answer on a conference call like this is. Probably a tough question for her doctor to answer as well. If I were her doctor and seeing or I'm not sure I would have more information. But I feel like I have so little information that I can't really answer that one.

Becky: Great. A lot of our patients talk about this insatiable itch. What do you tell patients to help with that itch, whether it's on their legs or their hands, especially associated with pemphigoid? Is there anything over the counter that helps or is there a prescription that can help? There's patients that say that it's enough to literally make them crazy.

Dr. Korman: So the way I would answer that Becky, is it kind of depends on the state of the patient's disease. So if the patient has clearly active skin disease and they have significant itching that's one story. But if they have essentially almost inactive skin disease, and yet they still have significant itching, that's kind of a different story. So, in terms of over the counter therapies there's nothing great. I love the product Sarna which is an over-the-counter product that's got some menthol in it. It's essentially an over the counter lotion, but it's got some menthol in it and it's soothing. Sometimes even refrigerating Sarna can be soothing to people. I will put people on antihistamine so things like Benadryl over the counter, or there are prescription antihistamines that may work a little bit better. There's no simple right answer for itching. That's what I do as a dermatologist, I manage itching all the time. And I don't always manage it very well, unfortunately.

Becky: Great, thank you. That's a big help. And I like the idea of putting it in the refrigerator. That's genius. And I do that with aloe for if you get the accidental minor sunburn, but putting it on all the time is genius. Hacer says, the first sign of my disease was weepy eyelids and then oral lesions. Recently, my eyelids appear to be slightly weepy again. Does this mean my disease is getting worse? And also, how serious is the risk of developing cancer for patients on Azathioprine?

Dr. Korman: Well, certainly I would assume that this patient has pemphigus given the oral lesions, but certainly eye lesions in pemphigus are pretty relatively uncommon, not unheard of, but certainly uncommon. So I can't really comment on whether or not a little bit of weepy eyelids is the beginning of her pemphigus coming back or what. As far as cancer risks with

Azathioprine, all of the immunosuppressive drugs, Azathioprine, Mycophenolate, Cellcept, Methotrexate, those are the main ones that we use all of those drugs in theory suppressed the immune system and in theory might increase the risk of cancer. Very, very, very uncommon. I'm not sure I have seen anybody that I am confident develop cancer and that I feel confident that their cancer has a relationship to their immunosuppressive drug. And I've been using these drugs and doing this for 35 years. So I have treated thousands of people with pemphigus and pemphigoid. I certainly have patients who develop cancer but what I'm saying is, do I think any of them develop cancer because of the immunosuppressive drug, whether it be Imuran or Cellcept or anything else? My answer is I don't think so.

Becky: Great. Thank you. Are testosterone shots contraindicated in male patients that have pemphigus or pemphigoid?

Dr. Korman: Depends what it's for. If it's for a male that has a low testosterone, low T, and needs it, it's medically indicated, that's one thing. If it's a guy that's got to build his muscles, no way.

Becky: Great. Thank you. Brenda says, I'm confused about my immune system. Will an immune system booster make MMP worse? Are there any vitamins or supplements that are safe to take with pemphigus or pemphigoid?

Dr. Korman: So I can understand why you're confused about your immune system. I'm pretty confused about your immune system too. I'm confused about everybody's immune system, and I wish that we had things that we could do to so-called boost people's immune systems so that they could go out and buy something that would make it work better. But I don't think that's the case, unfortunately. I think that the big secret, if you will, the big confusion, the big unknown is, why do I get this disease? Why did my immune system go awry, such that it's attacking me? Why am I getting blisters and my mouth and MMP or in my eyes or wherever I'm getting them? And the answer is, we don't know the answer to that. Many of us are still studying that to try to come up with reasonable answers. But, unfortunately, there's no great over the counter stuff. And I'm sure that no patient really has any or immune stimulants. When doctors don't have good answers to questions, there's always somebody on the web that claims they have a good answer. You can find those ads, all of us have been up at 1 o'clock in the morning and thought stupid things. I've done it too, we've all done it. I would discourage most of you from doing that, even if you're frustrated with us as your doctors, because we don't give you all the answers. There are usually not great answers out there from some company that's selling you something for 20 or 50 bucks.

Becky: Great. Our next question has to do with vitamin D. I've heard that autoimmune disease is associated with low vitamin D levels. I don't think my doctor has ever tested me for vitamin D. So should I take an over the counter dose of vitamin D and if so, how much should I take?

