Amethyst: Welcome, everyone! This call is now being recorded. I would like to thank you for being on the call this evening and to our Sponsors Genentech, Principia Biopharma, Argenx, and Cabaletta Bio for making today's call possible. Today's topic is the A Multidisciplinary Approach to Treatments and Care of P/P.

Before I introduce our speakers I want to take a quick poll to see how many of our listener's see a dermatologist and an Oral Medicine Specialist or Dentist to help treat their disease?

If you could take a quick moment to answer the poll while I introduce our speakers for this evening.

Dr. Donna Culton completed her medical degree at the University of North Carolina at Chapel Hill. While there she also received her PhD in the Department of Microbiology and Immunology where she studied autoreactive B cell development and regulation. She continued her training at UNC and following her Dermatology residency she completed a postdoctoral fellowship applying her knowledge of autoreactive B cell pathophysiology to pemphigus by studying B cells and autoantibodies from patients. Her laboratory generated a novel murine model of pemphigus allowing for a better understanding of mucosal pemphigus vulgaris. In her current position as Associate Professor of Dermatology at the University of North Carolina at Chapel Hill, she serves as the Director of the Clinical Immunofluorescence Laboratory at UNC and sees pemphigus and pemphigoid patients from North Carolina and neighboring states in her specialty Autoimmune clinic. She has served as an investigator in clinical trials in pemphigus and has contributed to consensus statement publications as part of the International Pemphigus and Pemphigoid Committee.

Dr. Joel Laudenbach received his Doctor of Dental Medicine from the University of Pennsylvania, School of Dental Medicine. He then completed postdoctoral residencies in general practice at Cedars-Sinai Medical Center in Los Angeles and Oral Medicine at the University of Pennsylvania. Dr. Laudenbach is appointed to Atrium Health as an Associate Professor of Oral Medicine and attending medical staff in the Department of Oral Medicine in Charlotte, North Carolina. He practices Oral Medicine at the Carolinas Center for Oral Health and is a Diplomate of the American Board of Oral Medicine.

So it looks like based on the poll, it looks about 60% of our attendees that they see both an oral medicine specialist and a dermatologist to help treat their disease. So that's great.

Now, it is my pleasure to introduce Dr. Donna Culton and Dr. Joel Laudenbach and back to answer your questions today. Thank you guys for being on the call.

Amethyst: Before we begin, I want to ask you guys both, to explain a little bit more about your specialties and how long you guys are. I'm sorry, and how you guys work together to treat patients with.

Dr. Laudenbach: Dr.Culton, you want to start off?

Dr. Culton: I'm at UNC Dermatology in Chapel Hill, North Carolina, and have been seeing patients with pemphigus. Over time, I developed a special interest in the oral mucosa mostly pemphigus patients, but some other oral conditions as well. Then I met Dr. Laudenbach through the IPPF and quickly knew he was a great person to partner with to see some of these complicated patients. As a result, we share many patients, and I have really enjoyed his expertise in helping, helping to guide their treatment.

Dr. Laudenbach: Wonderful, well, thank you Donna, it's been a real pleasure to work with you, and I think all of our patients know, we're all lucky to be able to work together and to have you as a big resource for us. Our patients in Charlotte oral medicine is a sub-area area of dentistry, really. So I'm a dentist by training and practice dentistry as a general dentist for sometime in the past, focusing on oral pathology, and particularly managing patients that have skin conditions in the mouth. As well as some pain, oral, and facial pain problems. So that's the type of patient population I see. And luckily, at the hospital in Charlotte, I also get to see inpatients and a wide variety of both people who are ambulatory walking in with problems. And then people have even more complicated, more interesting, you know, complicated issues as well in the mouth, in the hospitals. So, we do refer patients to Dr. Culton and I was just talking yesterday about a newly diagnosed patient, and talking about how a local dermatologist, just as an example, you know, kinda got the patient to myself. We took multiple biopsies, some serum, made a diagnosis, and then, now it's OK. Should they see the same dermatologist or go see someone who really has experience in these areas, so, we were talking about you in case your ears are ringing or burning or whatever they're supposed to.

Dr. Culton: I think patients ask a lot. You know, why, why should I see both, or what's the benefit? And I always explain that we really come from different training backgrounds and so we kind of see the disease through our own personal lens of our training and our experience and there's approaches that Joel has that, you know, I don't tend to use. And so it's nice when we can kind of cross-pollinate our ideas and I think patients just benefit from it. And, you know, I definitely think it leads to better patient care, and we can talk about, you know, so much of, it depends on disease severity and kind of how the patient is doing. Because even though we're both in North Carolina, it's, you know, a good 2 to 3 hour drive between us. So, it does beg the question of, do I really need to drive three hours to go see this other doctor? I think most of us who see these specialty diseases are used to seeing patients maybe less frequently, but doing more on the computer telemedicine, and kind of managing somewhat remotely, but having the option to get the patient in front of us. So, anyway, that is just an introduction to what we're about to talk about.

Amethyst: Awesome, Well, that's great. Yeah, and that kind of answered our first question, you know. Is it important to have a team of doctors? And if so, how do you facilitate, or how do you recommend a patient facilitates that their doctors in different specialties do communicate about their treatment care plan?

