COVID-19 Vaccines and Updates- Patient Education Webinar Transcription

Becky: Welcome, everyone. This is the COVID Update and COVID Vaccine Patient Education Webinar. We are now being recorded. I'd like to thank you for being on the call with us today and a big thank you to our sponsors, Genentech, 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, everyone's situation is unique. The IPPF reminds you that any information found on the internet or during any of our presentations should be discussed with your own doctor or health care team to determine if it applies to your specific situation.” Before we begin, I just want to start with a quick poll so if you wouldn't mind answering a quick question for us. If you've had COVID-19, how severe were your symptoms? If your symptoms were mild, you had a low grade fever, nasal, congestion, sore throat, dry cough or mild body aches. Moderate would be considered a fever of higher than 100.4, a persistent cough or temporary sharpness of breath. Or were your symptoms severe where you had constant trouble breathing, persistent chest pain confusion, or needed hospitalization? This information is important to share with researchers and doctors in our community so that we can learn more about how COVID-19 affects people with pemphigus and pemphigoid. And while you are answering that poll, I'm just going to introduce our panelists today. You should recognize them from past COVID-19 calls. Dr. Maverakis is an Immunology researcher at the University of California, Davis Department of Dermatology. There, he runs a clinic that specializes in the treatment of patients with severe immune-mediated diseases involving the skin. Next, At the University of Pennsylvania, Dr. Payne is a Professor of Dermatology, Director of the NIH-funded Penn Clinical Autoimmunity Center of Excellence, Core Director for the Skin Biology and Disease Resource-based Center, and Associate Director of the Medical Scientist (MD-PhD) Training Program. Dr. Payne’s clinical practice specializes in the diagnosis and treatment of patients with autoimmune blistering diseases. Our third panelist is Dr. Mary Tamayko. She is a physician scientist who specializes in the diagnosis and treatment of autoimmune blistering disease and other immune-mediated skin disease. Dr. Tomayko is a director of dermatology education at Yale University School of Medicine.

Becky: So I'm going to close our poll, thank you for participating. It looks like about 63% of those who've had COVID and are listening had mild symptoms and about 29% with moderate and 5% that had severe disease. Thank you for sharing that. Now, before we get into the questions, I just want to go over some housekeeping items. (REVIEWS HOUSEKEEPING…) We have received many questions, so we'll try our best to try and answer as many as we can. Now it is my pleasure to introduce to you Dr. Payne, Dr. Tomayko and Dr. Maverakis to present to you information about COVID-19 and COVID vaccines and to answer your questions.

Dr. Maverakis: Sure. Thank you for inviting me, again. It's always nice and it's nice seeing patients and them saying, hey, I signed up for your webinar. I guess you're reaching lots of

people if our patients are even telling us about this. Can we go to the next slide or do I have any control over the slides? So I'm gonna start off by talking about vaccine efficacy, then Dr. Tomayko is going to talk about safety, then Dr. Payne is going to discuss research on pemphigus treatments and vaccines and then we're going to be open up for a panel discussion. Usually, the interesting questions come in during the panel discussion. So please wait until the end because that's probably where everything is going to become clear.

Dr. Maverakis: You probably know there's 3 COVID vaccines. They're fairly similar in efficacy and timing, but there are some significant differences. The Pfizer vaccine has been approved for kids 12 and older and for adults from children. It's two shots separated by three weeks. And usually, people are considered protected after about 1 or 2 weeks after the second vaccine. The Moderna vaccine is for people 18 and older and that's also two shots. But this time it's separated by four weeks and usually you're considered protected two weeks after your second shot. And then finally, the Johnson and Johnson is just the one shot vaccine for people 18 and over and usually you're considered protected after two weeks. Both Pfizer and Moderna are RNA based vaccines and Johnson Johnson is a virus based vaccine. So let's go to the next slide.

Dr. Maverakis: So how did we get these vaccines so fast? There's something called emergency use authorization and this is during a public health emergency. Emergency use authorization allows the FDA to give approval for unapproved drugs and these are things that could be used to diagnose and treat or prevent various illnesses. This is not that the vaccines or the drugs have not been extensively studied, there are many, many criteria that have to be met. In fact, before the vaccine was released, they actually changed some of the criteria and made them collect even more data. So, we do have a lot of data on these vaccines, even though they're officially not approved under the normal pathway. So, all of them have this emergency use authorization, which is a kind of approval, but it's not official approval, which we'll talk about in a little bit. They've all demonstrated very good efficacy. They've all been shown to have benefits that likely outweigh the risks and there's adequate and approved alternatives available. We didn't have a vaccine, we needed a vaccine, and we couldn't wait forever before we got these vaccines. I want to point out that usually, adverse events associated with vaccines occur in 30 days. Before these drugs were approved, they collected, I believe 60 days of follow-up on the patients. So there was plenty of time for, at least the most, common and severe adverse events to present themselves within those 60 days. To gain full approval, basically you need six months of follow-up data. And, I told you that they had about two months before these vaccines came out. Now, the Pfizer and Moderna vaccines are expected to apply for this full approval, which is called a Biological License Application that they're submitting. I expect that both these vaccines will be fully approved in the upcoming months. Next slide.

Dr. Maverakis: So, how do the vaccine's differ in the one mile view of them? They all have proven to be pretty safe. They all lower the risk of hospitalization, they all lower the risk of death, and they lower the risk of severe illness. The main difference in terms of the dosing is that the Johnson and Johnson just has one dose and the Moderna and Pfizer are given in two doses. Next slide.

Dr. Maverakis: If you look at the trial results, it looks as if the efficacy is slightly different. It looks like the Johnson and Johnson has a little bit less ability to protect you from a symptomatic infection, but they all seem to be pretty good at preventing death from COVID and they all seem pretty good at preventing severe disease with Pfizer and Moderna, possibly being a little bit better. Of course, the studies were done under different conditions. So, it's hard to say exactly that Pfizer is better than Moderna but I think both Pfizer and Moderna have better efficacy than the Johnson and Johnson vaccine. Next slide.

