Becky: Welcome everyone. Thank you for being on the call with us today. This call is now being recorded and a special thank you to Celgene and Genentech for sponsoring this call today. Our speaker today is Dr Kyle Amber, assistant professor of Dermatology at the University of Illinois at Chicago. Thank you for joining us today. The call today will focus on treatments for pemphigus and pemphigoid. First let me introduce you to our speaker. Dr Amber is an assistant professor in the Department of Dermatology at the University of Illinois in Chicago. Dr Amber was born and raised in Miami, Florida, where he attended medical school at the University of Miami Miller School of medicine. After completing medical school, he completed a transitional year internship in Chicago, followed by his residency at the University of California Irvine, Department of Dermatology. Dr Amber currently leads the skin immunology lab at the University of Illinois at Chicago where he studies the role of, uh, local skin inflammation in pemphigus and pemphigoid. In addition, he runs a specialty clinic for the treatment of autoimmune blistering diseases. Now, it is my pleasure to introduce Dr Kyle Amber to answer your questions on treatments of Pemphigus and pemphigoid. Welcome.

Dr. Kyle Amber: Hi everyone. I just, I thought it would be good before answering the question just to sort of give you my biases, my perspective, on treatment, why I do what I do and how I view treatment. Because I think it'd be almost dishonest to say, oh, you should do this, you should do that. I think the first thing to understand is sort of what I view is what different aspects of disease are we treating. I really think there's three aspects of disease treating what you have today, what your body is trying to make during the next two months, and what your body makes in two months to treat the disease. You really want to focus and choose your treatment at that time. For example, if you say, I'm going to be very aggressive with the treatment that works in three months, it's not going to do anything immediately.

I try to compartmentalize those things. The other thing is just sort of the goals of treatment. If you look at traditional treatment, steroids. If steroids don’t work, you add something. If that doesn't work, you change to something else. I try to avoid failures that are expected failures of treatment on the traditional approach. I sort of think of things in terms of the expectation of frequent relapse, the expectation of being on remission, on medication, and what really is my goal is long-term remission off medication, which requires a lot more aggressive treatment and a lot longer treatment. But I think to be able to hopefully be disease free for the foreseeable future with being off all medications is certainly something I would

want if possible for my patients. So, I just say that because that sort of will tie into a lot of my answers regarding some of your guys' questions.

Without further ado, I guess I'll start from the written questions here. Is it possible to have negative results on the Desmoglein in one in three blood tests, but still have had biggest Pemphigus Vulgaris flares? Yes, absolutely. About 10% of patients will have a negative Desmoglein and there was the older concept with that. This is a disease just caused by an antibody. Single antibody targeting Desmoglein. That's the only thing important, et cetera. And that was sort of propagated for maybe 20 plus years with like a small diff dissenting voice and it's grown over time. And even we had actually shown a few antibodies that could cause disease, for example, that we see in about 40% of patients with pemphigus. It's probably hundreds of antibodies all contributing together while guest Desmoglein is certainly the most prominent of them.

Dr. Kyle Amber: There are others. So that's why in this case, can you explain why flares would occur in this scenario? If it correlates, but it's not perfect. and it certainly doesn't catch all patients. Next, what is the correlation between stress and Pemphigus? Is there any relation to disease and the level of stress? 100%, absolutely. Yes. And this is true beyond Pemphigus is true in pemphigoid history and mucous membrane pemphigoid is really true in most dermatologic diseases. There is a strong neurologic link, between would the skin. For example, we see patients who have say autoimmune hair loss, they get stressed, they lose their hair, they're not stressed, the hair grows back. Why does this happen? We have absolutely no idea. But it's a real phenomenon and is one of the things as best as possible. You know, during this time you have to try to reduce stress because it does make the disease better.

Dr. Kyle Amber: But of course, you know, you're on steroids or something, you're not going to be very happy. And so the cycle sort of goes, so it's easier said than done certainly. But stress is absolutely, related to it. Next question I had, is there a causative relationship between Pemphigus and radiation? The interest kind of, so radiation can induce stress to the skin which can then sort of unmask pemphigus if it was sort of undetectable or if somebody has it, it can cause relapses on its own. It shouldn't cause it. If you are not predisposed to having pemphigus and you get radiation it shouldn't make you all of a sudden get pemphigus. But certainly if you were predisposed or had it already, it can make things worse. Next question now we're getting more treatment questions.

Dr. Kyle Amber: How many rounds of Rituxan without remission do I do before giving up on this therapy? I think this is an important one. because I think there's a view with rituximab. I'm thankful it got approved. I'm thankful that people put in effort to, to study it. The problem is I think there's one article that came out and said, Rituximab, a magical bullet for pemphigus and it's not the issue with Rituximab is what I was saying in terms of what do you treat disease now, treat what you're making. In two months or treat a what you have at two months. The reason is our body has some called plasma cells and plasma cells make the antibodies that attack the skin. Rituximab does not kill those plasma cells at all. It kills the precursor. So only when your own plasma cells die, does rituximab start to work.

Dr. Kyle Amber: The longer you have disease, the longer that's expected to happen. In a patient who let's say has disease for less than two years and you give them rituximab, their plasma cells don't last for very long. Lasts a couple of months and usually three to six months and the patient's clear they're there. Ideally in remission or at least the disease is quiet. Then, the problem is let's say you have a disease for 20 years and you give Rituximab. It's shown that those plasma cells can live almost two or three years. Sometimes people will keep giving cycles of Rituximab, without, in someone who didn't respond, and the problem is, will you, you wiped out the precursor cell, but you're not able to kill the cell that's making the antibody. I don't know that a lot more rounds of rituximab will help that other than time because you're looking at basically the two to three years for your own cell population to die out.