Dr. Laudenbach: Yeah, that can be, a dicey one. Sometimes, for example, the case, just, recently, the referring provider is in the dermatology world, and so, I think they have some experience in this area. I do believe, as a provider, for consistency, that they should continue with their provider. Maybe, Doctor Culton, you can speak to this from the Durham World. I don't really know. In dentistry it would be common to see a General dentist and even a periodontist for gum specialty care and these days, there's alternating dental visits and the periodontist. But, I don't know, in the dermatology world, would it be reasonable? I guess you need someone local for the common stuff and how does that work on the Derm side. Do your patients have two Dermatologists sometimes?

Dr. Culton: Often they do, I think the ones who live kind of near to Chapel Hill. Sometimes, I'll end up taking over their general dermatology care too and doing their skin checks and other things. But in general, people who live further away have their regular dermatologists. Then I kind of do more of the treatment and management of pemphigus and pemphigoid.I think what you hope between all your doctors, whether they're in the same specialty or in different specialties, is that they're willing to take the time to communicate with each other about your care. It does take time and effort. And I do think some doctors are kind of more willing to put in

that time than others. But I think that's, that's what you want, right? As a patient, you want your doctors all on the same page, you don’t want to be getting mixed messages.

I think, sometimes, it's appropriate to have you be the conduit between your providers. But more often, I think the powerful decision making comes when the doctors can get on the phone together, and talk. I think every patient deserves to have that. So, certainly, I share patients with other dermatologist. I play well with others. Like I'm a team player, I'm excited to be on your team, I'm never calling the shots on my own. It's always a group decision, and that's, that's kinda what you want.

Amethyst: That's great. Have you guys -either of you- noticed any differences with things being a little bit more telemed? Has it been easier to be able to communicate with doctors that may be a little bit more remote from you two?

Dr. Laudenbach: I would say, from my perspective, when we were really trying not to see anybody in the office, it was, I think I'll speak for myself. There was a lot more downtime, so to speak, not having to be physically in with patients all the time.

So that was actually a time where you could kind of communicate a little bit easier and find each other. But since then, some providers are back in the office some are working remotely only depending on your specialty. Then there's the ones who are in only certain days of the week. When they're in, they're actually remote. That's at least from the dentist perspective. So you know, the dental offices are closed. I don't know how much on the medical side did. So it's been an increasing return to being able to communicate with everybody. And how about you, Dr. Culton ? How's it been on your end?

Dr. Culton: Yeah, I feel the same. We realized early on that there were going to be some patients we just needed to see in person, even when most things were shut down. We were mostly shut down. But we still, we're seeing some patients, but we learned how to do telemedicine. Really quickly, I joke that we had a whole committee that was going to work on telemedicine and getting up and running, and then we expected it was going to take them a year. We got going in a week. All of us, I think it did open that as a possibility. So I've had several patients that now that we're back in the office, and mostly seeing patients in person.-Many patients with pemphigus and pemphigoid are immunosuppressed and if we can keep them out of the office, that is helpful. Now some of my patients that live far away, if they're pretty much doing well, we can do a telemedicine visit. We still have that as an option. But as I think we would both agree, it is hard to see in the mouth, you can't send really good quality

pictures, and it's hard to like get up close to the camera on the computer and show your mouth. So, it's just not easy to diagnose and treat over telemedicine. So I think it's better suited for patients who have a known diagnosis, who are doing fairly well and are just kind of doing a med check in maybe some small tweaking to the treatment plan.

Amethyst: Wonderful. Well, we've had a few questions come in. We have a patient who says that they're in the early stages of their disease and currently do not have an official diagnosis and who should they seek to confirm their diagnosis? And they said that they already saw a rheumatologist and are now seeing a dermatologist. Can the dermatologist solely treat their condition? Then they said they are also experiencing oral lesions. So, should they see an oral medicine specialist?

Dr. Laudenbach: Well, I would just say, often, I find that the path of least resistance to get in with one of the two specialists, who is more familiar with this area, is probably better for the patient. You know, holding out several more weeks to see one or the other. Just my opinion, especially when some of these rare conditions need to be diagnosed early it would be better, I think, to get in, you know find out who the person is in both areas and who you can get into. Whoever you can get into first because my experience is usually the dermatologist. If they don't do the oral biopsies or they need help with it, they're going to reach out and ask for the person and get you kind of in there quicker. Then, on the flip side, if I can't do it I'm going to say, you know, I know Dr.Culton does some oral biopsies, but also does skin, you know? And then we'll work to get them in there. Dr Culton what are your views on it?

Dr. Culton: Yeah, I agree. I think it's a case by case basis and I do think the diagnosis like getting the biopsy done is critical because really, if you don't have the diagnosis, we're kind of guessing at the treatment. So I completely agree, getting into any Dermatologists is not the same as getting into somebody that kind of knows and loves these diseases, and does oral biopsies/ Obviously If you have skin lesions, you know, any dermatologist would be likely to do a biopsy for that. But I agree. Kind of getting your foot in the door anywhere, It's critical, and then both, being your own advocate to get that biopsy, but also asking your doctor to advocate for you, so it might be that a patient sees a dental provider and the dental providers. And I really think you need to go see Dr.Culton and you need to say, Can you call her office and tell her this is urgent? Because if you just as a patient just ring up and call the office, it might be a two month wait. But if I know that you have one of these oral conditions, you know, we oftentimes will work people in more quickly and it always goes a little more smoothly if the doctor calls and says, Hey, I have a patient that needs to get in quickly.