Dr. Maverakis: That was the trial data and in the US, the data's never going to be quite as nice as the trial data, where everything is very controlled. You can imagine that people in the real-world, people getting these vaccines might have some issues with their immune system. The very, very elderly are not going to have the same repertoire of B cells and T cells as somebody in their 70's or especially 19 or 20 year olds. As you get up in age, your immune response is going to differ. Also, you can imagine all the people who have coexisting conditions that might affect their immune system or people who are on immune suppression. So it would be unreasonable to think that you're entirely protected if you get one of these vaccines, if you're on some amount of immunosuppression. In the real-world, it looks like these vaccines are very good, again, at protecting from death from COVID, and they seem to be very good at preventing severe disease. Some people are still getting symptomatic infections but that seems to be around 10% or less.

Dr. Maverakis: So how do you know if the vaccine was effective? Now, I think this is a real issue because I'm in support of dialog between conservatives and other groups on vaccines and who should be vaccinated and who shouldn't be vaccinated. And I think these are all relatively important discussions to have. But I do believe that there is this narrative out on some of the radio shows right now that says that, basically, if you're vaccinated, you're protected and you shouldn't be wearing a mask anymore or something to this effect. That is somewhat true. So, if your immune system is healthy, most likely, you're pretty well protected. But obviously, that's not all of us and obviously there are many people on this call who are on some form of immunosuppression or had some immune suppression in the setting of within a couple of months of receiving these vaccines. So, your protection is probably not the same as other people. And as we get into the stage where there's going to be fewer people wearing masks, this is something to know, that possibly, you're not going to be as protected as some of these other groups. So, if you're not on any systemic immunosuppression, even if you have

pemphigus, most likely you're going to be protected if you get the vaccine. But it's hard to know if you're protected. The reason being is that we don't have any test that says that you have sufficient protection from this virus. The tests out now that look at antibodies don't really tell you what your level of protection is. Now, of course, if the test comes back entirely negative, then that probably means you don't have much protection against the virus. But definitely for the vaccines, the jury's out in terms of the ability to test for how well the vaccine worked in you because the antibody tests are not well universally accepted yet. So, for example, in our hospital we were offering it, then we stopped offering it, and I don't even know what the current status is. There's no specific measure of protection as far as we have, based on what we know today. Also, if you're getting an antibody test, that's not going to necessarily tell you how your other cells of the immune system are responding to the virus. There's all these different viral proteins, the immune system has different types of cells that respond to different different epitopes of the protein. You have your antibodies that make an antibody response and those antibody responses protect you because they prevent the virus from entering the cell. But there are a bunch of other cells like T cells, and these T cell responses, which are going to be also important if you get the infection, are not measured by antibody tests. And also, the specific part of the domain is not necessarily measured by all antibody tests. It's not necessarily that you just have an antibody to a certain protein of the virus, it has to actually be the right region of the protein of the virus to give you full protection. So, in summary, I don't want to lead you down any weird ideas right now, but I wanted to let you know that if you are not on any systemic immunosuppression and you have received the vaccine, most likely you're protected but there's no real good way of testing to make sure that

Dr. Tomayko: All right, thank you Dr. Maverakis, hat was very clear. So, now we'll talk about vaccine safety. So, next slide, please. One question that people are asking is: what are vaccine side effects? Also, what's the difference between a normal side effect and an abnormal side effect? Can side effects be serious? Am I going to be at risk for side effects? So side effects, reactions to the vaccine are common. You can imagine that when children get vaccinated, it's not uncommon for them to get a fever afterwards. They might get some swelling, a baby might get swelling in their leg where they got a vaccine. These sorts of vaccine reactions are a side effect, but they're not worrisome side effects, they are not problematic side effects. So with these vaccines it is quite common to have pain, redness, swelling, sometimes even itching at the vaccine injection site. It is quite common, especially after a second dose to have fatigue, fever, chills, even shakes. Muscle aches or pains, headache, nausea. Some people even get belly pain. So these effects are quite common. Not everybody has them, some people have no reaction at all, but these kinds of effects are things you should expect. They are self resolving and limited. Next slide, please.

Dr. Tomayko: There are some very rare, serious side effects. So let's walk through what they are. With the J&J vaccine, which is this adenovirus based vaccine, there are rare clotting disorders that have been observed. These clotting disorders are most common in younger women or women under the age of 50. So that is a potential risk. It's important to balance that

against the fact that we know COVID-19 infection markedly increases your risk for having serious blood clots. So yes, the J&J vaccine does have a risk of blood clots, that's very rare, particularly, in younger women, but still the risk of the same sort of problem with the infection itself is much higher. Could you advance, please, Becky?

Dr. Tomayko: Another thing to consider is, especially in young men, young boys, mostly adolescent and young men, young men like military age recruits, it is possible to get inflammation around the heart. For boys, age 12 to 16 this is something to consider with either the Pfizer or the Moderna M-RNA vaccines, there is a very, very low risk of what we call myocarditis. Again, infection, actually getting COVID-19 disease carries a risk of heart inflammation and sudden death.

Dr. Tomayko: What are the recommendations? So, the IPPF asked all of the advisory board physicians to weigh in on what our opinion was about the risks and the benefits of the vaccine. The IPPF Advisory Council came out with a very strong statement saying that we really do support patients getting vaccinations. Importantly, there is no clear evidence that vaccination will flare pemphigus or pemphigoid. We do know that vaccination generally decreases the risk of COVID-19 disease, and hospitalization and death. Vaccination is critical if we're going to re-open society. And long infection, long COVID is an issue. So there were several specific questions that people asked that I think really boiled down to these, but let me just kind of go over some of them again. So what are the risks associated with the vaccine? Mostly it sees annoying side effects that are self resolving. However, there is a small risk of blood clotting if you're a younger woman with J&J and there's a small risk of inflammation around your heart if you're a boy. We don't have evidence that you are at high risk of having your disease get worse if you're immunized. There are many, many, many questions getting down to that point but there is no clear risk of worsening your disease. Is there anything I can do to avoid a flare ahead of time? No, because we don't think you're going to have a flare from the vaccine. Will. How long after getting the vaccine will I be susceptible to having a flare? Again, we think that the things that are controlling your disease activity are not going to be directly related to the vaccine. Is getting COVID more dangerous than the possibility of the side effects from the vaccine? Absolutely, handsdown, unequivocally your risks from getting COVID-19 disease are much, much, much higher than your risks of having a side effect from the vaccine. Can we go on to the next slide, please?