Dr. Kyle Amber: And the Rituximab, it works pretty much 100% and wiping out a, the B cells, it's just you need to actually get rid of the next step to sort of repopulate. How many rounds before giving up? I think it is a bit difficult to answer because I wouldn't say, you know, non-responders do exist for sure. The question is, its non-responders at three or six months or is it non-responders at like five years? It depends on the disease, how long it's been there. okay.

Becky: The next question is that she was diagnosed as cicatricial pemphigoid in November of 2008. She's been taking dapsone 25 milligrams for seven months and using flu canonized a gel on her gums as well and she'd like to get off it both. How would you recommend doing this? She has had side effects of yeast, canker sores in her mouth, which are under control after taking an Antifungal Med and a to know her mouth blisters are much better but are not completely gone.

Dr. Kyle Amber: So, the problem is, dapsone works very well for sort of that immediate phase of disease. So your body is still making the protein set attack. You're scanning or Mucosa and then you're masking the effect of that to ideally quiet. I don't know how realistic it is to get off those with that line of therapy only. Basically, you're not doing anything to stop antibody production. You're just masking it. That said that sometimes if it's a mucous membrane perfectly that's not very aggressive, I strongly recommend that approach because sometimes you can get overzealous about wanting to try to put the disease in remission that you cause way more harm with the medications involved. Dapsone, 25 milligrams is a very, very tiny dose. And sometimes in a case like this, if there's still disease, I would go up to 50 and once it's a hundred, like to get it less.

Dr. Kyle Amber: If somebody is on 50 and smooth sailing and completely disease free, that is going to be, you know, it's always pick your poison when it comes to any medication and any goal. If things are more aggressive, especially eye involvement, then you need to get a lot more aggressive than that. The yeast is most likely a result of just the fluids. So that's where sometimes if you just go up on the Dapsone, you no longer need to use topicals. I don't know what that alone that is realistic to get off the to without expecting a flare, but I wouldn't worry a ton about the Dapsone, especially at 25 milligrams, which is really a minute dose. I mean we go up to 200 a lot of times.

Becky: Great. Bonnie also said that she has Graves' disease and takes levothyroxine. Are there drug interactions between the DAB zone and the levothyroxine?

Dr. Kyle Amber: There shouldn't be. It's always unpredictable. Dapsone is one of those, you know, if of all medications, I probably respect it the most because it's 99% of people tolerate it great, and then the 1% can be catastrophic. I definitely check labs a lot more frequently and I'm a lot more careful probably with that than any other medication. It also can do sort of weird unexpected things. It wouldn't surprise me. For example, if there happened to be some changes to TSH with the Dapsone, I have had patients who did complain of some changes in mood, especially at higher doses. It's kind of weird. There's not a lot of data of why and it's all small amounts of people.

Becky: Great. Sarah is asking, I would like to know if it's more common to see longer remission periods after each round of Rituxan treatments for BP. My skin was clear after eight months between my first and second treatments, 13 months between my second and third. And I'm hoping this trend continues.

Dr. Kyle Amber: The big issue is Rituximab is always going to be relapsed. It's about 75% of people relapse. In this case you're getting sort of these growing periods that will likely continue and then shortened back up. The problem is, every reef flare you have, if you think of things as sort of like giving yourself a vaccination, it's sort of like every time you have a flare, you're giving yourself a booster. At some point the immune system really wants to essentially be immune to the skin. And so those plasma cells start to last longer and then the Rituximab doesn't clear them as well. With every new relapse, that's one thing I worry with Rituximab is I see a lot of these relapses and they can be more stubborn to treat. I'm glad it's going on the longer side, but I don't know that that will last forever.

Becky: Okay, great. We're going to just go back to this next question is about dapsone. How long does it typically take to see dapsone results? I've been taking it for almost two weeks and I haven't seen improved me yet.

Dr. Kyle Amber: It always depends a bit on the dose. 25. I rarely see much. 50. I tend to see some improvement. I really wouldn't start at a hundred. I think the side effects are intolerable. I'm at starting that high. Generally, it's disease dependent. So in dermatitis herpetiformis it's two days. Epidermolysis bullosa. You can see improvement within a few weeks in bullous pemphigoid sometimes like two to four weeks. It really is an issue of the dose though since most of the time we start with a low dose to make sure everything is good in the bone marrow. Sometimes you notice a minimal response to two to four weeks, but then we boost up the dose to something that will actually work a little better. If you just start too high, sometimes you get a lot of low blood cell abnormalities.

Becky: Okay, great. Next questions says- I just finished up being weaned off all of my medications for bullous pemphigoid. When inquiring about the Shingrix vaccine for shingles, it was determined through blood testing that I have no immunity to chicken type packs. My dermatologist said I need a chickenpox vaccine, which is a live vaccine. And eight weeks after the chickenpox vaccine confirm immunity to chicken tax with a blood test. And then once that's positive, proceed with the Shingrix. But she's a little confused on all of this because she's had practitioners tell her in the past that autoimmune disease patients should avoid live vaccines. She's just wondering your opinion on that.

Dr. Kyle Amber: Yeah. Live vaccines with auto immune disease on their own, are ok as long as you're not on any medication or have any long-

lasting medication that with use to treat it. For example, if you got rituximab for your disease and then two months later you say, okay, well I'm off of treatment and then want to get a vaccine, you can't do a live vaccine at that point because you're still actually immunosuppressed from the prior medications. It does depend a little bit on the medication washout period for live vaccines.