Amethyst: Awesome, Great! Um, so we have an oral question here. Trish asked, why is Cellcept used more often for oral MMP more often than methotrexate. Also, do you need a prescription for chlorhexidine? Is there a specific brand of chlorhexidine that does not stain in your teeth?

Dr.Culton: I can maybe take the first question. So I actually use tons of methotrexate for MMP. I like it a good deal, I think it is, while it's immunosuppressive. It's a little less immunosuppressive than cellcept or mycophenolate, So I kind of pick each patient's treatment based on their comorbidities, their own kind of risk factors for other conditions and the severity of their disease. So I don't I wouldn't say that across the board that cellcept or mycophenolate is used more often than methotrexate. I think, you know, you might just ask your physician why they may have chosen that particular medication, specifically for you, and then chlorhexidine. I'm going to differ.

Dr. Laudenbach: Certainly happy to take the question, for those that don't know, chlorhexidine is an oral rinse. It's a prescription rinse, and it is used both in the outpatient setting that your periodontist or your dentist may prescribe to really decrease bacterial counts in the mouth. It can also actually kind of modulate and keep yeast or fungal overgrowth down to a lower level. So it has a couple of very favorable properties, but I always tell patients when I prescribe it, the two potential side effects are staining the teeth, and usually standing of the teeth is anticipated. As long as you're going to the dentist, certainly if it becomes enough, where it bothers you, know that you're seeing it to get a cleaning, and try not to wait on that, because it's usually amenable to a cleaning. Then the other potential side effect is a change in taste. Usually it's temporary, just while you're on the medicine, and most often resolves after stopping it, it's a swish and spent twice a day. Most commonly and classically, it's been for two weeks and stopping, But there have been some studies that show it decreasing the bacteria that cause cavities. So there are some, you know, groups that actually recommend higher risk patients to rinse for a week, a month.

It's kind of interesting, Chlorhexidine has come a long way, but in any event, in terms of brands, there is one that I know of an alcohol free version that's commercially available, I believe it sunstar, or gum or butler is the company. There was a recent shortage I heard due to the COVID-19 pandemic, but anyway, that one alcohol free in this patient group is very important. Alcohol Rinses certainly, when anyone I talk to with these conditions, is usually only going to get you either discomfort or into more trouble. So, the alcohol-free version is preferred, but often, it's only available and dispensed at a dental office.

So that's how the company has had it set up. If you're near a major medical center, I don't know if Dr. Culton, your medical pharmacy downstairs can make it available for outpatient prescriptions. I know some big medical centers do that. Depending where you are like UCLA, I think, does that in different places. But other than that, it can be tough to get the alcohol-free version, but I do recommend that one.

Dr. Culton: Now that's good to know but I'm not sure that our hospital offers that.

Amethyst: Ok, great, thank you. Speaking of mouth rinses, Kathleen says that she heard people talk about using Magic mouthwash. What is Magic Mouthwash? And what is the ratio of each product in it? And how often should she be using it?

Dr. Laudenbach: That is a great question. I think it evokes a smile from Dr. Culton and myself, probably simultaneously. Magic Mouthwash there is no real folklore to it, but it is important to keep in mind from the patient perspective, that if someone's giving you a magic mouthwash, it can be really a combination of anything, and it can be, usually, it's at least 1 or 2 items mixed together but more commonly, it's 3 to 4. It really can be usually something like an anti-inflammatory which is a steroids, an anti-bacterial, antifungal, and something to numb the mouth.

Sometimes, it's also a coating agent, like maalox liquid, something like that. Also Liquid Benadryl also numbs the mouth. So, magic mouthwash, as a catch all phrase should contain the question- Ok, what's in it? That's important to know, because when you go to the next provider, they're going to say, Oh, well, what did you try? And then most people say, well, Magic Mouthwash and then I'm, you know, scratching my head there wondering which and there are a few that actually have names like Duke's prescription and so we sometimes prescribe that.

Anyway, so in general, the way I look at it is what are we trying to manage here? Is it pain? In that case, I'll try and focus ingredients in a mouthwash to things that numb the mouth encode it.

So if my quote, magic mouthwash, I won't call it that, you probably could guess, but I would ask them to put in equal parts of lidocaine, which numbs the mouth, Liquid Benadryl. Then Maalox Liquid. I more commonly will use lidocaine for numbing the mouth. If we're going to use anything else, steroids or an antifungal, we're going to use it individually. So yeah, I know

what we're using and what you're responding to, Dr. Cullton. You've probably heard this, maybe more than I have,

Dr. Culton: I do the exact same thing. They say, I've used Magic Mouthwash, I was like, What was in your magic mouthwash? I don't know. Why? It's, you know, I'd say it's the kind of everybody's own little secret recipe that the pharmacist throws together unless it's one of the named, kind of like Duke's or something, but I agree, I like knowing what the main problem is and then giving a swish for that particular problem. I do think that, you know, we, as providers, think, we don't think this, We know you don't have infinite time. It's easy to prescribe things. It's hard to do them. So if you have four swishes that you're supposed to do twice a day, people then call me out on it, and they say, Well, which one am I supposed to do when and like I'm going to be swishing all day long here I get the beauty of a mix. Like, I get it, because then you can, like, do it, and be done. And you're not swishing all day long, but it is, it is hard to know them what you're responding to.

Dr. Laudenbach: Yes. I agree.