Dr. Korman: So that's a good question. Vitamin D, I think it's not a lot of data in pemphigus and pemphigoid regarding vitamin D levels. I don't think there's a whole lot of evidence in these diseases that we're concerned that low vitamin D levels are going to be playing a role. But certainly anybody who has a level of concern about this can ask their doctor, can you please check my vitamin D level? Then if you come up with a low-level then, it's going to be very reasonable to take a relatively small amount as a supplement. Do I think it's an okay idea to do that if you haven't had a vitamin D level test? I doubt that a small dose of vitamin D is going to do you harm. I just think you'd be better off if you actually get the data, have your vitamin D level checked, and then when you find out it's normal, then you don't have to worry.

Becky: Great, Thank you. Robin says that in February she started to get lesions on her back, torso, lower back and other parts of her body. She's been treating them with Clobetasol and Mupirocin ointment since then and new lesions kept appearing. She had previously been lesion free after 2 Rituxan treatments and 4 IVIg treatments in 2018. Her desmoglein 1 and 3 are now elevated. Though the sores are uncomfortable, she is worried about them getting worse. She's wondering if she needs to get Rituxan infusions again and can you make any other treatment recommendations?

Dr. Korman: Well again, this is the kind of question that would be best answered in the doctor's office with me seeing and examining the patient and trying to understand how bad the disease is. So now I'm not going to answer a question, because it's too specific and it's hard to make a judgement. But the answer is, if the disease is progressing and she continues to get more and more, it would be not unreasonable to do something therapeutically. Whether or not that's something is another course of Rituxan is obviously a more challenging answer that I can't commit to right now.

Becky: Great. Graham says that he used to get 2 to 3 months blister free and then get a flare, but he's having them more regularly now. He has been diagnosed for 7 years and was wondering if this is normal for it to occur more often down the line?

Dr. Korman: I think the answer is everybody's normal for themselves. So sounds like Graham's having a flare now, he's getting them more often and it's hard to know what to expect in the future. In general, if you're having a flare he needs treatment and so I would

encourage him to talk to his doctor and get back in touch and talk about what are the appropriate ways to manage this current flare.

Becky: Great, thank you. Iqbal also asks, is it necessary to have a maintenance dose of Rituximab after 1 year of 2 doses of 1000 in 2 weeks, and how many milligrams as a maintenance dose?

Dr. Korman: Nobody knows the answer to that question. It's a great question. If the patient is doing great, I certainly would not do it. But I've certainly talked to other members of the Medical Advisory Board, other people like me, who do a lot of this, and there is not consensus on this. Different people have different opinions about it, and there's not enough data to know the answer.

Becky: And I imagine a lot relies on what you've experienced, and what you've seen work in your own practice as well, and that influences what happens with the next patient.

Dr. Korman: Totally.

Becky: Richard asks, can you talk about the low dose naltrexone as a treatment. Is it effective or an alternative to prednisone or Rituxan?

Dr. Korman: I've actually used low dose naltrexone for a few diseases. I've never used it in pemphigus or pemphigoid and I'm not aware that anyone else has talked about it or used it so I have no comment, I don't know.

Becky: Great! Thank you. Amal asks, how long does it take to see positive results on Dapsone and methotrexate? The doctor wants to change to Cellcept, so how long for a positive effect with this medication? And what is the trigger point for us to jump from one treatment to another treatment?

Dr. Korman: Did Amal tell you what disease he has?

Becky: He did not, I'm guessing probably pemphigoid but I can't say that for sure

Dr. Korman: So that is important. So that's what I was going to jump on. That's what I would guess too. If it's pemphigus, that not a great idea, we don't use a whole lot of Dapsone in pemphigus. I mean occasionally, so the answer is, if he's not getting better with what he's on, then maybe it's time to step it up. And, again, exactly what to step it up to, depends upon how severe, how much disease activity there is.

Becky: And it takes about 6 to 8 weeks, right, for Cellcept to see an effect if it's working or not?

Dr. Korman: At least, if not more.

Becky: Okay, the next question says that we have a question about the amount of Rituximab you should receive for the 4 different times. Is it, 250 milligrams and four doses? Or is there another way to keep heart rate down during infusions?