Dr. Tomayko: So people have questions about, I have allergies, can I get the COVID-19 vaccine? In almost all cases, the answer is yes. Go ahead, please.

Dr. Tomayko: There are a few situations that are different and we'll go through those in detail. I'm sure you have read that there have been some situations and people having a severe anaphylaxis reaction after getting the vaccine. It's very, very rare, but because it happens, the guidelines say when you get your vaccine there's a 15 minute observation period. You'll go into

your site and there will be a big waiting room, maybe it'll be the high school gym and everyone waits there for 15 minutes before they leave. There will be an emergency setup to deal with anyone who has this effect. But I'll tell you in our entire county where we have now vaccinated close to 70% of the population, we have not had any anaphylaxis reactions yet. But that is a potential risk that we all take very seriously when we're delivering the vaccine. Can you advance, please?

Dr. Tomayko: So what if you already have a history of having severe allergies, nut allergies, bee pollen allergies? What if you already carry an epi pen? What if you've had a severe reaction to another vaccine before? What if you've had a severe allergic reaction to a medication? Well, in that case, you get put into the group that needs to wait for 30 minutes. And again, it's the same thing. You sit in the high school gym and you wait for your 30 minutes instead of your 15 minutes. And if you advance the slide we'll go through a few more details about allergic reactions. What kinds of allergic reactions and histories of allergies would preclude you from being able to have the vaccine? They're very rare. But what are they? So if you have a history of a severe or immediate allergy to polyethylene glycol or polysorbate-80, then you may not be able to get vaccines, but again it's not all of them. So now you might have to choose which vaccine you're going to get. If you have a severe allergy to polyethylene glycol, that can preclude you getting a Moderna or a Pfizer vaccine, but you would then be eligible for J&J. If you have an allergy to polysorbate-80, then that precludes you from getting J&J, but you can get Moderna or Pfizer. So, how would you know? Maybe you don't even know what these words are. Polysorbate-80, which is in the J&J vaccine, is in a number of different vaccines and medications. Allergies are very rare, but it's in influenza and hepatitis vaccines, the new shingles vaccine, Shingrix. It's in a number of medications that we use for skin disease like Stelara or Remicade, Tremfya, Simponi, and it’s in Rituximab. So, if you have a severe allergic reaction to Rituximab it's worth asking your doctor if that allergy was thought to be due to the polysorbate-80, or more likely the reaction was due to something else. But that's worth asking about. There are some polyethylene glycols that are in some medications that you might be aware of. Most likely Miralax, if you have a severe, life-threatening allergy to Miralax then that's worth asking you're a doctor about. But, again, because we have a variety of vaccines that are available, you should be able to, even if you have one of these severe allergies, you should be able to get a different type of vaccine. Can we go ahead, please?

Dr. Tomayko: So, if I have a choice, is there a brand that's better? I would say no, there is not one brand that is clearly better. Their efficacy is incredibly similar. Their risks are perhaps slightly different, but no one more serious than another. So, all of the vaccines are effective and very much their benefits are so high and their risks are so low that really, they're all equal. Could you go ahead, please?

Dr. Tomayko: When should you consider having Moderna or Pfizer, which are the two shot vaccines instead of J&J? Consider that if you're a woman under 50 or if you have a clotting disorder, because those are potential rare side effects of the J&J, consider doing the Moderna

or the Pfizer or if you've had a severe allergic reaction to Rituximab. But again, talk to your doctor first. Consider getting Madonna or Pfizer if you've had an allergic reaction to other vaccines before. Then on the flip side, you should consider getting the J&J, if you've had a severe allergic reaction to Miralax or any injectable glaucoma medications or if you only have time to get one shot because it's more convenient. People asked, specifically, Is there a brand that's preferred for pemphigus or pemphigoid patients? No, there's not. These are all good vaccines. What's the difference between the different brands? The main differences are what Dr. Maverakis spoke about which is the Moderna and the Pfizer vaccines use this M-RNA technology versus the J&J uses something called adenovirus technology. It's a different way of developing and delivering the vaccine. All three vaccines, prime an immune response to the same part of the virus, which is probably why they all have such equal but also such excellent efficacy. They're all going to stimulate immune responses against the spike protein of the virus. And just to reiterate, because again this is another question, is there one that's more effective than the others? The answer is no. So that's it and we can advance to Dr. Payne.

Dr. Payne: Thank you so much Emanual and Mary. That was a great introduction covering the efficacy and safety. So now, we'll move on to questions that you had about what research is ongoing on pemphigus and pemphigoid treatments and how it affects the vaccines. So, we can go to the next slide.