Becky: Great. Thank you. Pat says, my husband has pemphigus vulgaris and vegetarians on his scalp and after having lesions in almost every part of his body, mouth and throat Rituxan has eliminated all but the scabs on his scalp a will multiple infusions of Rituxan work to eventually clear this or is there another solution for this type of Pemphigus?

Dr. Kyle Amber: Sure. Going back to sort of acute phase disease to the issue. So in patients with these disease, you have antibodies that bind to your skin and once they are bound to your skin, there's sort of localized inflammation and Rituximab doesn't undo any of that. It just stops you from eventually making new antibodies. Some areas like the scalp and, and oral Mucosa are just much more stubborn than others. So the problem is even if the Rituximab is let's say it's worked perfectly, sometimes you're left with the stubborn areas that need to either have time to burn out, which can take like three months or so, four months or then you have to do steroids to really clear up that local inflammation. I don't know that more, I would depend on seeing the patient and seeing how the scalp changes with all of that. I think just sort of an acute treatment would be needed to clear up that last body. Even sometimes if it's small, just like an intralesional steroid or something. There's sort of have to treat it as the antibodies are already there, so you can't undo that part. Great.

Becky: Thank you. I'm going to group a few questions together here. We're getting a lot of questions about can you take rituximab without taking another medicine, specifically prednisone, but any other medicine and then how do you determine if Rituxan can be used on its own or if you need to have another medication?

Dr. Kyle Amber: Yeah, so you can absolutely do it. It's not probably the best way to go. The reason is, when you have sort of active skin disease, the Rituximab is going to take three to six months before you really notice a ton of improvement or ideally clearance. You're not really fixing what's there right now. For someone with very minor disease, I think a few spots here or there. I don't necessarily think it's worth doing the whole Shebang with the prednisone because you're looking at several months of high

dose prednisone. The question is- what are you achieving at that point? If it's severe, I'd say there's really no way of getting out of the steroid on that front. The ideal patient populations would, rituximab without prednisone is really going to be sort of more mild disease where you're okay with it taking longer to avoid the side effects of the prednisone. Now the reason I'm even in those cases, not a big fan of it is sort of the immunology front of it. So the steroids actually can really improve the course of the disease faster. Even in the clinical trial for Rituximab, they still gave steroids. You were able to just give a lot less to bring the remission. Presumably relapse rates would be a lot higher. If you're not using prednisone because again, this sort of smoldering disease makes the immune system a bit more stubborn.

Becky: Right. Thank you. Nina says that I've been on prednisone since the last 40 or 50 days, but I'm down to 20 milligrams a day with little to no symptoms. Could I get away with no systemic immunosuppressants?

Dr. Kyle Amber: I wouldn't. The reason is just the natural history of these is you, you start tapering steroids and at some point, you sort of run into a wall. The problem is you get stuck at a point phase day. It's, you tried to take her from 20 and you go to 15 and flair. Okay, you go back to 20 and you try it again, you get stuck. And the problem is the systemic immunosuppressants take about two months or so to kick in and sort of give you the better chance of getting off the steroids entirely. I always find that if there's a choice between steroids or say cellcept or azathioprine, the azathioprine or something, I think the prednisone should be the first one to go just from long term side effect profile. If you're at 20 milligrams a day and optimistic that you can completely get off the steroids and be in remission. Sure. But that that's unfortunately a minority of the cases, in which case I, I usually don't like to pull away the immunosuppressant until month off of, or at least actually years off of the steroids.

Becky: That's great. Thank you. Carol says, I was diagnosed in 2016 with oral pemphigoid. I've been treated with IVIG for the last two years and as I get closer to my eight-week confusion, I noticed my gums start getting soft again. When using IVIG can treatment be modified to eradicate the auto antibodies?

Dr. Kyle Amber: Yeah, so the big trick with IVIG is just the right number of infusions. So if you look at the published protocols on IVIG that resulted in remission at like years and years out from treatment. It was almost an average of two years of, of infusions to get

there. A modification, I presume that this person was tapered down to every eight weeks from every four. If not, I'd say every four certainly works better than, than every eight, at least in the initial period. As far as the, the tape, at every eight weeks, I would keep it there just for a little bit longer before moving to every 12 weeks if they're on that protocol. But as far as beyond, making sure it's the right dose, which is two grams per kilogram, making sure it's monthly. There's not a whole lot you can manipulate with IVIG beyond that. It's just, it works very well, but it just needs time.

Becky: Okay, great. And thank you. Beth is asking if sets up a cellcept is still a good choice for pemphigoid? Is there or is there a newer or better drug available?

Dr. Kyle Amber: Cellcept is what I use. A lot of people on the east coast use methotrexate. I think both are reasonable choices. I think the side effect profiles they'll slip is better. The issue is, can we use Rituximab for both Pemphigoid? Absolutely. Data shows and my experiences, it's not as good as for pemphigus. The other bigger problem is the realities of our unfortunate healthcare system. Getting it covered can be a lot bigger of a challenge since it's off label. I find for like really chronic pemphigoid I like IVIG with cellcept is really my, my preference of bringing remission. I don't think there's a new great way of getting away from the felt up unfortunately.

Becky: Great. We're getting a bunch of questions that are asking about, how long can you be on cellcept and what are the long-term side effects of Rituxan?

