

## March 3, 2020 Patient Education Call Transcription- Dr. Fairley Treatment Q&A

**Becky:** Welcome everyone, this call is now being recorded. I would like to thank you for being on the call this evening. Our Speaker today is Dr. Janet Fairley. Thank you for joining us today! On the call today we will discuss treatments and side effects. But first let me introduce you to our speaker. Dr. Fairley' is John S. Strauss Professor and Chair of the Department of Dermatology at the University of Iowa. She completed medical school, residency, training and a research fellowship at the University of Michigan. Dr. Fairley's interests include autoimmune skin blistering diseases, such as bullous pemphigoid. She has published over 110 articles and book chapters. Dr. Fairley is a diplomate of the American Board of Dermatology and a member of the American Academy of Dermatology as well as the Society for Investigative Dermatology, for which she serves as a member of the Board of Directors. Her certifications are with the American Board of Dermatology, Iowa Board of Medicine, Michigan Board of Medicine and the National Board of Medical Examiners. Dr. Fairley also has Fellowships with NIH Research, Cell Physiology, Dermatology, University of Michigan, Ann Arbor. Now it is my pleasure to introduce Dr. Janet Fairley to answer your questions about treatments and side effects. Welcome Dr. Fairley.

**Dr. Fairley:** I am happy to be here. A lot of good questions tonight.

**Becky:** Absolutely, so in light of concern about CoronaVirus, are patients with pemphigus or pemphigoid at greater risk when they are on or off treatment?

**Dr. Fairley:** Great question, I know everyone has questions about CoronaVirus these days. The truth is we don't understand a lot about this virus yet. Certainly patients with pemphigus or pemphigoid have an autoimmune disease which means that the immune system isn't working as well as it should be which means that we have to assume that more than likely you may have more trouble handling something like the CoronaVirus should you get infected. Now whether you are better off on or off treatment is something we don't know for sure, we do know that the CoronaVirus survives on surfaces and things like that for quite a period of time so my intuitive response to that is if you are in good shape right now you are probably best not to go off your medicines or do anything like that and risk having a poor barrier, skin and mucous membrane barrier, that the CoronaVirus might more easily get into. Yup, so probably overall anybody with pemphigus or pemphigoid is at a little higher risk. My gut reaction is most likely you are going to get better off if you are in good control. And probably what you need to do is be really rigorous in hand washing, not going to places where you might become infected or put yourself at high risk in large crowds. But just doing all the kind of routine, wise things we do for things like Influenza.

**Becky:** Great, I heard today on the news they were talking about how long to wash your hands and they were saying that 20 seconds is the amount of time that you need to wash your hands and it's the equivalent of singing "Happy Birthday" twice. So just a tip for those out there. We

also have had a lot of questions before the call about getting vaccines when you are taking an sort of treatment for pemphigus and pemphigoid. Can you just go over what kind of vaccines we should and shouldn't be getting. And if we get them before or after or during treatment and what is safe for our community?