Dr. Korman: So if you're getting the once a week Rituxan for 4 weeks, then the dose is actually based on how much you weigh and how tall you are. It's dosed based on what's called your body surface area, it's a calculation. So if you are five foot and way 98lbs you're gonna get a certain dose and if you're six feet 4 inches and you weigh 260lbs you're gonna get probably 2.5 times that dose. I made that number, but you're gonna get a lot more. Yeah. So, it's very much dependent upon your body surface area, which is a calculation based on your height and weight.

Becky: Great, Thank you. Barbara asks, is MMP an autoimmune disorder that a dermatologist can treat or will my periodontist treat the symptoms? Her dermatologist's office insists this is a periodontal issue and that the low dose steroids rinse from her Periodontist, has no effect on her blistering gums.

Dr. Korman: Yeah, unfortunately that's an example of a dermatologist that just doesn't have a comfort zone for this disease. Obviously, Becky, as you know, serving in the role that you do at the Foundation, there is a good amount of people who are not comfortable taking care of this disease. Obviously, if the patient lives in an area where there's other options in terms of practitioners, I would certainly encourage them to find one. And you can figure out, Becky, where they live and you can help them hopefully find somebody. But if you live somewhere where there's no access, it's a challenge because I do not think that generally speaking,

periodontists are really comfortable treating this or if they claim they are, most of them don't have enough good experience doing it.

Becky: We COVID-19 and this is just my question, with COVID-19 has telemedicine made it easier for patients who live in rural areas to contact you, or is it still a little bit of a hassle and some hoops that need to jump through to be able to get a telemedicine appointment?

Dr. Korman: It's great that you brought that question up because I was thinking of actually bringing it up myself and saying that I am actually right now starting to look into that. The answer is, I have not done anything. And the answer is the telemedicine that I'm doing now almost entirely because I've been practicing for 35 years, which means I'm not 19 years old and I'm concerned about my health minimizing my exposure to the live patients. I'm doing telehealth, almost solely, and I'm now considering the idea of looking into the idea of trying to make myself available for patients in other places rather than just the metropolitan area of Cleveland or a 50 or 75 mile radius, or 100 mile radius. Whatever it is. But there's all kinds of rules and regulations, so I haven't started to look into them yet. So could I see people in rural Kentucky virtually, and then could their insurance pay for them to see me, and all those kinds of things. What I'm gonna do is, once I figure it out, Becky, I'm gonna let you know, and if you want you can certainly make that known to the community that I can see people in the following states and that I would be happy to do. So far I have not found a whole new coterie of people from afar, but I think it's a great idea. And I think it would help a patient like this enormously. Sometimes the challenge is, though, that, if we haven't been seen by somebody who knows about the disease, they're probably going to need to visit nonetheless. They're going to have to traipse up to Cleveland from wherever they are, at least once, which they might be willing to do.

Becky: Absolutely. And I think that brings up another interesting point, in our community is that the undiagnosed community, where there is a suspect that they have the disease. But with dental offices being closed right now and slowly starting to open in some areas of the country and even dermatology offices. Getting that biopsy is a tremendous handicap right now. So what can be done for those patients who symptomatically or that doctors feel might have pemphigus or pemphigoid? Is it safe to start treatment, or what happens in those situations?

Dr. Korman: An amazingly wonderful question with no great answers. It's going to be comfort zones of individual physicians. As a general rule, most of us are a little gun shy to say, I think that's what you have. Here you go, let's put you on some super potent medicines and hope for the best. Right? So it's a tough question and I don't have any simple answers and I can't tell

you what I would do routinely. I think routinely I would make each decision on a one-on-one basis.

Becky: Sure. Thank you. That's an honest answer so I really appreciate it. Our next question comes from Vicki. And she says, what is your opinion regarding the Dexamethasone oral elixir? Does it help to treat MMP? She says, my mouth blisters seem to become irritated and swollen after swishing for 5 minutes 3 times a day. And she's been using it since January without resolution of her symptoms.

Dr. Korman: Well, if she's doing worse using this, then it's time to stop using it. It may not be that the dexamethasone elixir is actually making it worse, it just may be that she's getting worse and she's not getting better because she's not on the appropriate therapy and the appropriate therapy means a more aggressive therapy than just a swish and spit. This is a systemic disease, and typically what I would call a topical treatment doesn't do the job. So I think she needs to be treated a little more aggressively.

Becky: I've heard a doctor saying, I don't remember which doctor it was but if you use a topical medicine, you treat the lesion. If you use a systemic medicine, you treat the disease, is that a fair statement?

Dr. Korman: Sometimes the topical medicine doesn't even treat the lesion. So certainly the systemic medicines treat the disease, that is absolutely the case.