Dr. Payne: A lot of questions came in about how do the treatments for pemphigus and pemphigoid affect the efficacy of the vaccine? The answer to this is always that systematic studies are needed. Ideally, you will have thousands of patients who are on various different forms of therapy, we will follow them out over time, we'll see what the responses are and then we'll see what the actual incidence of COVID and severe disease are in those populations. Right now, we don't actually have year-long follow-up data on all the pemphigus and pemphigoid patients who'd been immunized but we do have emerging data from smaller studies. So that's basically what we're reporting on here. There have been two publications that are highlighted on the bottom of the slide. There have been a few others as well, but I just wanted to summarize what it's shown so far. Basically, if you're on prednisone or other forms of steroid, there is a reduced efficacy of the vaccine. On the whole, they've noticed in some of these studies that there could be as much as a 10-fold lower antibody response after vaccination if you are on a steroid dosage even 5 milligrams or higher. Mycophenolate, Azathioprine and Methotrexate they've seen reduced efficacy. It seems to be about 2-3 fold lower in regard to the antibody titer. These studies have largely only looked at antibody titers and not T cell responses, which we'll get into in just a little bit. Then Rituximab is associated with reduced efficacy and this seems to have the greatest effect on antibody levels, which is to be expected because basically the way Rituximab works is it wipes out the B cells that are producing the bad antibodies in pemphigus and pemphigoid but it also stops for making other types of antibodies, including antibodies against the COVID vaccine. This is the population where they've noticed the greatest effects. When they've looked at Rituximab treated patients they noticed over a 30-fold lower level of antibody titers in Rituximab treated patients. Conversely, if we look at IVIg, there's unknown impact on the vaccine, however, there have

been some studies on IVIg and other vaccines. A lot of times that only becomes relevant because I don't know if everybody knows this, but how IVIg is actually produced is by pooling good antibodies that are collected from hundreds of different donors. If that donor has actually been exposed to COVID-19, which is currently relatively rare, because a lot of times they're going on batches that were collected months and even years ago, then it only will be predicted to have an effect on the vaccination if the person that donated had COVID before. If that's the case, the concern is if there's a lot of circulated COVID antibodies around it could actually neutralize the vaccine and prevent its efficacy. So, in general, what we recommend is that let's say you're getting IVIg every 6 to 12 weeks, which is probably where everybody falls, it may help to actually space your IVIg so that it's a minimum of one month before the vaccine and also one month after the vaccine. So you might have a minimum of an eight week window where the vaccine comes right in the middle. If you were going to do that and that would probably be the safest way to handle it. If you can afford to go out even farther, that could be even better but again, you ultimately have to control your disease at the same time so you would talk to your doctor about that. In regard to Dapsone or doxycycline, it's unknown whether this has an impact on the vaccine but we wouldn't predict that it would affect anything. So right now we feel that those are probably perfectly fine.

Dr. Payne: Question came in about, should I delay getting Rituximab infusions in order to get the COVID vaccine? So again, this is very complicated because it depends on the severity of your disease, as well as your level of risk for contracting COVID-19 because what we're doing now is balancing relative risk. This is where we really can't give a blanket recommendation, you have to talk to your treating physician. But I think it's important to note that no systematic studies have addressed that question. Secondly, if your disease is severe enough that you're going to land in the hospital and you're going to have to be treated with some form of the immunosuppression regardless, I usually just say by all means, get Rituximab because it is from clinical trial data the most effective treatment that we have so far. Conversely, if you are basically completely controlled, you have no active disease and you are just going to go in for routine maintenance and infusion and your level of risk for contracting COVID-19 is very high, then that might be a situation where you might want to talk to your doctor about whether or not you need the maintenance dose of Rituximab to just prevent a disease flare. But if we think about the way that Rituximab works, how this works is after Rituximab your B cell count is expected to go to zero within about two weeks of getting Rituximab and then it's going to take about 6 to 12 months for the B cell count to start coming back. We know from data that has been actually done in pemphigus patients, this was done out of Emory with Ron Feldman that if we look at responses to flu vaccine after Rituximab, people can respond after about five months. If you do the vaccine immediately after the Rituximab, when your B cell count is completely zero, there is very little chance you're going to develop an antibody titer. So based on that data, again this is not COVID data, this is not specific to this particular question, we think that about 4 to 6 months you might be able to make a small response to the vaccine. So under that guise, we're basically saying you may want to wait about 4 to 6 months after Rituximab to receive the vaccine to give you the greatest chance of responding. Conversely, if you've already received the vaccine and now your disease is flaring, again, talk to your doctor

because if it's a severe flare of disease we don't want to land you in the hospital and end up throwing you on high dose prednisone and other things that will also shut down the vaccine response. But if you have a little period of time, it's good to wait at least 2 to 4 weeks after the last shot to receive Rituximab although this may result in a shorter duration of protection. So we'll go into this a little bit later. But studies show that after the first shot of the Moderna or Pfizer vaccine, your antibody titers will go up by 10-fold. After the second shot of the COVID vaccine, it goes up 100-fold. So that's a huge increase in protection between the first shot and the second shot. We know from the clinical trial data so far that that actually lasts pretty well out to six months. For those of you that follow the literature, there's people that are doing mathematical modeling that basically, if you can see what the peak response was and then how much it fell by six months, then you can extrapolate out and see how far you think it will fall by 12 months, 18 months, 24 months, et cetera. And so based on that, that's where people are trying to predict when they think people might need a booster. But again, at this point, they're all predictions. What we don't know is that if you get the first shot and then you get the second shot, then you get Rituximab about two weeks later, we know that you're protected but the question is, how long will it last? As of right now, none of us know the answer to that and it could be shorter. Next slide.

Dr. Payne: A lot of questions came in surrounding this issue and I know that this is a tough question, the news says the new COVID-19 protection lasts for a lifetime. Why do we need to get the vaccine if I already had COVID-19? So this data was based on a paper that was published, actually probably two papers that are, that are at the bottom of the slide. One was from Michelle New Science Lab, and another one was from Wash U, the Ella Betty Lab. What this showed was that memory B cells and so-called long lived plasma cells, which are the antibody producing cells, are detected 6 to 8 months after infection. They're called long lived, because in certain circumstances, they can last for a lifetime. But this is where the media sort of ran with the title and then people started retweeting the title. But if you actually look at the data in the paper that’s attached to lifelong protection, what they actually showed was that the protection lasts for 6 to 8 months, 6 to 8 months is not a lifetime. What we know right now, is that we do see these memory B cells. We do see these little with plasma cells, we do know that the protection lasts for at least 6 to 8 months, and that's all we know right now. So, I think the title kind of got away from us a little bit and a lot of that got retweeted as being lifelong protection. Secondly, we do also know that real-world data suggests that reinfection within one year from natural infection is relatively uncommon. So we do know that natural infection in a lot of circumstances will protect you from reinfection within the calendar year. So that is basically the reason why these questions have arisen as to, why would I need to possibly get the vaccine? If we go forward, these are all of the reasons that people will provide for a counter-argument. Number one, we do know that serum antibodies if you just follow the titers will fall after 4 to 6 months, that's considered normal. So whenever you get a natural infection, they'll kind of peak and then they'll fall, and then if you were to ever get reinfected, they would come up again and then they would fall again. That's how your immune system naturally works to protect you against infection. But we do know that they fall, and the question is if they fall low enough, that you're no longer protected and you get infected again? That's ultimately the real