**Dr. Fairley:** Sure, and I get a lot of questions about vaccinations as well. First of all the big three that people worry about are the shingles shot, influenza, and the pneumococcal or pneumonia vaccine. Obviously we hope there will be a CoronaVirus vaccine too but that will be a ways off. The difference is there are some vaccinations that are what is called a live virus vaccines and then there are others that are what we call recombinant or killed viruses. The ones that are safe for anyone with an autoimmune disease are the ones that are killed or recombinant. What we don't like folks doing or getting if we can help it are the live vaccines. So shingles, some of you out there may have had old shingle shots where it was just one shot and that was sort of inactivated. It was relatively safe but not as effective as we like. The newer shingles vaccine, Shingrix, that one is what we call a recombinant virus. It is absolutely safe, you can't get shingles from it and I do recommend that folks go ahead and have the Shingrix, new shingles vaccine. Even if you had the previous shingles vaccine or even if you have had shingles yourself we still recommend that you go ahead and get the Shingrix because you can get shingles more than once. The difference between the old vaccine, the old vaccine wasn't as effective as this newer one. If you got shingles after you had the older vaccine it wasn't as bad as people would get if they had no vaccination but the new one is much more effective so I would go ahead and have that. Influenza vaccine again, if you get the shot, that would be perfectly safe. No worries. The old inhaled vaccines which they mostly don't give anymore that one is live and you shouldn't take that one if you are a patient with an autoimmune blistering disease so go with the shot. I know none of us like shots but that one is much safer. And same thing with the pneumococcus, pneumonia, vaccination that one is also very safe to get. Now ideally you would be all up to date on vaccinations before you are starting treatment but if you are not, then I would discuss that with your physician. In general it is still safe with these killed or recombinant vaccinations because they can't they can't give you the infection. The issue is particularly with Rituximab, Rituximab can make your "take" of the vaccination so to speak a little less effective and it is not clear how long that effect is but probably for six months after their last Rituximab infusion you may not get as much benefit from the vaccination then you would if you hadn't that. In general when somebody comes to me as a new patient and is just getting ready to start and we are trying to go through all the approvals with insurance and things we try and get the vaccinations all up to date during that window of opportunity. But if you have any questions I would discuss it with your physician but in general the vaccinations are usually more benefit than risk.

**Becky:** Great, that was a lot of information in a short amount of time so thank you so much for answering all of those. Our next question is about Rituximab, since you were just talking about that. The question is do all patients require long-term use of maintenance drugs after Rituximab?

**Dr. Fairley:** The answer to that is no, in fact we really hope that for many patients Rituximab will put them into a remission that allows us to withdraw the other medications and make Rituximab do the work, that's one of its advantages. So I would say no is the answer to that. Recently the approach is if you are going on Rituximab and I will say this, most of our data when we are talking about Rituximab is for pemphigus, a little less clear in some of the other autoimmune blistering diseases but in pemphigus, generally we stop other medications when you get Rituximab. If you are on Azathioprine or one of the others you will usually stop those once you get the Rituximab. You might stay on some prednisone but the goal is to have you off every other adjunct within six months of completing your Rituximab. That is the goal so that is what we hope for.

**Becky:** So that is great. Our next question is still about Rituxan. "I have PF, if you have the Rituximab infusion and then go into remission, when do you typically recommend having another series of infusions?"

**Dr. Fairley:** In general I do not recommend an additional infusion unless you start to flare. If you read all the medical literature some of the European folks like to give another infusion at 6 months after completing it but that is generally only if you have 2 cycles of Rituximab at the beginning. They tend to go 2 cycles of Rituximab at the beginning and then another cycle at 6 months whether you need it or not. In the United States a lot of physicians now just give the 4 infusions at the beginning and then don't retreat unless you have to. And that is because there is some data that suggests the 4 dose initial treatment gives a longer remission than the 2 dose followed by 1 six months later. So in general I tell my patients we are going to do 4 and then we are not going to treat you again until we have to. And that has to, at least in pemphigus on average is about 18 months later.

**Becky:** Great, thank you. The next question says, "My 17 year old daughter will have Rituxan has her first therapy. She has been diagnosed with pemphigus vulgaris. Can you talk about general care after a Rituximab series of what we should expect and need to do?"

**Dr. Fairley:** Well Rituximab has maximal benefit after about 4 months. So for a lot of folks it ramps up slowly. Part of it sort of is patience to wait to see that maximum effect. Some people will get an effect more rapidly but in general I recommend to folks, hold tight we are going to see where you are at 4 months. Now during that period of time as I think a previous person asked in general I get rid of things like Azathioprine and I will bridge with enough prednisone, gradually tapering over that period of time, it's going to slow down and the prednisone goes down. So hopefully by 4-6 months after the Rituximab your daughter would be off all medication other than the residual effects of the Rituxan.