Becky: Our next question is from Mo and he says, if I'm taking a low dose prednisone, less than five milligrams a day, doxycycline and Nicotinamide for remission for therapy for pemphigoid, over the next couple of years is it an acceptable low risk medications with minimal side effects and infection issues, or should I be converting to Cellcept or get out of the prednisone altogether.

Dr. Korman: Well, my goal is always to get people off prednisone. Am I able to do it always? No, but I always prefer to get people off prednisone. So in general, if somebody's on say, prednisone and Cellcept the way that I approach them and the way most of us approach it is, let's get you off prednisone. Let's taper and taper until we've got you off prednisone. So now you're just on Cellcept. So that would be my scenario here. The doxycycline and the Nicotinamide is not particularly immunosuppressive so that doesn't concern me at all, but it's the prednisone. We didn't specify what dose, right? So the higher the dose, higher my level of concern is.

Becky: Great. Our next question asks, do you feel there's an association with certain foods and PV flares, including foods from the allium family, or bananas, avocados, nightshade vegetables, etcetera, and is sugar very bad due to the impact on inflammation?

Dr. Korman: Sugar is very bad for the fact that we have all these people on prednisone and way too many of them get insulin. They get insulin resistant and higher risk of diabetes. I don't think that I buy the kind of lay story that's out there, that sugar increases inflammation and that it's going to make things worse. I think sugar is not good for us, in general. As a pre-diabetic, I can certainly attest to that. A pre-diabetic who doesn't have pemphigus or pemphigoid but a pre-diabetic nonetheless. As far as night shades, vegetables, that whole world, there's a whole set of data out of the European literature that says that many of those dietary products can make pemphigus worse. And I'm not sure that I buy that either.

Becky: Great. There's also a question about gluten, is there an effect on the disease's if you cut out gluten from the diet?

Dr. Korman: I have not seen any data on the value of gluten. I think gluten is just like the world's most popular thing to eliminate from your diet to solve all of your world's problems and I don't think that's correct.

Becky: Great, thank you. George is asking, when you have a serious underlying illness, such as lung disease, are treatments such as Rituxan or Imuran used? When your immune system is reduced, are your pneumonia chances increased?

Dr. Korman: Yeah, absolutely. If you're immunosuppressed you have a higher risk of infection, and pneumonia is a serious infection, so, definitely, that's the case. So it's a risk versus benefit kind of story as to whether or not it's safe enough to do this and do that. A lot of times I work with the patient's other physicians, their primary care doctor, their internist, their infectious disease doctor to say here's what I need to do, what do you think? Do you think this is an okay idea? I need to put this person on 60 milligrams of prednisone. And the other doctor might respond, does it have to be 60? Could you get by with 30? It's a negotiation and I listen to the primary care doctor and I listen to the other sub specialists, and then we work together. Then two weeks later, we might have to revisit and say, it's not cutting it, I tried your 30 milligrams and they're getting worse. I need to go up, is that okay? It's a balancing act. I'm old school, I actually talk to my patient's other doctors. I feel it's critical to make that happen. And it's also very hard, and especially a lot of the younger doctors you can't talk to, you can't get near them. They won't return your call or their staff won't let you near them. So it's a challenge, but I think,

especially with our patients with pemphigus or pemphigoid who are on aggressive medicines, it's a critical part of their care.

Becky: Great. So we have a couple of questions that have come in regards to this. What is the outlook for the CAAR T therapy in our disease space, and what do you see as the most promising 1 to 2 drug candidates in the research and development area right now?

Dr. Korman: So I think the CAAR T therapy that's being developed by Dr. Payne and her group at Penn, is extremely exciting. I think that it's a great basic science translation into the clinical realm and she's studying this and we're going to have some answers, and I'm very excited about it. But it's a slow process. Any new therapies they're very, very slow on the horizon. In terms of other exciting new therapies, there's a trial that I imagine, of the 83 people on the call, I bet you, 10 or 20 of you guys have heard about it, maybe 1 or 2 or even on the therapy. It's an oral drug, it's called a BTK inhibitor. And it's being studied in a big trial and is in the last stages of the trial called phase three trials. So after the results of this study are completed, if the results are promising enough it may actually get on the market a few years from now, 2, 3, 4 years, something like that, perhaps. And if it works as nicely as it suggests that it might, it will be a very exciting new therapy in terms of how it falls into the mix with Rituxan and prednisone, and other steroids sparing agents. I don't think any of us can answer any of those questions now. Those are all the follow up questions that everyone will want to know and I don't know the answer right now.