Dr. Kyle Amber: For cellcept long term, it's really just decreased immune systems. Whether that has an increased risk of cancer that's been shown in azathioprine and hasn't really been shown in cellcept, which are comparable drugs. I feel like in practice, just seeing a dermatologist, I still see skin cancers anyways, the people who are on azathioprine and just sort of tend to sprout more skin cancers than those on cellcept. I prefer to switch to that. It's not ideal to be on it lifelong because it does increase the risk of infection. The older you get, the bigger risk of infection there is. The goal is really to control or prevent the relapse. When is that ideal time that you can pull the trigger and take away the cellcept. There's no good test and that's the most terrifying thing is when somebody's been good for years and you say, okay, let's try to stop this step and see how it goes. If there's not a good solid answer of long-term risks of them, we know infection now a long-term risk with Rituximab as well. We think probably less in the way of long-term risks. You get to the

same immunosuppression, but that immunosuppression can last for a much longer time, that can last us for a year or two years. And some patients don't quite bounce back as much as you would like with the treatment, presumably shouldn't carry that cancer risk or carried longer term risks.

Becky: This is another question that is ultimately about cellcept. Sheila says she was diagnosed last July with bullous pemphigoid. In October of last year, she began treatment with IVIG and saw only a 50% improvement and then took in December, began started taking two grams of cellcept and 10 milligrams of steroids, currently down to two milligrams. Now she's seen great improvement with no signs of bullous pemphigoid anywhere but on her toes and she has like about five blisters. Should she continue to stay on the 2000 milligrams of cellcept or maybe change to Rituxan. And then as a follow up question to was- do I need to be off cellcept before I begin another treatment?

Dr. Kyle Amber: The issue I see here is the taper to steroids from 10 to two, without clearance of the disease. So, I'm always very cautious to try not to taper if there's disease activity because what's going to happen as you lower the dose. In this case, I'd say if there's still involvement, it's almost a guarantee. Things will get worse when you strip something away. The question I guess would be, is if still such is being used with IVIG, I think they should always be used together. If you're doing IVIG to some rebound phenomenon we see, but I would not get off cellcept with any active disease. I think you actually have to be more aggressive because if you just believe that little bit of activity there and pull things away, they can spiral out of control.

Becky: Great. Thank you. This next questions says that she's currently fluocinonide Ointment, 0.5%, and it does not help with the itch. Can you recommend anything that might help with the edge?

Dr. Kyle Amber: For itch, it's difficult. The problem is, it depends on the disease, but for bullous pemphigoid for example, if the disease, if the itches severe, it's really a sign that the bullous pemphigoid is systemically very active. And I think you need a systemic approach rather than a topical approach. I think the topical is sort of nice as a band aid. But with most of these diseases, they're actually a very steroid responsive from itch. I mean, which is probably the most complicated thing. They're like 40 pathways of itch. For simplicity purposes and blistering diseases, it’s fairly simple. You have to just reduce the inflammation enough so that things aren't itchy. And now you could go up in strength from fluocinonide and clobetasol which

is a minor increase and may be helpful. It's generally a sign that just the immune system is sort of overwhelmed and needs of systemic treatment.

Becky: Great. Thank you. Fabio says that he has pemphigus that ended in the past three years. He's had three atrial fibrillations. His cardiologist raised a question and asked, is there a link between Pemphigus vulgaris and Adrial? Is there relation or is there a connection to Afib?

Dr. Kyle Amber: There shouldn't be. The only thing is sometimes rituximab can cause some cardiac arrhythmias, like afib, that are sort of more transient during infusions. There are cases I believe in like cancer treatment where it's ongoing, but the disease itself really shouldn't have any association.

Becky: Great. Thank you. George asks a timely, and I think a really great question, is sun exposure like at the beach or swimming a trigger for bullous pemphigoid and what can be done to protect the skin when you're out in the sun? What recommendation?

Dr. Kyle Amber: Again, I think pemphigus it's far more of a trigger than bullous. Pemphigoid but absolutely both. And I've unfortunately seen patients who are, say for example, misdiagnosed and then got ultraviolet therapy and then they just blew up with bullous pemphigoid all over their body. It's definitely a trigger. I feel like I take a different standard than many dermatologists. I'm like, live your life still be outside. Don't hide from the sun, but take calm like good precautions, which is basically going to be, if you can keep the areas covered, for example, a cool long sleeve shirt that would be preferable. If you're like me and get very warm and would never actually do that, I would really be judicious with sunscreen on. Generally, the sunscreen would be like, are going to be a zinc and titanium base. The problem is they tend to be pastier. The benefit is well they don't cause rashes and they work a little bit better. I would say titanium sunscreen, an SPF 50 or higher. It is unfortunately a trigger.

Becky: Great. Thank you. We've also gotten quite a few questions about are there any foods or beverages that can help treat or natural treatments of pemphigus and pemphigoid, or are there any things that should be avoided?

Dr. Kyle Amber: I'm glad you asked it because we finally publish the study. The patients on who filled the survey, they had finally some recommendations for diet with some evidence. One of the hardest things is a patient comes in and they'll say this food makes my disease terrible and the next patient says that fluid

helps me. We did a study on 200 patients from the IPPF. The sort of consistent things that made things worse than about a third of people were spicy food, citrus food. Interestingly, deep fried food was also another one, green leafy vegetables. And I believe it was dairy actually. Some people found a beneficial about 10 to 15%, so that's as best data as we possibly have for Diet and these things. As far as homeopathic things and like that, I have to be skeptical because a lot of them are advertised as they do this.