**Becky:** Great, thank you. So we've got a couple of questions about both pemphigus and pemphigoid being limited just to their mouth. Is it a good idea to get Rituximab when it's only in the mouth? And a patient with MMP says she has been on 3 grams of Mycophenolate for

approximately 8 months and has 2 Rituximab infusions with injected steroids and she has not had a blister in 10 days. When should she start reducing typically the Mycophenolate dosage?

**Dr. Fairley:** I guess part of that would depend on how recently that last Rituximab infusion was. Definitely with the Rituximab we hope that you are going to have a good response and would be able to get rid of the Mycophenolate. 10 days might be a little early but probably within 21 days after not having any blisters I might ask about reducing that Mycophenolate down. Again, if it's done its work we hope to get you off all of that within a couple of months after giving the Rituximab.

**Becky:** Great, and if it's just in the mouth both of pemphigus and pemphigoid is it a good idea to get Rituxan?

**Dr. Fairley:** So the issue with, I think that it's different. With pemphigus, the problem is it usually starts in the mouth and very often if it is not treated more aggressively, it can move from the mouth to more generalized disease. The immune system kind of gets amped up and creates more problems in other areas. So I think a lot of people at this point, with the information we have, early treatment with Rituximab has more benefit and is actually probably better for you than treating it later on. I think a lot of people have Rituximab treatment for pemphigus if it is just localized in the oral mucosa. When you say pemphigoid only in the oral mucosa I presume you are talking about mucous membrane pemphigoid because straight up standard bullous pemphigoid isn't usually just in the mouth, it's pretty rare in the mouth. That's a little more controversial because we don't have as much data on the use of Rituximab in mucus membrane pemphigoid. Personally, I am a really big fan of Rituximab in bad mucus membrane pemphigoid especially if it is in the eyes or posterior part of the throat and the larynx, I think it is incredibly helpful in those disorders. I think that it is a little more on the fence now if it is limited to the mouth and so in general I think it depends on how bothersome it is. I work with an oral medicine doctor who is also a dentist and sometimes if it is just the gums he will make special trays that patients can use their medication on, that are held up against the gums and sometimes that can be incredibly helpful. But I think that if someone is really having a lot of trouble, if they are losing teeth, if they are losing weight because they can't eat, those are patients that I think that the use of Rituximab is probably more beneficial.

**Becky:** Great, thank you. So our next question is again still about Rituximab and the patient is asking, how hard is it to get a medication like Humara or Rituximab covered through Medicare if it is only FDA approved for PV?

**Dr. Fairly:** Well, that is very dependent on the state. I will tell you I have less trouble getting Rituximab than I do getting Mycophenolate in the state of Iowa. Yeah, it's crazy! Medicare here is really difficult here with Mycophenolate and I sometimes say this and I shouldn't say it out loud but I don't think some of the people who are screening don't know the difference between pemphigoid and pemphigus, I think they think it is all the same thing. So I don't have a lot of

trouble here getting Rituximab for mucous membrane pemphigoid or for resistant bullous pemphigoid patients. I do know that other states have more trouble.

**Becky:** Wow that is great, sure. Our next question has to do about the itching. They want to know what treatments are recommended for the severe itching?

**Dr. Fairly:** That is probably one of the most difficult things for people. I mean there are studies out there that show that bad itching is every bit as detrimental to people's quality of life as pain is. So it is difficult and understudied. Most of the time I think when people are having a lot of itching, it means their disease is probably still active.

**Becky:** Okay.

**Dr. Fairley:** But besides addressing the underlying disease, there are a number of topical agents, one called Sarna that's actually even available over the counter. It's got a little bit of a topical anesthetic in it. It's very safe to use. You can use it as often as you like. So that's something that can sometimes at least give some temporary relief. Antihistamines can sometimes give some temporary relief, especially at bedtime so you can sleep and the itching doesn't wake you up. But in general, I think if somebody is still having a lot of itching, it probably means the disease may need to be treated a little more aggressively.