Becky: Great, thank you. Barbara says that she has bullous pemphigoid and she's on IVIG every four weeks for two years and still getting lesions. She's also on Imuran and her white blood cells dropped to 2.5 to 3. Have you had patients on Rituxan and IVIg where this is a common thing to have her white blood cells drop?

Dr. Korman: So, I heard two different things. I heard that she was on IVIg and Imuran and that she dropped her white cells, which makes sense. Then at the end of it you said I had people on Rituxan and IVIg, who dropped their cells. So that's two different things, right. So Imuran is known to lower the white blood count, totally normal. We certainly have to watch it and I'm sure her doctors are watching it very closely. It's definitely low, but it isn't necessarily so low that it needs to be instantly discontinued. It's a fine line, walking the fine line and you watch it very closely and monitor it regularly, every two weeks, every four weeks and see how it's doing. So I wouldn't necessarily institute that you have to stop your Imuran and tomorrow because your white blood cell count is below the normal range.

Becky: Okay, this question is from Melinda. How do we treat lesions at home? My father is 66 and is rapidly deteriorating. He has covered from scalp to foot and the blisters look like second

degree burns. He is unable to eat and hold things in his hand. He's unable to sleep related to blisters just covering his back. How do we dress or bandage these large areas?

Dr. Korman: Sounds like her dad is in a serious state, and not necessarily somebody that should be managed at home. But, of course, we didn't hear about what other treatments that he's on, and what the choices are and what needs to be done. But, this sounds like a patient that might need to be admitted. We don't do that a whole lot, but it sounds like this patient is very, very severe. I don't think there's any simple, easy at home remedies that I can recommend over the phone here.

Becky: Great, thank you. Our next question says I've found some information about the maddening itching being related to an undiscovered variety of shingles saying that it is the virus attacking the nervous system. I'd like to share this information if it could be helpful. And is it true that pemphigus affects the nervous system as well?

Dr. Korman: Well, I don't think there's any definitive information that there's a connection between the skin condition, pemphigus and the nervous system, at least nothing that comes to mind right away. Certainly a disease like shingles is a skin disease, but it's a virus that is hiding in the nerves and then when it gets reactivated, it comes out as a skin eruptions. So that's the connection between the skin and the nerves. But in terms of pemphigus I don't believe there's much of a connection there.

Becky: Great! Another question comes from Deborah and she says, I was diagnosed with MMP over a year ago and more recently with chronic lymphocytic leukemia. In your experience have you seen a linkage between these diseases?

Dr. Korman: No, I have not. But certainly people can get things and they don't always correlate. Lots of us have various medical conditions and not every single one is related to the other. People just get unlucky and get stuff. I don't think that's a relation between MMP and chronic lymphocytic leukemia.

Becky: Great, thank you. I just want to check with you, we have some more questions that are coming in fast and furious and I know our hour is up and I want to be respectful of your time. Would you be willing to stay on for a few more minutes and answer just a couple more questions?

Dr. Korman: Sure.

Becky: Great. Steven says he has cicatricial pemphigoid and I am taking 150 milligrams of dapsone and my blood work shows that my hemoglobin and hematocrit continue to drop below the normal range. My doctors suggest continuing the dosage, but should I start taking iron supplements?

Dr. Korman: Yeah, typically anemia, low blood count due to dapsone is not corrected by an iron supplements. My rules for when I worry about the low blood count caused by dapsone is when the patient says, I'm totally wiped out. I can't function. Or if the numbers get really, really low. If Steven's doctor is comfortable enough with the numbers, I don't think that's worthy of panic, and I don't think there's any benefit in iron whatsoever.

Becky: Great. Thank you. Sue says that I have developed osteoporosis after seven months of high dose prednisone for PV. Do you have a recommendation of a best osteo med if she developed osteoporosis from steroids?

Dr. Korman: So the standard drug that we use is called Alendronate or the brand name as Fosamax. But certainly would not be unreasonable for her to see an endocrinologist or a rheumatologist. Usually endocrinologists are the best specialists to manage osteoporosis. And that they would be in the best scenario to make the best decision because there are many other drugs besides this Alendronate or Fosamax. As a dermatologist, even though I use a ton of steroids and have been doing it for 35 years, I'm not an expert in choosing which one of those drugs to manage osteoporosis would be best for an individual patient.