Dr. Kyle Amber: If they do 20 different things for you, they probably don't do a lot. So, I'd say things like anti-inflammatories like say fish oils, turmeric and things like that. I think common sense would say they probably actually do have a beneficial role in the disease. Nobody's proved it. Bu that doesn't really matter. Common sense kind of prevails for that one. There are a lot of different things. For example, I mean every supplement out there and, and I get asked frequently if this is an autoimmune disease, what can I do to improve my immune system? There is no supplement that actually demonstrates changes to the immune system. And by definition, auto immune disease, your immune system is actually working too well. So even if those supplements work, that would theoretically make the disease worse rather than better.

Dr. Kyle Amber: I don't think there's a lot on that front. Definitely Diet and a lot of patients will report changes in Diet. And I think the most important thing with diet is really, I don't care what works for someone else. I care what works for you. If you notice a constant trend, like every time I eat this I get a flare, stop hitting it. And even sometimes food journaling can be helpful just to sort of try to find associations because I think there's a lot more to it than we know. And I don't claim in any way to know every food that may make somebody better or worse, but I think it’s very patient dependent.

Becky: Great. Great answer. Thank you. Betty says that I treated the early identified spots. She has bullous pemphigoid with a Kenalog ointment, and it will dry it most of the time, three times it just developed into a bubble and left a discoloration spot. And she wants to know should she continue to apply the cream once the bubble appeared or should she just protect it with a band aid? And her follow up question is that I have been applying this cream sparingly for approximately about a year, still in the same tube with my fingertips. Is this going to be detrimental to my fingertips in any way?

Dr. Kyle Amber: I would not be shy at all with triamcinolone. Triamcinolone is a medium to week strength of steroids. We always warn people about sending of the skin and I think that's a very real thing, especially if people put it on the face, in the armpit or in the groin. For thick-skinned areas like the fingers, for example, you could really get away with using triumphs and alone for years and not actually notice anything. It's even if it's the top of the hands that you start worrying about after a few years. The actual palm sides. Really. I don't think I've ever seen a single person who had any thinning of the skin there, even who may have used steroids for 40 plus years. I would be less cautious and make sure you're treating accordingly. Now the area's dry up.

Dr. Kyle Amber: They leave hyperpigmentation. That dark spot is in theory done. So there's nothing to treat at that phase. The only thing I warn you is sometimes there'll be a dark spot, but there'll be a little hint of red to it. Then it is still active. I would always for if time someone's enough to do it, I would really lean on the side of overtreating cause you're not really going to do harm by treating a few extra days with the triamcinolone. Whereas if you don't, things can spiral a bit out of control for fingertips. I would wash your hands after application. I really wouldn't be worried about it.

Becky: Roger says after having successfully completed remission through a four-week treatment of Rituxan remission might be extended or could remission be extended by periodic one-time infusions every six months.

Dr. Kyle Amber: Controversial. Whether to consistently give it every six months to try to just keep permission forever without a flare versus sort of following and seeing if a flare happens. I don't have a great answer. I do worry about just chronic treatment because essentially about 25% of people, if you do a single course, will never get the disease again. To commit to lifelong therapy when you could be in that one quarter would never need another therapy again. The problem is it depends on the duration of the disease. I'm not sure how long they had the disease for if it's a new diagnosis, they, within a year I would be okay totally watching after the, so I would do the one month and I would do a booster at the six months. That would be it. I wouldn't give a chronic treatment. Now if you had the disease for 10 plus years, I would probably do every six months for just a couple of years just because the likelihood of relapse is just much, much higher.

Becky: Great. Thank you. Jenny's says that she's a 40-year-old female diagnosed with PV. 13 years ago. She went through standard

steroids and immune suppression, suppressant treatment first, when she was diagnosed and over the years completed four courses of Rituxan therapy and one IVIG works well to eliminate my symptoms, but PV antibody titers are still above normal. Does rituximab therapy decrease effectiveness over time?

Dr. Kyle Amber: Not really. If the disease is in remission on therapy the issue is, I never followed titers because I think if the titer is still somewhat elevated, that doesn't necessarily mean if you stop treatment you're going to flair and vice versa. So, I really try to treat the person and not, not the titer, but it is difficult cause once you have the result you really don't know what to do with it.

Becky: Great. My dentist said, recently did a biopsy and diagnosed me with pemphigoid and is treating me with Clobetasol. How do I know when it's time to try another medication or systemic treatment?

Dr. Kyle Amber: In these cases, if it's pure, just mucous membrane pemphigoid sometimes the treatment is worse than the disease. When you get more aggressive. For example, it's just pure oral pemphigoid and Clobetasol works, I would be content there because you switched to other things. You started taking other side effects. The problem is if it's another mucus sites involved or if its skin involved, I really think then systemic therapy makes a lot of sense. If you're getting like a lot of yeast, oral yeast infections or if the Clobetasol doesn't quite do it. I don't think it's a bad idea to see a dermatologist who, who treats these things and you can basically get an idea of what the side effects are. And if they're right for you, there's no right answer because it's always picking your poison. But I think if things are not well controlled, I would lean on the side of systemic. If things are well controlled, I would lean against it.

Becky: Great. Thank you. This is another question about Clobetasol Is it okay to use Clobetasol on broken skin?

Dr. Kyle Amber: It depends on the broken skin because of blistering disease. Absolutely. The skin is broken of the inflammation from the disease. In that case it is required in order for that skin to heal and speeds up the healing broken skin. If there was an injury or a wound, I wouldn't use it on there because that slows healing down.

Becky: That's a pretty clear cut answer for us. There is another question about what is a pemphigus score index and which countries use that score?