**Becky:** Well, I think that's good news and it's bad news. Yeah. So we're all trying to get off treatment and thinking our disease is controlled but when you still have the itch, that's good to know and we should probably let our doctors know how bad it is to then.

**Dr. Fairley:** Exactly.

**Becky:** So back to the Rituxan questions that have come in. So after 3 infusions of Rituximab each 6 months apart and Mycophenolate, my potassium, hemoglobin and iron levels are low. Is this common with this medication?

**Dr. Fairley:** No, it is not. The Mycophenolate typically doesn't make the hemoglobin or iron levels go down. It can cause a specific type of the blood cells called lymphocytes to be low. I would be concerned that if you're not well controlled, you may be losing blood through the skin if you've got lots of blisters and some of them are hemorrhagic. I think that deserves an investigation to make sure it's not due to something else. I wouldn't just accept that as being from the Rituximab.

**Becky:** Okay. And our next question says that, my white count has continued to stay low even though I've been off steroids for 6 months. Will they come back after I'm done with all of my treatment. I'm currently weaning off IVIG.

**Dr. Fairley:** In general, if your counts are suppressed because of the treatment, it should come back after you're off all your treatment. It's another one of those things that if you're off all your treatments for a number of months and they're not coming back, I think that's something that also deserves a little more investigation to make sure there's not something else going on. You know, folks with autoimmune diseases there are also other autoimmune diseases that can affect the blood count dependent of things like pemphigus. So again, should go away, if it's from the treatment within a couple of months of ending.

**Becky:** Great. Thank you. Our next question asks, can flare ups happen with blisters developing over 3 to 4 hours without any other previous skin symptoms? This mom says our daughter is nonverbal, so we don't know if she felt itchy or anything before her blisters appeared.

**Dr. Fairly:** Okay. The answer to that may depend on what underlying disease she has. If it's a young girl, then more likely it's pemphigus or something called linear IGA disease. And linear IGA can be itchy. Pemphigus, as one patient already wrote in and asked about can be itchy but a lot of times I don't think people with pemphigus get as many symptoms before the blisters show up. So it's very individual. I'm guessing if she had a lot of itching she will probably be trying to rub her skin and do other things to indicate that it was itchy or uncomfortable before the blisters appeared. I have quite a number of patients whose blisters show up totally unannounced, they wake up in the morning and there are 3 new blisters. Less common and pemphigoid, there is usually itching before those.

**Becky:** Okay, and another Rituximab question is this patient has pemphigus foliaceus and they want to know if there is a dose limit or a number of maximum times that you can receive Rituximab?

**Dr. Fairley:** Well, so far we haven't seen any limit to the number of times you can take it. If you take it and you're getting a good remission, thus far there is no feeling that, oh, you could only have three cycles or six cycles of it. So far there is not any indication of limits. I would say my, I just looked at this in some ways. I have a couple of patients who've done up to 5 cycles but . But I've been using Rituximab now for probably 15 years, but as long as they do well, I'm okay with it and they are okay with it.

**Becky:** Great. Thank you. Our next question is how long would remission have to be to conclude that the PV is not coming back?

**Dr. Fairley:** That's a tough one. I would say...

**Becky:** We are not easy here...

**Dr. Fairley:** The longest amount of time I've had a patient go with absolutely nothing going on and then the pemphigus came back is nine years. I have another patient at the nine year level that hasn't relapsed yet. But the immune system I like to tell folks has a really long memory. So I'm not sure I ever am totally sure the pemphigus is never coming back. Our colleagues over in Europe believe that we cure people. I hope I've cured some people. Maybe that gentleman out at nine years is cured. But, I am always looking at the bright side of it. Whereas if you've been in remission for years and you're not having to see your doctor every couple of months and you're feeling fine, it's as good as being cured. And if we have to retreat for another cycle in general, folks do just as well with the next cycle. So I think, enjoy it and I hope that, I hope some people are cured, but I can say the immune system has a really long memory.