Amethyst: Wonderful. Thank you. We have a question from Joanne, and she says that She has BP. And it's affecting her mouth. Her dentist said that there is research on antibiotics, and the microbiomes that show antibiotics are a hindrance to good health. And he suggested that she should reduce her doxycycline to 20 milligrams per day, but her dermatologist says, that, the Doxy, at a higher dose is effective. She is currently using 50 milligrams 2 times per day, and temporarily uses Prednisone. Is there any research on the mouth and gut biome and it's importance to responding to flare, ups, and drugs.

Dr. Culton: I can start with one part, and then I'm going to hand the baton to Joel. There is some evidence that oral, antibiotics, systemic antibiotics, like doxycycline do more than just anti bacterial. They have anti inflammatory properties, as well, and there's been research that shows that it can be quite helpful for Pemphigoid. We as Dermatologists struggle with this all the time, we love doxycycline and minocycline and we use it for acne. Patients end up on it for months, If not, longer. We all know it's probably not ideal for a global sense community population. You don't want to be having everybody on long term antibiotics because it definitely does mess up the gut flora. And the mouth flora. But I think, on an individual basis, it's one of our least risky system treatment options, right? So if you're not doing doxycycline, then the next step you're looking at is methotrexate or acfiber. Then all of a sudden, it gets really serious. For that reason, we sometimes are willing to overlook, especially if it's working for a patient we're willing to overlook. Yeah, it's not ideal. You'd be on a long term antibiotic, but this is actually safer for you, and it's working. So let's call it a win. I don't think there's much

evidence on the low dose doxycycline efficacy in pemphigoid , so low dose doxycycline can be used for other things like Rosacea. We know that it works pretty well. But for pemphigoid, I don't think that data's there yet. In that regard, you know, I think it becomes a personal decision and certainly, you don't want your dentist in your dermatologist fighting about it. I'm going to pass it to Joel now to talk about microbiome in the mouth and how that might play a role.

Dr. Laudenbach: Very good. That was really helpful for me to learn from you. From my perspective, I didn't completely, the first part of it from what I gather, as a dentist when I hear doxycycline at 20 milligrams. I start thinking about and we'll forget that my father's a periodontist and my brother too. But there's some periodontal literature and I'm not up to date on it currently. But I believe low dose doxycycline several years ago was something that from a collagen sort of protective standpoint within the periodontal gum tissue region of the mouth was thought that low dose long term doxycycline was helpful to help maintain periodontal or bone surrounding teeth. And, so, I'm not sure if you said in the intro, if it's the dentist that was thinking a lower dose or if it's the physician. But, I think you said that. There may be this thought pattern from the dental side which is totally different then what Dr. Culton was talking about, which is all the other benefits that can be had at higher dosages for all these other skin conditions and other inflammatory conditions. I mean periodontal diseases and inflammatory condition, that may be part of where that idea of the low dose. Even just keeping it on as, if you were gonna drop it anyway. I don't know if the literature now says, you stop at three months from the periodontal standpoint, but that may be from where that came from.

Dr. Culton: I do think, if you're doing well on the high dose or on this intermediate dose that you're doing now, I would say a high dose or what we would consider normal dose is 100 milligrams twice a day. And so, if you're doing well on 50 milligrams twice a day, why not try to go down and see if you get the same benefit for less overall antibiotic exposure. But, if you're not doing well, you might have to have that personal decision making about whether you want to go back up to the higher, normal dose or switch to a different treatment.

Dr. Laudenbach: And I would just throw in here, this may come up later, but I know common questions about swishes that control lesions in the mouth. There's always this question of should I stop at some points? Should I taper down? Should I go every other day and there is sort of a tailoring from my perspective with each patient as we tapered, we find out what gets under control and out of the woods for severe outbreaks. And then we taper down as well as we can, and then some folks can do on and off treatment. But others need it once a day or so. it's kinda the art and the science.

Amethyst: Wonderful. Augustine asks, what's the prognosis of blood filled blisters occurring in the mouth during flare ups of Pemphigus?

Dr. Culton: I've definitely seen those more. We call them hemorrhagic vesicles or bullae in the mouth. I have definitely seen that in Pemphigus, you can see it in Pemphigoid as well. I don't think it's like, Patent Mnemonic, like, not diagnostic or one or the other, and I don't think that it being filled with blood necessarily has any prognostic value. It just means that you're having a flare. I don't think it means that you have like the worst disease or bad things are gonna come in the future, I think it just some people just tend to have more blood filled lesions.

Do you agree Joel?

Dr. Laudenbach: I can't be very helpful in answering this question. Usually the areas that I see in the mouth of blisters have usually burst. When we see one in the mouth, it's very helpful, diagnostically. But whether or not that has blood filled or not, I can't help on that one, but it helps when I see the lesions, because it points me in this diagnostic direction.

Amethyst: Great. Thank you. We had a patient write in and they said that they developed joint stiffness after Rituxan especially after they tapered off of prednisone. Can this be due to the Prednisone stopping and if so, how long should it last?