question. Secondly, the reason why people are recommending vaccination is that the vaccine is expected to provide longer lasting protection than natural infection and it induces neutralizing antibodies. So when you get infected with the coronavirus, I think at this point all of us have seen that picture of the spiky virus. Your immune system doesn't really know what to do when it's naturally infected. It's just kind of going to throw antibodies all across that virus. You're going to make neutralizing antibodies and you're also going to make non neutralizing antibodies. However, with a vaccine they're only immunizing you with just the very specific protein that's required to make a neutralizing antibody response and that's actually really good. So for example, if you were to get a natural infection where you made a whole bunch of different antibodies, and then you got the vaccine, you would actually specifically be boosted just for the ones that are intended to protect you and it would ignore all the other ones that you might of abarantly made that aren't actually protecting you. That's actually why people feel that if you have natural protection and you get the vaccine, you're super protected. That's why people are recommending that. It's also thought that vaccines may protect against variants that are the natural infection. So you've heard about all of these variants, where if you've been naturally infected before and you made an antibody response against that particular virus, that you may not be protected if you come across a variant. Whereas again, because the vaccine is boosting against these very specific antibodies that are felt to be neutralizing which do have a certain amount of cross reactivity that may help protect you a little bit better. And finally, if you're immunosuppressed, you may not have made a pretty good response after natural infection and the hope is that the vaccine would boost that specific protective response. So if we go forward.

Dr. Payne: A lot of questions came in about, do I need both shots or is one good enough? So the recommendation is that both shots are recommended, particularly with these more infectious variants circulating. The idea is that if you have a very high antibody titer and each one is slightly less effective at, for example, neutralizing a variant, a more infectious variant that might come along, then the higher the better and that's pretty well accepted. So that's the reason why people are recommending that you complete both of these shots. I think that where this question is coming from is a study that was published, there was one out of University of Pennsylvania which is cited here, where they showed that in so-called naive individuals, or people who had never been exposed to COVID before that after one shot, your antibody titer went up by 10-fold and after the second shot, it went up by 100-fold. If they look at people who had had COVID before and they got the two shot vaccine series, what happened is after the first shot, it went up 100-fold and it stayed at 100-fold after the second shot. That's where this thought came out that maybe if you had COVID before you actually only need one shot. So, that's basically where that data's coming from but, again, I'll note that this response may not be the same in immunosuppressed individuals. In immunosuppressed individuals one shot may not be enough. And again, it's the reason why people are still sticking with a general recommendation that both shots are recommended, given the variance and given that people are immunosuppressed or have other medical conditions where they may not have mounted a sufficient response to begin with. What can be done if I had a lesser immune response to the vaccine? Will I ultimately need another one later on? So as of right now we're going to say stay tuned, because we're following the data on this one. A booster shot may be recommended and

we believe that these may be ready by the fall of 2021. Moderna and Pfizer are already working on these booster shots. We think that they're going to be ready sometime around that time. Basically, we're just going to follow the science and listen to the CDC and the NIH and the medical guidelines to see what they ultimately recommend. Also trials are in planning right now to evaluate the role of these two vaccines, particularly in immunosuppressed individuals because from a lot of the published data that we went over, we know that immunosuppressed individuals are not making a good response in many cases. So Rituximab and steroid treated patients in particular as well as Mycophenolate and Methotrexate. So there's a number of things that people are interested in testing, including number one if you go and you get a third shot, a booster shot will that actually be enough to protect people who were previously immunosuppressed? And secondly, people are interested in trying questions such as, does it help if I hold Mycophenolate, or Azathioprine or Methotrexate surrounding the time of the vaccine? Will I make a better response if that's the case? Again, as of right now, we are not making any medical recommendations on that because it depends on how severe your disease is. We don't necessarily want you to flare if you've been in good control, all of these sorts of things. But it could be something to ask your doctor about. A question came in saying, if you test negative for antibodies, is there a protocol to follow of whether you can get another vaccine series, either 1 or 2 shots? So as of right now, no formal protocol, but the trials that are in planning are meant to evaluate that.

Dr. Payne: A lot of questions came in about, what activities can we do or should we avoid now that a lot of societies are reopening and getting rid of mask rules, getting rid of any kind of restrictions on gatherings? So number one, the answer will always be, follow your local and individual institutional guidelines because local guidelines will differ across the country. And furthermore, even if the local guidelines are particular way, individual institutions may have different guidelines. So, for example, most hospitals are requiring people to have masks when they enter, even if the local guidelines have a no mask required role. So if we think about things that are lower risk, if people are gathering, but everyone's vaccinated. If there are smaller indoor gatherings where you may not know the vaccination status of everyone but it's smaller and people remain masked and or distant, that's probably lower risk. Outdoor gatherings, particularly if people remain six feet apart, if they're eating, drinking, shouting, or singing, I think we've talked on earlier webinars that anything that would cause you to accidentally spit on somebody, we've all done that in a social setting. It's more common if you're shouting, singing, etcetera. So anything that would cause that to happen, would be a slightly higher. So if your distancanced when that happens, that's lower risk. And it's lower risk if you were not on systemic immunosuppressive medications at a time of vaccination because that means that you're more likely to be protected. Now, if we go forward, on the flip side, what are some things that we still consider to be on the higher risk side? If there's large gatherings of people with unknown vaccination status, it's all a statistical argument. You'll know that on average, X percent of people could have the chance of being infected, so what's the chance that you'll come into contact with them? If there's very high infection rates in your community and low vaccination rates, that would also be something that would make those larger gatherings more dangerous. Anything that makes you in close proximity to somebody who's unmasked, again, in