**Becky:** Okay, great. Good answer. Good information there. And I'm hoping that a lot of us patients get past that nine year mark.

**Dr. Fairley:** Yeah. Amen. The other thing I would just add to physicians who are treating pemphigus and pemphigoid if there was a way to reset the immune system in a way so that you're truly cured and we know you're cured. There is work going on along those lines right now. I think people have tried cellular therapy. There's a couple trials going on now. Folks who participate we're trying to sort of reset your own immune system in some of these ways and that's what people would really like to do. So you sort of induce what we call tolerance of the immune system, and it doesn't want to attack your skin anymore. That would be the very, very best thing. So that's, that's what we'd all like to see happen eventually.

**Becky:** Yeah, absolutely. Our next question says in the past month I've been getting itchy skin on my legs, arms and if you small blisters. I had sepsis, severe sepsis and septic shock in late August and September. I was in the ER ICU and a regular room one week and then one week of inpatient rehab. Could the new BP symptoms be related to the sepsis.

**Dr. Fairley:** That's an excellent question. We recently had found that a lot of pemphigoid patients with a fairly nasty staph organism. And so I do have concerns of sepsis and all that may have been related to the pemphigoid and colonization. That being said, I'm not sure that the chicken and the eggs there. I think probably the pemphigoid is there first and then you get colonized with this nasty staph which can cause problems like sepsis. So I do think that if you're starting to get a lot of itching and blisters I think it's definitely worth going in, having things checked and probably getting therapy again. We see it so regularly, a lot of times we will concomitantly treat pemphigoid patients with antibiotics because I think it does help keep down the staph colonization and we hope to prevent things like the sepsis.

**Becky:** Okay, great. Thank you. The next question says I'm currently being treated with a cream that I apply once a day inside my mouth and it is called Clotrimazole and Betamethasone Dipropionate Cream. I am also on 75 mg of Minocycline twice a day. I have been on these two

meds for a month now. How long should it take for the pain in my mouth to completely go away? And I feel that some of the pain is actually due to a yeast infection. Do you have any thoughts on this?

**Dr. Fairley:** Certainly yeast infections are not uncommon in folks who are using steroids in the mouth. And the Betamethasone Dipropionate is a steroid. The Clotrimazole is an antifungal, but sometimes in folks who don't have a normal barrier because of their blistering disease Clotrimazole may not be enough to get rid of yeast overgrowth. And sometimes we have to go with an oral anti yeast medication to try to get it to go away. So I do think it's worthwhile getting that checked out if you feel like it's not getting better. A month may be a little short to expect everything to go away. And some people do require more than just topicals if for treatment. So again, I would probably give it another month. I don't know when you're scheduled to see your physician back, but if you've used it for two months and you're not getting significant relief that I think it definitely deserves a reassessment.

**Becky:** Great. Thank you. Our next question says I was on prednisone for almost 3 years and slowly out of it last July and I've had some withdrawals from that. Like what was mentioned on our last call with my knees hurting and I cannot stand or walk for a long time, will I ever become normal again? And how long should it take?

**Dr. Fairley:** Yeah. Prednisone boo, it's a two edged sword. It can be great acutely, but we don't like it long term. Part of it depends on what the symptoms are coming from. It is true, Prednisone itself will mask a lot of symptoms of plain old osteoarthritis or other things. So when you take them away suddenly folks go, holy smokes, I have more arthritis than I ever knew I had. So that one thing that could be going on and if that's the case, then other things other than prednisone can be used to help that arthritis pain. The other question is if you can't stand or walk for a period of time, if that's from the pain or just from weakness and some people will get steroid myopathy, which means their muscles don't work properly because of the steroids. If that's what's going on then physical therapy and things like that may help you regain your strength. The one other thing to bring up, and again, since I don't know the full history there, a lot of people are put on bisphosphonates for osteoporosis when they're getting steroids. And a fraction of patients on bisphosphonates can also get a lot of muscle pain and joint pain as a side effect. While they're trying to prevent bone loss, it can cause some other problems like that. So without knowing your full history, I can't be sure, but I think those are at least three things I'd be thinking about if one of my patients came to me after going off steroids and said, hey, here's the kind of symptoms I'm having.