Dr. Culton: I think in general, Rituximab is pretty well tolerated. We worry about, obviously, immunosuppression afterwards, So there's like side effects that we think about could happen, or infusion reactions, but in terms of side effects, Like joint pain is not very common. And I think there is Prednisone as an anti-inflammatory for lots of things. And, I often chalk up joint pain after coming off of Prednisone was probably helping everything feel nice and not inflamed. And then you come off of it and your body misses that a little bit, and those aches and pains that you would kind of learn to live with and maybe even weren't even feeling that much anymore. Now, all of a sudden, they're back with a vengeance because you can feel every little thing again, and so I do tend to chalk it up to the prednisone kind of being tapered off. At that point, I will ask patients to hook up with their primary care physicians and make sure there's not something else going on, right? Most inflammatory joint diseases like that we think about rheumatoid arthritis or psoriatic arthritis. You know, I have a couple of patients that have rheumatoid arthritis and Pemphigus and Pemphigoid should help, both, so joint pain after Rituximab it's pretty unusual and we just need to make sure there's nothing else going on.

I mean, that being said, I think most of my own patients know I'm not a doctor who ever says There's no way. There's no way, right? Because you could be the one person that has terrible joint pains after Rituximab and maybe it indeed was due to the Rituximab and it's just something that's not been reported before. So, while it's possible I think it's, it's less likely and certainly our duty would be to make sure it's not anything else any other inflammatory joint disease.

Amethyst: Great, thank you. Another question on Rituxan. Aruna says that she had a severe reaction to her Rituxan but was wondering if it would be safe to try IVIG as a treatment option.

Dr. Culton: I do think Rituxan and IVIG are very different medications, Both are given IV and so it really kind of depends on what the severe reaction was. Things that are similar, is that, if you can have an infusion reaction to any Infusion. So, if it was an infusion reaction, you know, maybe it's going to be less likely with a completely different agent, like putting IVIG in your infusion versus putting Rituxan in your infusion. But, infusion reactions are always possible with any infusion.

So, while I don't think it, maybe it's a little more likely you would have an infusion reaction, IVIG, given that your body already did that to Rituxan, I don't think that's a guarantee that that's going to happen. And otherwise, that's the main similarity between the two. Otherwise, I think of them as being very different with really different risk benefits. And so, side effects of IVIG. Afterwards, you know, it's not immunosuppressive, but there are other things that it can do, being a big protein load and big volume load. You have to make sure you have a good heart and kidneys that need to be able to handle it.

I would ask your provider that particular question. I've had patients who have rechecked the Rituximab who had severe issues with it. And we kinda dig into what exactly happened. And many of them have successfully rechallenged Rituximab with some changes to the protocol, different infusion rate, different pre medications, even patients who have a true anaphylaxis reaction, there's ways to desensitize patients to it. And thankfully I've never had to do that. But I have colleagues and allergy and immunology who have said we would be willing to work with you on that, you know, try to do it in a hospital setting. So, I know there's some patients who Rituximab is the only thing left on the table for them and then they have a terrible infusion reaction or even anaphylaxis. It's risky but it doesn't mean that it's totally off the table to retry It.

Amethyst: Great. Thank you. We have a question here. Linda asked, Is oil pulling recommended for Pemphigoid?

Dr. Laudenbach: I'll weigh in. I'm curious about what Dr. Culton's heard. But oil pulling for those that maybe are not familiar with it or I've asked patients well what do you mean by that because it's certainly not something that was taught and recommended for management. And so, rinsing with an oil or some sort of natural product is certainly not a new concept. And I had the luxury of practicing in Southern California for several years and had patients who are interested in trying lots of different natural products. Asking me, is there any research on this product or that product? And actually, one of the products or I should say, you know, aloe vera gel. There's actually some data in another skin condition, like Lichen Planus where there's actually a little bit of support and a few papers out there that with a certain combination prepped by a pharmacist, you know could be helpful. So as a provider, I usually try to hang my hat on no treatments and management strategies that have data to support their use. We try all those, and then they're the things where people don't respond, and they try other stuff. Now, with oil pulling and rinsing with different oils, I've had patients tell me more commonly, and recently coconut oil seems to be the latest one. And oil pulling is, as I understand it, rinsing in the mouth. I don't know really how much time. But swishing and spitting out, and it may be more than that, so if anyone else can guide me that's great, but I keep asking patients, I really haven't seen many lesions of concern. In these patients. There have been a handful over the years where they got white patches and we've biopsied them just to make sure they weren't a-typical or pre-cancerous and they haven't been. So, I don't know that there's really data to support their use generally in the mouth. For other conditions, let alone these diseases and I haven't really seen many side effects other than a few patients with white patch lesions that we occasionally biopsy. so, I can't really advise patients one way or the other.

Dr. Colton, what are your thoughts or experiences on this one?

Dr. Culton: Yeah, I had to look it up. So, I saw that question and I thought, what is that? And then, when I saw it was just rinsing with oil, I thought, Well, that's fairly low risk, I would imagine. As you said, I don't recommend it as a treatment, but if somebody wanted to try it, I can't imagine that would do anything terrible. I don't know. I do know some patients with severely dry mouth. one of our mutual colleagues, UNC School of Dentistry, will recommend rinsing your mouth with oil to just kind of keep up the lubrication. And so, you know, in general, people, try all kinds of crazy stuff. This is one of the lowest risks, in my opinion, so I don't recommend it from my own treatment algorithm. But if somebody said they were doing it and they were liking it and they wanted to try it, I wouldn't have a problem.