Dr. Kyle Amber: A pemphigus score index is based on an extensive list used for clinical trials. I don't think people really use it for routine practice. I think the only reason you would use it for routine practice is if you think you're going to go back and like review charts for a research study, then it's nice to have those numbers. But it doesn't really help me a whole lot because if I say, okay, there's a score of this and that because I scored 40 different sites and the degree of extent, the reason these scores exist is nobody wants to fund clinical trials where there's not a clear cut outcome. If a physician says, yeah, they look better, the patient's happy, that's not good enough for getting approval. If you say, well, the patient's score improved by 75%, the drug is effective compared to nothing, then it gets approval. They do it I think a bit more in Europe. Switzerland and Germany and in Australia there are a few people who sort of publish and do these things a lot, but it's more geared towards the clinical trial setting and not in routine practice.

Becky: Thank you. Mark says his father is 96 years old and has the condition in one eye. He has to wear a full contact. And we have, as well as see as ophthalmologist and they're having to frequently pull eyelashes. His overall health isn't good and he does have prostate cancer. They're looking for some ideas or some treatments to relieve the constant discomfort that he is experiencing. Additionally, his eyelids are turning in and scraping his eye.

Dr. Kyle Amber: In these cases, if the comorbidities are problematic, it would depend obviously on all the specifics. But dapsone is helpful first symptomatic relief. It's not particularly disease-modifying. For example, in somebody who I'm worried in with eye disease about blindness, I would not do that as a monotherapy because it's almost just a ticking time bomb. But when comorbidities limit you and you're looking for sort of a treatment for the next year or two to just keep things under good control and really get symptomatic relief, that I think is one of the more helpful ones. Sometimes I would probably maximize something like a Doxycycline and Dapsone to see if that's adequate for symptomatic relief. IVIG is also actually quite helpful. The downside is it just takes a long time to work and that's at least not contra-indicated with having a cancer and doesn't increase any of the risks. It does depend on sort of expectations of treatment and disease progression.

Becky: Great. Thank you. Bonnie is asking, what are the side effects of Rituxan?

Dr. Kyle Amber: The biggest one is going to be infusion reactions, that can be high highs. Sort of like anaphylaxis, like swelling of the lip and shortness of breath and all of that. Which is more common than usually the first infusion that you can control with you. It depends on how much thyroid you give before the infusion and you adjust accordingly. I noticed some infusion centers where my patients go will be, unfortunately, they'll give less than had wanted and then a higher risk of the infusion reactions and then others do what I want in and fewer infusion reactions. Just decreased immune system. I mean you're knocking out an entire line of immune cells. It certainly increases the risk of infection and probably more so than cellcept arrays, the thiopurine. Then the rare, the scarier one is agony and basically just cause cardiac arrest during the infusion. And that doesn't have to do with, you could have a terrible heart, or you could have a perfect heart, that can happen. It's a very rare, thankfully though, but it always gives you a little more pause about choosing that as a therapy.

Becky: Great. Thank you. The next question is, will methotrexate cause discoloration on your tongue? And she says that she's also using a magic mouthwash and I brush my tongue, but that hurts, and it doesn't always remove it all.

Dr. Kyle Amber: Too difficult to answer that question because the thing is with discoloration of the tongue are actually multiple discolorations because yeast can do it. You can have overgrowth from other things. I would see the methotrexate on its own really shouldn't. It's of all of them, it probably decreases your immune system the least in some respects. Getting like a yeast infection or something probably wouldn't cause that, or it wouldn't cause the issue. It's basically if there is a yeast infection, you can scrape all you want but you really need treatment for it. And the magic mouthwash is symptomatic treatment but doesn't actually, it's sort of a band aid. If it doesn't fix what the original problem is, which I can't tell you on that one.

Becky: Thank you. Another question. Do you like dapsone at the first sign of pemphigoid or is there another treatment that you use first?

Dr. Kyle Amber: I am not a big fan of dapsone overall. I think my issues with it is probably it's overall very safe, but if someone's going to have a bad reaction to it, it can be life threatening. I don't reach to that first unless it's a disease that particularly responds well as a first line. Now pemphigoid responds somewhat well. I think it's, if you look at, it depends on who you ask. Some people will say it's the most amazing thing that ever happened in pemphigoid.

Other will say it's useless and I'm probably somewhere in between. I think it certainly has a role depending on severity. I really do like doxycycline. I think the side effect profile of those is so far superior to any other systemic treatment. The recent study showed it's not inferior to steroids, which in in practice I think it is inferior to steroids to some degree, but basically, you're sort of picking your poison if doxycycline and niacinamide enough to be disease free that's going to be the choice. Now if the patient doesn't want the sort of long-term stuff and control and say that didn't work or a steroid dependent, then certainly adding dapsone on board is helpful. I'm just not a big fan of it as a first line.

Becky: Great. Thank you. Our next question is in addition to BP. Trisha pemphigoid with scarring connecting the left eyelid to the eyeball. What is the best treatment for my eye?

Dr. Kyle Amber: It's difficult because the treatment that you are on for the pemphigoid overall is the most important thing. For me, sort of by definition when the eyes are involved, I'm basically doing either Rituximab, IVIG or Rituximab and IVIG. I don't really play around with anything less because I think it's probably for me is always the most frustrating because I am not an ophthalmologist, but I certainly treat a fair amount of it. So, the end of the actual therapies for they have like amniotic membrane transplant, all of that. I'm not equipped to answer this specific as once the eye is already damaged, but it's really how to prevent it. And I think as a dermatologist, you see it's like 1% body surface area, but you're giving them the strongest thing, which is always unsettling. But you really do have to be as absolutely aggressive as possible or else it can progress irreversibly.