**Becky:** That's a lot of great information to take back to the doctor to start asking about too. This next patient says, I used to get blisters in my mouth and my private area more often. Now I get tiny blisters in my mouth two to three times a year. In my private area I get tiny blisters or tiny cuts maybe once a month or less with an itch that lasts two days. The itch doesn't intensify. Is it because I don't agitate the skin by scratching?

**Dr. Fairley:** That certainly could be. It may just be that your overall disease is less active now too. But it could be one or the other. So certainly the more you scratch your skin will sometimes respond to that by causing inflammation. So avoiding scratching is about the hardest thing of the universe if something really itches. But if you can avoid it, that's good. But if you're getting more blisters, if each time they occur, you're getting more and more, it may mean your skin is heading towards a flare and then it's probably good to get that reevaluated.

**Becky:** Great information. Our next question says, I am now really curious about how 5 weeks into CellCept therapy. I can go several days without a blister and then they erupt. They will be at not as painful or fully formed as before. Are there triggers? And how do I begin to identify them? She says walking and being out and about and doing errands seems to bring on the symptoms. And even the softest of clothing that touches them now. It seems the very thin skin that brings them on as well.

**Dr. Fairley:** Five weeks into CellCept is still a pretty short period of time. So I'm thinking you're most likely still getting blisters now and again when you agitate your skin that's bringing them on because you're not really getting the full benefit of the CellCept yet. It has a kind of an early, what I call anti inflammatory effect where the skin isn't as irritated as it would be but to get the full anti immune system sort of effect sometimes it takes up to 10 to 12 weeks. So it may be a little longer into therapy that those symptoms will start to decline and the skin will feel normal. It's interesting though, a number of my pemphigus patients they'll be totally healed up at all during the examination and they don't report and blisters and still have some discomfort that lasts for a period of time. And I have to believe it's probably nerve endings in the skin that has been disrupted as well by the inflammation there. So I do think sometimes it takes longer than you'd like, but it's still pretty early for the CellCept.

**Becky:** Great. Our next question says that I'm a 69 year old woman with pemphigus. In April of 2017 I had some balance issues about a month after the two infusions of Rituximab and had to go to physical therapy. About a month after the second set of infusions in September of 2018 I suddenly had intestinal issues including irritable bowel syndrome and had to go on meds. After this last set in December of 2019 I suddenly have had itching and burning all over my skin with no rash and with no explanation. All of my blood tests have come out good. Is it likely I opened Pandora's box each time I do an infusion? Is Rituximab causing these things to happen or is it my compromised immune system that is doing this or just purely coincidence?

**Dr. Fairley:** Yeah, that's a difficult question. I think the fact that they were sort of different symptoms each time makes it less likely that it's all just due to the Rituximab. Certainly some people can have an allergic reaction to the Rituximab and itching and burning of your skin. Could that be a sensitivity to it? Possibly, but I would think that to me it would be hard to put all

those, just the Rituximab. So it may be a combination of things. Your immune system which is compromised as you correctly say and some addition of the Rituximab as well.

**Becky:** Okay. Well, something to investigate then and bring to the doctor's attention.

**Dr. Fairley:** Absolutely but I do think it's reassuring the lab tests all look good and they don't really crazy going on there.

**Becky:** Yeah, absolutely. Our next question says, I take care of an elderly family member has been diagnosed with bullous pemphigoid. This person has been successfully treated with doxycycline monohydrate, Clobetasol Propionate as a topical and Niacinamide. The family member has been dealing with the condition for almost a year and we've gotten the blisters under control. But she can continue to have the itchiness and rashes that haven't completely dissolved. What are the side effects of continuing her on the antibiotic and corticosteroid? And could the rash be something else other than the pemphigoid, but in how do you figure that out?