the setting of no vaccination that would be higher risk. Similarly, indoor gatherings where you are tightly packed in and not masked and people are not vaccinated, that's a higher risk. And higher risk as well, if you are immunosuppressive like Prednisone, Azathioprine, Rituximab at the time of vaccination because we believe that most likely, you don't have the same level of protection as people that were included in the trials. Just so everyone is aware, immunosuppressed individuals were actually excluded from the COVID vaccine trials. So, we think that they would have a poorer response than the percentages that were shared earlier in the presentation, which fundamentally looked at an otherwise healthy, or not an immunosuppressed population rather. If we go forward, now let's say that you're faced with one of these higher risk gatherings but you want to know what to do and maybe you are an immunosuppressed individual and you did get the vaccine. Let's say you're contemplating one of these higher risk gatherings on the right and you're wondering what you can do to still be able to do what's on the right side of the slide. Number one thing you can do is vaccinate yourself but again, you may not be able to fully respond if you're immunosuppressed. Number two thing you can do is vaccinate everybody around you, so if you're not vaccinated but everybody else around you is vaccinated, then the things on the right actually become a little bit less dangerous. If people are able to mask and physically distance that also makes that a lot safer for you. If it's outdoors, it makes it much safer. Again, all of the standard things apply, so if you wash your hands when you're in that setting and you don't touch your face with unwashed hands. Also, continue with testing. I know that in our earlier webinars, we talk all the time of testing. It seems like testing is not going on quite as much anymore, but if any of your close contacts have symptoms, or if you have symptoms go and get tested. Hopefully this helped answer some of the questions. I know that there were a lot of very specific questions, like can I go to my local gym? Can I go out to eat at a restaurant? I think that, a lot of times you can, for example, if you're at the gym and you're not wearing a mask,but there's no one within 6 feet of you and then you put on your mask right after you leave the machine and go out and wash your hands and leave, it's not unreasonable. Eating in a restaurant, I think that if you're eating with a close contact, who's a household contact who you're always around anyway and you're physically distant from people around you, I think that that's probably fine. Now we can go to questions from here.

Becky: Great, can you just reiterate, whether or not the vaccines will keep you safe from all of the known variants of the coronavirus at this time?

Dr. Payne: I think that they will help keep you protected. So, basically, a lot of them have partial cross-reactivity with all of the variants, so they will protect you. One of the things I forgot to mention on the prior slide is that we've mentioned this on prior webinars, but there's two ways that your body is able to protect you from infection. Number one is with antibodies and that's what all of the tests actually look for. But number two is the T cells and T cells are pretty effective at killing off viruses. We think that antibodies might be a little bit more important but T cells can actually provide a decent amount of protection in addition. We think, again, this is very preliminary data, that T cell responses even in Rituximab treated patients are detectable after

vaccination. So, this is why it's very difficult to ultimately make these recommendations. We know that your antibody titer could be 30-fold lower for example in certain cases. Your T cell response may be okay and ultimately, what we have to do is follow people out over time and understand what the instances are of people who are treated with immunosuppressants versus people who are not. And based on that, we can calculate what your risk is.

Becky: Great. Thank you. Along that line, there's a few questions that have come in that these people are fully vaccinated and they are considering starting Azathioprine or Mycophenolate for their disease now. Are there any recommendations or is there a possibility of that medicine wiping out the antibodies that they've already developed if they're already fully vaccinated and then start those medicines? Rather than the flip, which is usually the situation for our community?

Dr. Tomayko: I think Dr. Payne presented some information earlier that would say that we don't really know for certain. I think that most likely, you're going to have protection that's going to last at least for some time but we really can't say. I don't think we can say what's going to happen for the long term. Most likely, a portion of the immunity that you made from that vaccine and I'm thinking specifically about things like the long lived plasma cells, are probably going to be mostly functional at least for a period of time. But I think this is something that we clearly need to have more studies on. We need to keep observing people, measuring antibody titers, but also measuring T cell function to see how durable it is, and to see how inhibited it is by the medication. That's like a great position to be in, right? To have been vaccinated, not on immunosuppressive medication. So that's terrific and wonderful, but it still is prudent to be careful and to assume that you are at higher risk than maybe another person.

Becky: Great. Rosanna is saying in Canada the AstraZeneca is being mixed with the Moderna. What would the efficacy be for tha? She says that she is eight months post Rituximab and had the AstraZeneca three months ago and is expecting a second shot, but now they're going with the M-RNA vaccine.

Dr. Maverakis: First of all, with Rituxan everybody's going to have a variable amount of time on how long their B cells are gone after the Rituxan. So, it's actually quite nice that you've waited so long for your second shot and that it just turned out that way, that you're getting your second shot and they haven't gotten COVID in the intervening amount of time. I think even if you are mixing the vaccines, hopefully they'll give you the second booster shot. But if not, you might be considered somewhat similar to that scenario that Dr. Payne said, where somebody had a normal COVID infection and then got the second booster shot of the vaccine, were there titers still raised. So we would think that, regardless of what mechanism that you are primed with, when you get that secondary boost you most likely are going to boost the response regardless

of how you are primed, if it was a natural response or another vaccine that they're now mixing it up with. It's still going to be a secondary immune response. Going back a couple of questions, in terms of the variance in how well these vaccines will protect against the variance. When we hear about these variants, it's important to note that they're not entirely different viruses. There's many proteins on this virus and these vaccines are targeting the spike proteins. These variants will have a single, so these proteins have many aminoacids and these variants will usually have a very few, possibly only a single change in the aminoacid of a one spike protein. So the vaccine has many spike proteins in it, and the variant may make it more contagious; however, the vaccine should still protect you, maybe not quite as well, but definitely the vaccines will protect you from the variance. Possibly, not quite as well, but they will still protect you.