Becky: Lauren says, we are given Rituxan biosimilars now in France instead of the a Mabthera Rituxan each hospital can get, can give different biosimilars depending on the deal is struck with the lab company. What are your thoughts on this or is there any brands that are better than the others?

Dr. Kyle Amber: I will say I have only a little experience with the biosimilars and unfortunately, they've all been bad experience. So in my experience, I think a two or three patients that I have to do the biosimilar, all of whom got way more of an infusion reaction than I'd really seen on average with sort of the regular Rituximab, I think it's quite a hit or miss. And the problem is the regulation on them is they have to be similar. They don't have to be the same. And they don't have to justify their side effect profile to the same rigor that the original drug had. In theory,

should it be completely fine like generic drugs? We pretty much have no problem. We know at least the active ingredients by law has to be the exact same and at the same amount with biosimilars, that's a little bit different. I usually try my best to avoid them just because I think they're more unpredictable. They probably do about the same thing though.

Becky: Great. Thank you. Rosa is asking, I have pemphigus foliaceous and have had two rounds of Rituxan and now I'm lesion free. Do I have to still avoid the sunlight and use precautions when I'm in remission?

Dr. Kyle Amber: Yes. The issue is they're in remission to the naked eye and in remission under the microscope. So even if to the naked eye or completely in remission, if you have sort of just the small smoldering disease and get a bit of Sun, that sun damage can be enough to basically unmask it and you're sort of stuck where you were before. Now if you're in total remission, in theory, if you get minimal sun, it shouldn't make a difference. But something like a sunburn, for example, causes enough damage to the skin that you're basically, again, sort of vaccinating your body with yourself and your immune system somewhere in the back of its memory knew that you had this disease and more than the average person wants it to come back. I would still absolutely be cautious.

Becky: Great. Thank you. Olivia says, is it true that there are cases where the disease, she's referring to pemphigus vulgaris contend to disappear after a certain amount of years. She says she was on an active on a constant basis for about 18 years and is now, has been inactive for about a year and a half constantly.

Dr. Kyle Amber: Not generally, if you look at the natural history of the disease is almost always to get worse and worse. As far as triggers of why it could potentially undo medications are by far the biggest one. If somebody was on something, sun is another one. If they had cancers, if there was a cancer that was treated, then sometimes that can calm down. In general, to have the disease and just to sort of go away on its own, it doesn't really do that. I don't doubt it if it can on, but that's just generally not the way it goes.

Becky: Great. Thank you. This question is coming from Bob and he says, what can I do to reduce the jittery feeling I have with 60 milligrams of prednisone?

Dr. Kyle Amber: There is not a great solution to it, unfortunately. Some people get more jittery than average. For sleep purposes sometimes if they can't sleep, you can give like a sleeping pill or something.

But from the overall jitteriness of the steroids, there's not a great option, which is why I try to be pretty aggressive to get off of those types of doses as soon as possible. The thing is sometimes adding thyroid sparing stuff like the doxycycline or Dapsone, which kind of work in a similar way be at much less, can help to get lower on that dose a bit quicker, more quickly. There's not a great therapy unfortunately for that. Jitteriness terrible.

Becky: Okay, great. Yeah, that's something that we all struggle with. With the prednisone, unfortunately. Marissa says I'm a 40-year-old female. I was diagnosed last year with PV. It was just in the mouth, but then it flared to the skin and other mucosal areas. I started prednisone, cellcept, and then Rituxan in April, and now I'm tapering off prednisone and the plan is to remain on cellcept until I'm in remission. My doctor is planning to do another Rituxan infusion after 16 weeks if I'm not in full remission. I'm currently at 12 weeks and doing very well. But I do still have some small areas of blistering. Would you recommend waiting longer than 16 weeks? If I only have minor blisters?

Dr. Kyle Amber: It's hard to answer because I never used cellcept and rituximab together. I think you're sort of doubling up on the same thing. I wouldn't extend longer. If there's still minor disease, that's not good enough. A lot of people are like, well, things are almost gone, almost gone as is, as far as your immune system knows. This is 100% still there. As far as tapering off, I wouldn't taper off with active disease as far as repeating rituximab. I don't do both. I would just do one or the other, that's sort of hard to answer that part for you.

Becky: Great. Thank you. There is a question. Do you know anything about the research going on about the gas six protein and will it be a potential help for PV?

Dr. Kyle Amber: This was a gene. I think they had found. There's not a whole lot, if I remember correctly, there was like a genetic study. But as far as I know, there's nothing even then like phase ones or anything related to that. So it's a pretty small thing.

Becky: Great. Linda is asking, can you take doxycycline with Methotrexate because I use 10 milligrams of prednisone with methotrexate, but my feet cramp when I use it with prednisone.

Dr. Kyle Amber: There should be no issue with using them together. The biggest thing is if you get too much stomach upset really is going to be to separate the timing out. You can try to take one in the

morning, one in the evening type thing, to see if that helps. But there shouldn't be an interaction.

Becky: Great. Thank you. This next question is I took prednisone and cellcept for about four years and have successfully weaned off this medication and have been in remission for three years without any reoccurrence. Is it possible that it will never reoccur in my system?