Dr. Laudenbach: There is a dry mouth that actually has olive oil in it, in addition to Xylitol, I believe, and some others. And it's out of Spain and it's been around for awhile. I mean if you heard me say go home and rinse with Pepto Bismol, I don't know if you've ever heard that one but severely dry mouth patients who have mouth ulcers that aren't from any skin condition. I mean I've learned from the group I work with the specialists here that some patients respond to that now Is there any data on that? We're probably going to have some data, because we're in the future, if we choose to do the study, But if it helps you and it's not hurting, and we're monitoring, know that it's probably ok. And we would tell you, I think I would certainly tell you, you know, if there's something that does, I'll tell you about the white patches and then you can choose if you want to do it. But yeah, it's a good question. It's a common question, more common now. Are there other oils out there? We don't have to go into CBD oil unless there's another question on it but there are patients coming in and asking me, can I use that for this and I give really the same answer.

Amethyst: Thank you. Lisa asked, How isn't IVIG protocol determined for PV patients and was trying to get into remission? Is it based on their IGG levels?

Dr. Culton: So, typically the IVIG protocol is pretty standard, two grams per kilogram, divided over a number of days, and the reason that dose is divided over a few days is just because as we talked about that big protein load and volume load. If you do it all in one day, there's a higher risk of severe headache. So severe that It's kind of like a terrible migraine and can even be what we call a septic meningitis, which is like an inflammation of your kind of lining of your brain and spinal cord. That's not an infection.

IVIG is typically a standard dose based on your weight, two grams per kilogram, divided over 2 to 3 to 5 days, just depending on everything else. Just the way it works, it lasts about 3 to 4 weeks. You would have to repeat it every month if that was the only thing you were doing. I will often use it as a bridge for somebody who can't use Prednisone, but needs something that's going to work pretty quickly. While something else is kicking in, right? Like while we're waiting for something else to finally take effect, I'll use it that way. There are some protocols out there where patients are maintained on IVIG monthly and that I think is fairly safe.

Some patients are able to get in remission on that. It's quite expensive and it's also quite time consuming for the patient, right? So you're essentially once a month doing 2 to 5 days of your life getting infusions. And so it just it's a lot of It's a big commitment, a lot of time. And so a lot of patients do home infusions if they're gonna do that. But I know there are some physicians

who feel that IVIG is kind of, you know, the safest way to go, even for maintenance. It's just not really how I use it but I would say it's not based on your IGG levels necessarily.

Amethyst: Great, thank you. Barbara asked, does IVIG cause gums to bleed?

Dr. Culton: Not to my knowledge.

Dr. Laudenbach: That's a great question. And you could probably tell by my reaction, my answer is I'm not sure. I have not come across that one and I am thinking about my patients that I see on a regular basis, let alone new patients. I don't have a lot of patients who are on the continuous IVIG probably kind of dovetails the discussion here. So, I guess I don't really know. I haven't seen it, but I also don't see a lot of people on a continuous IVIG.

Amethyst: Great. Thank you. Tony asked. How do you know if you are in remission and just do you have to do biopsy? She said that she was just put on prednisone.

Dr. Culton: You know remission I think is considered clinical, right. Remission is you don't have any more source or sensitivity and you know we think that your disease is kind of cleared up and we use different definitions. So, we have complete remission, partial remission and that's like are you getting any sores at all, you know, if they kind of come and go pretty quickly within a few days or even a week without changing any treatment then that is more considered a partial remission. If you just never get sores anymore, that's complete remission. And you can have complete remission or partial remission on or off therapy. So, that's another critical thing. I put patients on Prednisone all the time, and they come back and they have no sores in their mouth. They are in complete remission on prednisone but that's not the end of our plan. So we gotta get my friend his own and hopefully maintain complete remission, so how do you know because you don't have any sores on your mouth? The bigger question is, do you have a durable remission? Meaning, if you come off of everything, are you going to stay without sores on your mouth? Are you going to have a flare up down the road? And that's an area where we all, I think we don't have the crystal ball to know. There are more and more studies coming out to kinda look at who is more likely to stay in remission and who might have a flare up a lot of that depends on your titers. So, the blood work. But, no, I don't tend to do biopsies, because where are you going to biopsy, if you don't even have a sore, right? The biopsy is most diagnostic near one of your lesions. If you don't have a lesion, then we wouldn't biopsy, but blood work can be helpful. The titers I think, can be very helpful. So that's kind of my take on.

Dr. Laudenbach: And the only thing I would add about remission is just from the dentist standpoint for those patients that maybe are only being seen in the dental world. One of the important things that I'll make sure patients know is that there is this concept of remission, even if it's just a quote just affecting the mouth that patients should, I feel always be offered the explanation about remission and that if they do choose not to just do topical management, they should be explained. Really, from the medical side that there are these medicines that can help push this disease process into remission, however, that's defined. And then if the patient decides, you know, I have a few patients who tell me it's just affecting my gums, I'm really not interested. But I know about it. I try to get them for the baseline medically vowels so they know that that's an option because that's really important as these diseases can progress. I, as a dentist, can only really control local disease, not the systemic part of it.

Dr. Culton: I think that's a really good point. Just because the things I have to offer systemically are not always friendly. So, you really do have to weigh your own persona, how much disease you have, how much it's affecting your life, and do you want to take a chance on one of these systemic medicines that may have other side effects to control it. Some people say, I can't even eat. I can't even live my life, Yes, I wanna go for it. Other people say, it's just a few little spots here and there if I can stay away from any of those pills, that's what I want to do. And so, I support patients in both directions, so I agree with you.