**Dr. Fairley:** We'll certainly Doxycycline and topical steroids are a pretty safe long term treatment. We use the doxycycline, doxycycline is an interesting antibiotic because in addition to its ability to kill bacteria, it has another effect. It inhibits something called matrix metalloproteinases. We call them MMPs for short. There are too many MMPs in this world, but MMP's are what are released at the skin that chew up the basement membrane zone in pemphigoid. So when we use doxycycline for pemphigoid, we're mainly using it to try prevent the immune system from being able to chew up the skin. So that's why we use it longer term, it's not for the antibiotic per se, it's to prevent that splitting of the skin. And it is an antibiotic that's not used for a lot of other things, so we don't worry too much about resistance to it. There's almost very little that doxycycline would be needed for that nothing else could substitute. So I think that that's a pretty good combination. And these have less side effects than systemic agents do, particularly in older folks. The problem is if your relative is still having itching, then that needs to be addressed because as we talked about, itching is just really disruptive to people's lives. I just think it's probably one of the, a lot of my patients tell me the worst thing about their pemphigoid is when they just have this itching that they just can't stop.

**Becky:** Yeah. We hear that too at the foundation and they just feel a little helpless because you know that it's just such an innate itch.

**Dr. Fairley:** The interesting thing is there is a group at the University of St. Louis who is really focused on itch and really trying to dissect out what exactly are the chemicals in your skin that trigger that kind of itch. I'm hopeful that we're going to get some newer agents that may be really helpful for some of us folks with blistering disease.

**Becky:** I sure hope so. Our next question comes from Wendy and says that her husband is on Methotrexate and it is working to control his disease, but in the evenings, her husband's eyes water. He says it's fine, but she finds it concerning. Is this something she should be worried about?

**Dr. Fairley:** I think that might be something to check out and I think it depends on what type of disease he has? If he has to make this membrane pemphigoid and his eyes are watering, I for sure get them checked out because he could be having very little activity in his eyes. Pemphigus can involve the eyes, but usually only in the setting of lots of other activities. So I definitely think it's worth getting checked on it. You know, it could be something as simple as ocular allergies, allergies affecting the eyes, but still better to have it looked at.

**Becky:** Great. Our next question says that says she is a 57 year old female diagnosed with pemphigus vulgaris two and a half years ago. She just finished her second round of Rituxan and last August and was on 40 milligrams of prednisone. Most of the sores are healed with the exception of one and my blood test shows a huge drop in my desmoglean levels down from 368 to 23. However, I have no B cells left. What do I need to watch out for? I have major pain in my joints which is the cause of prednisone and I'm off now. Or is it not having the white blood cells?

**Dr. Fairley:** It's probably the withdrawal with prednisone I would guess. There is a drop in B cells can occur with Rituximab. Generally it's transient and they come back, but it sort of parallels the improvement. So we generally don't get too concerned about it. But again, those folks who do Rituximab don't have huge problems with infections the way some of the higher doses, but probably viral illnesses are the things we worry about or than bacterial infections with folks with Rituximab. So I would just be on the lookout for anything if you got something that feels like a bad cold and you're not getting better or coughs that persist. It's not just I got a cold cough, but I've got a cough that just really didn't clear up. Those sort of things are the sort of things you should be seeing the physician about.

**Becky:** Ann says, "I just got diagnosed with the flu. Currently I'm on 30 milligrams of prednisone and after being on 65, 50 and 40 tapering. Is it safe to take Tamiflu while I'm taking prednisone?"

**Dr. Fairley:** Yes, absolutely. Go ahead and take it. Hopefully it'll make you feel better. So yes, I don't think there's any problem with taking the Tamiflu along with that.

**Becky:** Okay, great. Thank you. And this is another one about Rituximab. Do I need to wait one year before becoming pregnant after treatment with Rituximab or is 3 months sufficient? What are the risks?