Becky: Great, Thank you so much. Alex is asking, is the clotting factor associated with the Johnson and Johnson vaccine the same as the disorder, thrombosis in combination with the thrombocytopenia associated with the adenovirus AstraZeneca vaccine being given in the UK and Australia? I think they are asking if the J&J clotting issues are the same as the AstraZeneca vaccine, with the thrombosis in combination with the thrombocytopenia?

Dr. Payne: I think that the thought is yes, that it might be the same mechanism for both.

Becky: Okay. You've talked this evening about a flare being caused by the vaccine, but is there any research or anything being shown that any of the vaccines can induce pemphigus or pemphigoid?

Dr. Maverakis: I can answer that. In general, there's a minute risk that a vaccine could cause autoimmunity. It's a very, very tiny risk, such that if you look in the medical literature or if you look in any of the databases for the influenza vaccine, a patient may have got this type of autoimmune disease after the influenza vaccine. But you have to understand that roughly 75 million people are getting the influenza vaccine so by chance there's going to be lots of people getting autoimmunity after an influenza vaccine. Now that we're immunizing so many people with this COVID vaccine there's going to be so many people getting autoimmunity after the vaccine but we expect that by chance. So, in order to find out if there is any real risk, then you have to do what's called a population based study and those are a little bit more difficult to do. Usually when these population based studies are conducted, they find that the risks that people thought were there based on case reports, they don't see in a population based study. That's easy to do with influenza vaccine because we know what months people get the influenza vaccine and then the following months, they don't, and then is the incidence any different between the active vaccination phase and the not phase? So sometimes after you subtract all these factors there is a miniscule increased risk of autoimmunity and only in certain diseases, most autoimmune diseases, they're not. So I highly doubt that there will be cases of bullous

pemphigoid or pemphigus vulgaris after the Moderna and Pfizer vaccine that are actually caused by the vaccination. You're going to see lots of cases just by chance. And in the end, there is some kind of increased risk and after you subtract that, it's probably going to be some minuscule number, like one out of a million or three million vaccinations where there would be a real association, but the vast majority of associations are just going to be there by chance.

Becky: Great. We've gotten a few questions asking, if I had a decent response with some of the side effects that you've mentioned such as pretty decent body aches, and a low grade temperature, and feeling tired and fatigued, does that mean that I had a good response and my antibody levels will be high?

Dr. Tomayko: I'll take that. So I would say that we don't know for real, but anecdotally, no. It does not mean that you're going to make a good antibody response. Now, remember, the antibody response is only a part of the response, it's what we can measure the most readily. So if you had a very strong reaction, you were having a reaction so the important question is, did you make a protective response? And that we just don't know. We just don't have the tools right now to really measure protective response. But I think there are a lot of people who worry, I didn't have a reaction. Does that mean it didn't work for me? Conversely, I had a strong reaction, is it protective? And I can say, there was a nice study at Johns Hopkins of a thousand healthcare workers and 999 made protective antibodies and one person didn't, and it was one person on Rituximab. So that's 900.99 out of a thousand and many of those people had no reaction to the vaccine. So having no reaction is not significant. But also there are people who feel very sick and then they don't have detectable antibody titers. But again, whether or not that means that they're not protected isn't clear.

Becky: Great, thank you. Our next question asks, if your IgG is below normal, is it better to wait until monocyte levels rise before getting the vaccine? This particular patient is doing subcutaneous Hizentra every two weeks, and their last Rituximab was about six months ago. So I don't know if that plays into the answer of that question.

Dr. Maverakis: I think they probably mean for B cell levels to rise maybe before getting the vaccine? Possibly they also have low monocytes that might be interesting as well. I'll answer and then you guys can correct me if I'm wrong. So in this case, going back to what the other experts on the panel said, is that the vaccine is going to raise different immune responses and these other immune responses are also going to have some kind of protection. So in this scenario and this is a scenario that we're all encountering with our patients, when should you be vaccinated? And usually I tell them, it depends on what their risk factors are for getting the virus. So if you're sequestered and you're not going crazy being sequestered, then it might be reasonable to wait a little bit until your B cell counts come back. However, if you're in a high risk

environment and you're living in a house where you have people working, people going out or maybe you have to go out in public a lot, or maybe you're even still working and interacting with the public, then I think in that case, any response that you're going to get from the vaccine is better than no response at all. So even if your B cell counts aren't back yet, I think you should get the vaccine. However, if you're able to be sequestered, you're not around any strange contacts, everybody around you has been vaccinated then you might want to wait a little bit longer to see if your B Cell counts come back. But then it's a waiting game, and you don't really know when those B cell counts are coming back because some patients I have B cell counts don't come back for like a year and a half and for some patients, they come back in six months. So, you just don't know when those B cell counts are coming back and you don't know when you're going to get exposed to the virus. So, under normal circumstances, at some point, you just have to get the vaccine because it's going to give you some protection even if you're not gonna get a great antibody response from it. Now the real experts could chime in and tell me what they think.

Dr. Tomayko: I was going to just say something practically following up on what you're saying, which is, we're probably going to have booster vaccines that are going to come out. Either it will be boosters with the same vaccines or it will be boosters with vaccines that are even better targeted for variants. So, even if on some level you think you need to wait, I don't know that you need to feel like you need to reserve this vaccine until it is the most optimal time because you're going to most likely have a chance or a booster again in the future also.

Dr. Payne: Yes, I completely agree with Dr. Maverakis and Dr. Tomayko said. Six months out from Rituximab, we think you should be able to make at least a decent response. Your T cells will be able to respond. I would just do it.