Amethyst: Richard asked how many milligrams of cellcept can a 68 year old man take daily. He's currently on 2000 milligrams per day. It has improved the BP but not cured it. He also wants to know what percentage of BP patients experience side effects from cellcept.

Dr. Culton: That's a good question I think in general mycophenolate or cellcept, a max dosing of 1.5 grams twice a day. So, three grams total. Know, the higher you go, the more immunosuppressed you are and the more chance for side effects. So, we kind of tip toe our way up by adding another 500 milligram tablet to work our way up and assess side effects. And I will say I've had some patients who don't even know they're on the medicine while they're on cellcept and other patients who have lots of side effects which cellcept is pretty well tolerated. But when you start to look there are side effects reported. So, it's not perfect, no medicine is perfect, they all have the possibility of side effects. So, what I just tend to tell patients is, whatever you feel that might be new, tell your doctor, ask them, Could this be a side effect of cellcept? You know, we often will look in the literature and say, Oh, that's never been reported with cellcept or maybe, yes, that's pretty common, actually. So, mostly what you're trying to get at is if what you're feeling is likely to be due to the medication, or not likely

to be due. Because if it's not likely due to the medication, you have to go looking for another explanation.

Amethyst: Great, thank you. And in regards to the cellcept are there any studies of any long-term side effects? Frank has been on cellcept for many years, he says.

Dr. Culton: We always worry about the risk of long term immunosuppression and I think the one that we worry about, the most is increased risk of malignancy. So, your immune system in addition to fighting off infections kind of patrols around the body looking for cancer cells. And you know, obviously not a lot of people think about the immune system having that role, but it certainly does, And so being immunosuppressed for long, long periods of time, years and years. We always worry about that. And so my strategy in general, Is just to make sure I listen to my patients. If they're having some news side effect of new pain somewhere, we gotta get it checked out. I think to try to always be on the lowest dose possible that controls your disease, right? So, you shouldn't just hang out at cellcept three grams a day. If you're doing well for years. You want to try to taper down to the lowest dose that you can get away with. And so that's my approach. There's some people out of the gates that risk of malignancy being out there, just worries them so much. And so I think it's just something you have to take into account. Certainly, increased risk of skin cancers is probably one of the most common things that we see with these immunosuppressive medications, and we see that with transplant patients too who are heavily immunosuppressed. They get loads of skin cancer more than they probably would if they weren't immunosuppressed. So that's the biggest one. And luckily, we can see that on the skin. You know, it's still not ideal to get loads of skin cancers, but at least that's something you can monitor externally.

Amethyst: Great. Thank you. Dr. Laudenbach, Carol says that she started taking cellcept in February, however, she does not see any improvement yet. She says that her gums are varyingly slammed in, our dentist does not know much about MMP. She's considering going to see a periodontist that day that diagnosed her, who is a little bit more familiar with her MMP? Is that a good idea or does it really matter who cleans your teeth?

Dr. Laudenbach: Sure, it's a great question. And it's great that there's a diagnosis and that really helps guide the management strategies. So, from the oral perspective, we usually counsel the patient and let you know that if any of us gets a build-up of plaque on our teeth, let alone calcified, Tartar build-up, that's going to cause inflammation and gingivitis and drive inflammation. So, we all have that risk without these conditions. Then you add an inflammatory condition. We’re hoping that medicines help knock down the inflammatory part of the skin disease. But, we also have to, at the same time, have the old-fashioned management of the

plaque build-up, the calculus. And sometimes, or I should say, more often than not. When patients are running into the diagnosis. They've gone six months, 12 months, 18 months where everything's getting more severe, which means they haven't been able to clean their teeth properly. They may have been the best you know at home care but unfortunately this gets painful enough, bleeds enough. And then they've gone to the dentist once or twice. And they can't clean well because it's painful and bleeds too much. Then, they're not getting a good cleaning. I usually tell patients from diagnosis. 2 for six months, at least from the dentistry side, the patient needs help medically with either topical steroids, systemic medicines, to help control the disease process. And that takes time, but it's only going to get so much better in the mouth. Until you're able to do the home care and go get your kind of quote first cleaning. And by that, I mean, since the diagnosis and getting some management started, and even that first cleaning, I usually say, No. I don't care if it's below the gums. Let's just get that above the gums make you tolerate it so you're ok going back, and so you can start some care. And then I also tell the patient, You may have only gone twice a year before, but now some patients have to go for the first few years to get back to where they need to be. You might need to go every two months, at least every three months. And that's usually a big eye opener. Insurance usually doesn't cover more than twice a year if that's an issue, dental insurance. So there are a lot of factors. So I'm supportive of her going to the periodontist. Some Periodontists are very well trained by their programs in managing these diseases with topical medicines too. And, if not, they usually know someone regionally, in the oral medicine world or a dermatologist specialist, like Dr. Culton, who could help out more so. So yeah, definitely supportive of the period of the patients in a periodontist, and stepping up the game on the home care. Dental, cleanings. It's rare that you get a severe bone loss and gum disease from these conditions, But there are exceptions. So it is important to have good general dental care, and sometimes periodontists on us as well.

Amethyst: Great, thank you. Meena. says that she has PV and she has oral lesions, but they're starting to move down her throat. It feels like razor blades when she swallows or eats. Can her dentist help with this, or should she see a different specialist?