Dr. Kyle Amber: Absolutely possible. The hardest part is to get where you are. I'm very happy you are where you are. Once you can taper off of the cellcept and get past about six months to one-year hump, the chance of it coming back much less now the caution is going to be you still want to avoid all of those triggers. You still want to be careful. If you have surgeries planned, for example, that's probably the biggest one I see is I always give people a two weeks script of 20 milligrams of prednisone. If they have a surgery, I want them taking it because you don't want to unmask the disease again and sort of be stuck where you are. Assuming you avoid the things that can sort of stimulate it coming back. Absolutely. There's a decent shot that you may be done with this for good.

Becky: Great. Thank you. What I think might be a little bit of a difficult question to answer. How does my doctor determine what treatment I should use?

Dr. Kyle Amber: Ideally data, but there's data, patient anecdote and experience. For example, I mean we're all human beings. If the data says drug a works really well and I use it in five patients consistently and all of them do terribly with it. And am probably going to use drug A again, probably not because I don't care what the data says in my patient population. That's not good. I think depends on who you talk to and how they translate severity. I almost have like a binary view that I'm like, there's very minor disease that is probably not worth treating aggressively.

Dr. Kyle Amber: And then there's more the more advanced disease that if you don't treat aggressively, you're just not going to get a hold of.

Some people will say, oh well it's moderate disease, I'm going to treat it, you know, is a certain dose of steroids and rather than this or that, which is not how I do it. There's a lot of different subtleties and then comfort with medication for example- I trained on the west coast. I used cellcept with both pemphigoids. Those people who train on the east coast mostly used methotrexate. I think it works. I think it works just fine. Why do I reach for that rather than the methotrexate? It's what I use and what I'm comfortable using. When there's an issue it's easy for me to adjust accordingly. You do something that you don't do routinely, you know the first step. But when you get to the second step real, I don't know how to exactly to adjust this safely.

Becky: Great. Thank you. This is coming from Rod. He's looking for the best way to reduce the dosage of mycophenolate. He's currently taking three grams and also wants to know how to reduce his dose of IVIG. He's currently on 180 milligrams.

Dr. Kyle Amber: That sounds odd. The IVIG I wouldn't try to decrease the dose. I would try to decrease the frequency. So basically, if you don't get high dose IVIG, which is basically two grams per kilogram or more, there's probably a little point because it just mechanistically it doesn't work at lower doses. But we find it if you can, if you're doing well for say a year or so and then taper to every other month and tapered every three months, that can go smoothly. For cellcept, I will say my view, which is probably different than a lot of people. I almost always do two grams per every person. I really don't think less than that is particularly therapeutic. I tend not to taper cause in my view there's disease or there's not disease. If I'm trying to control the disease, clearly, I'm not doing a good enough job. If there's a flare at say 1500 and let's say going from three grams to two grams, tapering down to that should be straight forward. Because like I said, I don't really find a huge improvement between two and three. I think I that's the best I can answer that question.

Becky: Thank you. Our last question is- Tanya says, I am interested in learning on how to be involved in clinical trials. What's your best advice for patients who are looking for treatment through clinical trials?

Dr. Kyle Amber: It's straight forward and easy when there's a website, clinical trials.gov and you can search by disease name and everything that's coming up that either has wrapped up and not released. Everything that they're enrolling or that they're going to enroll is available on there. And they're not that many. It's not too difficult to search through it. But that's really the best way to

keep up to date on sort of what therapies are on the horizon, as well as if you're looking in participating on what they are and what locations they are so you can see what the convenient or if they pay travel fees and anything like that.

Becky: Thank you so much Dr. Amber for being on the call with us today. I've learned a lot today from you, so thank you.

Dr. Kyle Amber: My pleasure.

Becky: I would also like to give a big thank you to everyone on the call that joined us today and of course thank you to Genentech and Celgene for making today's call possible. I do have a few last-minute announcements. The IPPF needs your help with our third quarter fundraiser. Funds are raised this quarter to support patients services such as this call today because the IPPF provides all of our services free of charge to the community, your small donation will instantly make a huge impact. Other patients' services like our peer health coach program and local regional support groups. Please consider visiting our website today and make a tax-free donation to support these valuable programs and assist the IPPF to provide support to pemphigus and pemphigoid patients.

Becky: The IPPF has also announced that we have opened our registration for the 2019 IPPF annual patient conference. The conference will take place in Philadelphia from October 11th through the 13th. This is our 25th year as an organization and we hope that you'll join us for an educational and fun weekend in the city of brotherly love. Early registration ends August 30th. So go online and register before then and take advantage of your discounted prices. Also, there's a discount for our healing heroes. Please mark your calendars and we hope to see you there. If you haven't heard of the natural history study, the IPPF has a study. If you have not registered for the natural history study, we encourage you to do so. The IPPF natural history study is a patient registry sponsored by the National Organization of rare disorders or NORD and the US food and Drug Administration (FDA).

Becky: You can register today at www.pemphigu.I am rare.org. This online data collect systems. A system collects, stores and retrieves patient data for analysis and research study. The more data we can collect, the better the information we can give to researchers and the sooner they can find better treatments. Help us to diagnose earlier and one day even find a cure. Our next patient education call will be on Wednesday, August 28th, from 9:00 AM to 10:00 AM Pacific Standard Time and this will

feature Dr. Donna Colton, associate professor of dermatology and co-director of immunofluorescence services at the University of North Carolina. For our question and answer session about Pemphigus and Pemphigoid registration details for the late August call, will be on our website. Lastly, if you have a question today that didn't get answered on the call or have additional questions, please email me at Becky@pemphigus.org or call me at (916) 922-1298 extension 105 and I'd be more than happy to help. This recording will be sent out after the call with a survey and the recording and transcription will be posted to our website as quickly as we can. Thank you again everyone for joining us on the call. Goodbye.