Becky: Great. A couple of questions have come in with the timing. Like you had mentioned about coming up on a year or six months into this that we're going to need a booster. That's also the flu vaccine season. Is there any talk about if it needs to be a space between getting the flu vaccine and the COVID vaccine or anything of that nature?

Dr. Payne: To be determined. I think that with the first round of the vaccines, they were recommending that you don't get any other vaccine within two weeks of the COVID vaccine to basically be able to better figure out if the adverse event was related to the COVID vaccine as opposed to the other vaccine that you got. My guess is that the same thing might be true. I think that one of the things that people are sort of interested in with these LMP vaccines, in general, is that it's easy to load them with different types of cargo. I think that this is down the road, once we get post-pandemic. I don't know if many of you have seen babies get vaccines but sometimes it's like shot after shot after shot, so the hope is if you could just actually load the vaccine with four different things here because you just get one shot ultimately. I think that one of the ideals that people are hoping for is that ultimately the flu shot and the COVID shot

could be combined into one but again, it's going to be down the road. So we don't think it's necessarily difficult from that standpoint but I think that they will likely keep them separate, just because of the adverse event monitoring, that they'd want to know whether it's related to one versus the other.

Becky: That makes perfect sense.

Dr. Maverakis: I would also get them in different extremities if you're in this situation because the vaccines are going to drain to the draining lymph nodes and if you got them in different extremities at least there should be little competition at that point. Then the only other thing I want to add is that the flu vaccine is usually what's called a split vaccine, that means that they grow up the virus and then they heat kill it or are they kill it somehow. So, it's actually a whole viral particle that has been then destroyed and made safe to administer. I think this goes back to some of the things that Dr. Payne was saying because in that case, your body makes an immune response to all components of the virus and maybe not all of those components are the best at protecting you. Whereas, in these more advanced vaccines, these M-RNA vaccines, they are only putting in the proteins that we know the antibodies can neutralize. Excuse me, they don't put it in the protein, they put in the instructions to make the protein. But it's only a certain region of that protein that really, if the antibody reacts to that, it protects you. So this is why I think that the influenza vaccines are probably not as effective as these new coronavirus vaccines, the M-RNA vaccines. They have an incredible effectiveness that we haven't, at least I don't think we've seen, with the influenza vaccines.

Becky: Great, Thank you. Another question is, would you suggest taking NSAIDs orTylenol before getting the vaccine to help with some of the side effects, like the body aches and pains and the fevers?

Dr. Payne: I generally don't recommend taking it in advance, only if you actually have the symptoms and it ends up being a problem. And usually, I recommend Tylenol first, then Advil, if that doesn't work.

Becky: Great. Thanks.

Dr. Maverakis: On that note, I can only tell you about my own experience. So, I got the first dose, I didn't have many side effects. Second dose, I felt I was still able to go to work and everything, but I felt fairly crummy. I thought it was going to be similar to the course of getting a cold or something like this where it actually takes you many days to get better but surprisingly, at least from my own experience, you could have a different experience, I went from feeling crummy to feeling totally okay and that transition might have taken two days or a day and a

half, but that transition was very abrupt where I was not feeling good and then a few hours later I felt totally fine.

Becky: Thank you. I had a very similar experience, Dr. Maverakis. For maybe 24 hours it was bad and then all of a sudden, it was like, I think I feel better. But, yeah, it was almost like a light switch. Thank you for mentioning that and sharing that with our community. That was very helpful. I cannot believe how quick this has gone, and I apologize, I just realized that we're already over by 15 minutes. So I apologize and I thank you for spending the extra time. I know there's a lot of questions that we didn't get answered and I sincerely apologize. I think you've provided us with phenomenal information and hopefully we can extrapolate some of the information that you've shared to answer some of the questions. Thank you to Dr. Payne, Dr. Tomayko and Dr. Maverakis for being on the call with us and thank you all for hanging and listening with us. And of course a big thank you to all of our sponsors, Genentech, Principia Biopharma, a Sanofi Company, argenx, and Cabaletta Bio for making today's call possible. Before we go, I would just like to let you know our next webinar will be on Wednesday, June 9th, a week from tonight and we're going to discuss Virtual Rare Disease Week on Capitol Hill and how you can advocate for the IPPF. Our panelists are Marc Yale, who is the IPPF Research and Advocacy coordinator, Katelyn Laws, the RDLA program coordinator, and Doris Chenier, a patient advocate and a patient with pemphigus vulgaris. This is a great opportunity to share your story with representatives as well as make a difference and advocate for legislation that will help pemphigus and pemphigoid patients have better access to treatments and increase funding to advance medical research for rare diseases. We hope that you'll consider joining us as the more pemphigus and pemphigoid voices are heard, the more of a difference we can make. I'm also excited to announce this year's Virtual IPPF Annual Patient Education Conference. This will be held on Friday, October 22nd to Sunday october 24th. And we hope that you'll join us for this exciting and educational event. More details are to come and registration will be opening soon. The IPPF also has several upcoming virtual support groups around the country that will be meeting over the next month or two. We hope you'll be joining us. And you can find more information on our website www.pemphigus.org and click on the News and Events tab.

Becky: Emory University Department of Dermatology is also conducting observational survey study to evaluate the changes in bullous pemphigoid disease in patients. Emory is looking for about 45 BP patients to participate in both face-to-face and remote visits conducted via Telehealth. If you're interested in participating, please contact Dr. Ron Feldman's research team at (404) 778-3084. The IPPF has been looking towards the future and how we can continue to help you and our community. But we need your help to grow the community of Healing Heroes. Healing Heroes fund the future of the IPPF community by making, sustaining monthly gifts to support our mission of improving quality of life for those who are affected by pemphigus and pemphigoid. No amount is too small, and your monthly donation goes a long way and continues to help us to provide great resources like this webinar for the greater good of our community. This call recording will be sent out with a survey after the call. 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. Thank you for joining us tonight. Goodnight.