Dr. Laudenbach: Well, I would just put out there that I usually tell patients that the part of the mouth and the throat, there's a part, kind of two thirds of that, that we as dentists can see really well and as we get back to the back of the throat and the what's called the base of the tongue, which actually I can't see. ENTs can look back there. Physicians are much more familiar with those areas, as well as the symptoms and managing medicines and related things like that. So, I would usually comment on what I could guide in the mouth part. That sounds like a progression of severe disease. I would want Dr. Culton or someone else who can actually evaluate it with Dr. Culton to decide, all right what are we doing here?

Dr. Culton: And I will just say that I also cannot see those places. And so I tend to refer my patients to either their ENT or GI, depending on where we think the pathology might be. Because obviously, an ENT can do a scope, where they kind of just numb and look down. Whereas what a GI does, they often have to, kind of, put you halfway asleep to really be able to look down in your esophagus. So, it kinda depends on where the symptoms are, but, I have patients that I share with both ENT and GI. Because, really what we need to know, I tend to assume like some patients, oh, if you're feeling stuck back there, it's probably your disease being active, but it could be something else. And so I just have one sad story where a patient's mouth got totally clear on my medicines but he kept having a sore throat. He was a smoker, and he had cancer back there and I kept telling them: You need to go see somebody. You need to go see somebody, anyone. He finally did. They found that so it's just to say leave no stone unturned. If you're having symptoms back there, we need somebody looking.

Amethyst: Great. Thank you. Marjory says I take a prednisone and cellcept for Pemphigoid. We're trying to reduce the prednisone and she's starting to flare. Should she be switching to IVIG?

Dr. Culton: I don't necessarily think so. So much of it depends on the timing of all this. So it's kind of this interesting little dance we do where we have the prednisone, it works pretty fast and then we're going to try to taper down. We started another medicine like cellcept and we're going to try to bring it up over time and we really just have to time it so that the cells that has become effective right when we start to pull the prednisone down and so you can't taper the prednisone too quickly, if the cellcept hasn't really build-up in your system enough to become effective. So, it's a hard question to answer, but I will say if you've been on a pretty high and stable dose of cellcept that is at least three months and you still are having trouble tapering down the prednisone, then it's probably time to look for another medicine.

Amethyst: Well, we have a lot of questions still. Do you guys mind if we stay on just a few minutes longer and ask a few more questions?

Dr. Culton: I can probably take another question or two, but then I have to jump off and go to the clinic, actually.

Amethyst: Great. Ok, well, Rosa asks, what is the best way to treat oral thrush? She's been using nystatin four times a day, and at night, she wakes up and her mouth is still very painful. She has a yellow flem and that persists throughout the night.

Dr. Laudenbach: Yeah, I would just say, I see lots of patients with oral fungal infections and it really is tailored to the patient. Nystatin swish and gargle and spit out over three weeks, is something four times a day is, it takes a patient with a lot of commitment to do that. And even then, conventional data doesn't say it's the best treatment, but it certainly is the easiest to do if I prescribe the lozenge for you to dissolve five times a day. Some people say, hey, that's easier. But then you need enough saliva to dissolve them. So, if your mouth is really dry and I give you something to dissolve. You can't dissolve it, so it's a challenge. We already talked about clorhexidina and how it has some antifungal properties. It can be more helpful I've found, in certain patients to prevent it from coming back but not as a treatment. So, I often find myself in more difficult cases working with the physician to go ahead with the systemic medicine fluconazole. Fluconazole has some interactions with other medications. So, it takes some legwork with me in the position to make sure that there are no issues there, but a good two week course of that, followed by either some preventatives, I think often will stamp it out and then we can prevent it. So, Dr. Culton, any thoughts there on your end?

Dr. Culton: Yeah, I agree. 100% with what you mentioned about a two week course, so I think sometimes patients come in. And first, I would say that we gotta make sure that it's thrush. So, I do swabs in the office that don't have to be sent. I go look under the microscope to see, just to make sure we know. And just because it's thrush there doesn't mean there's something else underneath it, right? We know many Pemphigus and Pemphigoid patients have their active disease, and then thrush on top of it. So making sure first that it really is thrush and then if it is, I think a course of fluconazole is always really helpful, especially if you're still trying to switch with like dexamethasone or something and then you're swishing with the Nystatin. Nystatin it's not working. like, go ahead and just take the oral fluconazole , but some patients will come and say, No, I already tried fluconazole and it didn't work. And that's because another doctor gave them the standard dosing for a vaginal yeast infection, which is like one pill. Repeat it in a couple of days. If you still have trouble, that's just not enough. I think, for this when you have a kind of raging thrush in the mouth, and you're continuing on other treatments that are just predisposing you to thrush. You need a longer course, so I agree with you.

Amethyst: Great thank you.

I would like to thank **both of you** for being on the call with us today. It was extremely educational having you on our call. I would also like to give a huge thank you to everyone on the call for joining us today and thank you to Genentech, Principia Biopharma, Argenx, and Cabaletta Bio for helping to make today's call possible.

I have a few announcements:

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**!

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 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.

Lastly, If you have a question that didn't get answered on the call, or have additional questions please e-mail Becky Strong, at becky@pemphigus.org, or call (916) 922-1298 x:105, and we would be more than happy to help.
This call recording will be sent out with the survey following this call.