Becky: Great. Our next question asks, does pemphigus cause lesions inside the nose and what is the best way to help those lesions to heal?

Dr. Korman: Absolutely, pemphigus can cause disease in any so-called mucous membrane. The nose is a less common one. The way to heal it is we've talked about it before. You manage the disease systemically with a systemic treatment. You don't put that drug that Becky Strong can't pronounce inside the nose. Remember that one. So that's a common drug that would be used inside the nose, thinking that's going to help. Typically, if there are lesions in the nose, nasal erosions, similar to oral erosions, it's not going to do anything. The patient needs to be treated systemically.

Becky: Great. Is there anything and just I remember when I had active disease and I had lesions in my nose, it was just irritatingly hurt. I used a saline spray and I didn't tell my doctor, but is that an okay thing to use to try and keep it a little more moist?

Dr. Korman: Yeah, it's probably harmless, as long as you're not drowning yourself in saline.

Becky: Kathleen says, I've had a severe flare of PV in early May preventing me from eating and drinking for three days. Then I was on a liquid diet for 10 more days. I started 80 milligrams of prednisone daily for a month, and now I'm on 50 milligrams of prednisone daily. How fast or slowly should I be decreasing my dose and my current plan is to be decreasing by 10 milligrams every two weeks.

Dr. Korman: So I am a strong fan of not doing that approach. So I'd like to taper the dose of prednisone based on how a person is doing not based on some random numbers that a doctor generates and says, here's your tapering regimen do this, and then do this, and do this. I bring the patient back, or I talk to them and I say, well, we did this. How are you doing? You are doing better, good, let's lower it a little. If you're not doing better, stay where you are. You're flaring, maybe we have to go up a little. So, there's not a simple, easy answer for it. And if this person is only on prednisone you probably need to be on something else as a steroid sparing agent in addition to prednisone. Otherwise, you're gonna get to some level of prednisone probably too high of a dose still, and they're gonna probably have a flare.

Becky: Great. Thank you. Our next question asks, what is your advice to control weight gain that happens with steroids? Things have gone very bad for me in the last four months since I've been diagnosed because of the Prednisone.

Dr. Korman: So, that's a known side effect of prednisone. That fits into my category of what I again as a doctor call nuisance side effects of prednisone. Certainly it is a nuisance if it's you, that's gaining the weight and it's very hard to lose weight while one is on prednisone. There is no simple answer to this question. The answer is you have to be on a steroid sparing regimen that will help to get you off prednisone that you can then be able to start to lose the weight again. That's the key.

Becky: Well, and I think prednisone too causes fat deposits, whether or not you are controlling your diet, right? And water retention and sorts of unpleasantness.

Dr. Korman:Absolutely.

Becky: Would you mind taking a live question? We have somebody that had their hand raised. Aruna I have you unmuted, but it looks like you have yourself muted. If you'd like to ask a question, please go ahead. Well, it looks like she's not answering, so, Dr. Korman I appreciate you going over on time with us, and thank you for being with us. As usual, I learned a lot tonight. You always have great information for our community, even though we're asking the toughest questions. Thank you everyone tonight, for joining us as well. And of course a big thank you to our sponsors Genentech, Principia Biopharma, Argenx, and Cabaletta Bio for helping to make today's call possible. I have a few announcements before we go. Our next Patient Education Webinar will be on Monday, June 22 with Dr. Ricardo Padilla, Associate Professor at the school of Dentistry at the University of North Carolina at Chapel Hill and Jennifer Harmon, a registered dental hygienist and Assistant Professor in the Dental Hygiene Program, Department of Periodontology at the University of North Carolina at Chapel Hill to answer your questions about the Effect of COVID-19 in pemphigus and pemphigoid Oral Care and Oral Health. You can register online today!

We want to thank everyone that donated to the IPPF's Hope Fund and to our generous matching partners, Principia Biopharma and argenx for helping us exceed our goal of raising \$40,000. With your generous support we are able to keep hope alive and continue supporting you and our community in the way you have come to expect!

Also, for those of you that do online shopping through Amazon, you have the unique opportunity to give back all while shopping. Visit smile.amazon.com and search for the International Pemphigus and Pemphigoid Foundation as your charity. Amazon will donate 0.5% of all purchases made through amazon smile to the IPPF.

If you have not registered yet 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 e-mail me, 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 with the survey following this call. Thank you everyone, good-bye.