**Dr. Fairley:** The risks are absolutely unknown frankly. There is no data to suggest that there's anything harmful about the Rituximab, but of course with pregnancy we are always incredibly conservative. It's not the Rituximab itself that's lasting in your body. That's probably gone relatively quickly. It's the effect on some of the B cells. And there's just no information on that. But in some ways I find that reassuring because I think if there were a lot of issues with post-Rituxan with pregnancies, you'd probably have heard about it by now.

**Becky:** Okay. Great. The next question is from Amrit and says, my mother is 63 years old, diagnosed with pemphigus vulgaris in February of 2019. Recently had a stroke last week. She's always had her blood pressure and lipid profile in control and she weighs 50 kilos gram. Can autoimmune disease be a probable reason? Maybe a small vessel vasculitis?

**Dr. Fairley:** Oh yeah, pemphigus itself does not cause vasculitis, but there's absolutely no doubt folks who have one autoimmune disease are more prone to other autoimmune diseases. So is it worth making sure she doesn't have any sort of either vasculitis or clotting problem that might've led to the stroke is probably not an unreasonable thing to bring up with her physician, especially if she sounds like she's had everything else under pretty good control.

**Becky:** Okay. Thank you. Dorothy from South Bend, Indiana says that she has MMP and after 2 years of heavy treatment with prednisone and methotrexate my physician from Indianapolis says that I'm now in remission. What is the likelihood of relapse or return?

**Dr. Fairley:** It's interesting, MMP is clearly not just one disease. MMP is triggered by at least four different auto antibodies. And I think to the answer that question depends on what auto antibody your MMP is targeting. And the problem is there's not great tests out there that are available to a lot of physicians to figure that out. If folks have one of the types called BP180, which is targeting a different region of the same protein that gives people trouble with standard pemphigoid. I think those folks tend to go into a good remission that can often times be permanent. There's other types that tend to recur more often. Luckily the most common type is that BP180 type that's similar to pemphigoid, a lot of people will go into a permanent remission. So we're going to hope your mom falls into that category and that she will be in a true permanent remission.

**Becky:** Great. Thank you. Let's see, the next question says I have BP and I've had Rituxan plus I'm on Dapsone. I noticed that my skin turns red or dark purple. What causes this and what can I do about it?

**Dr. Fairley:** That's a tough one to answer without a little more information. It gets kind of purple-y in areas that look like an odd bruise that's probably something called bateman's purpura. And that's from fragile blood cells up fragile blood vessels close to the skin. If it's a

more diffuse kind of bluish purple color, then I would want to double check and see how the blood counts and things are doing because the Dapsone can alter the blood's ability to carry oxygen out to tissues like the skin. So if it's kind of a bluish discoloration in a lot of areas I'd want to check and see if the Dapsone wasn't causing trouble. If it's just these funny looking bruises, that's probably a function of a fragile skin from a lot of steroids and things like that that are often used for this disease.

**Becky:** Great. Thank you. Linda's asking, besides prednisone, is there another inflammatory medicine you can use when you're having a flare?

**Dr. Fairley:** There's nothing else that works quickly. That's the major issue. We don't have good alternatives when people having an acute flare that will improve it rapidly. In Europe they have something they call immuno absorption that actually pulls the bad antibodies out of your blood and they keep rumoring that they're going to release it in the United States though I recently heard that they are potentially starting a trial on immuno absorption out in California as a prelude to getting approval to release it to here in the U.S. so we may have an alternative coming down the road. There's also a lot of medications that have been used for other diseases that folks are looking into to repurpose for some of the blistering diseases. Some of the medications that have been used for things like asthma or forms of eczema are being tested for their ability and it's possible if some of those work well enough, we may be able to avoid steroids. But unfortunately for the things that are actually approved right now, prednisone probably is still the only one that can cause more rapid improvement. We're stuck with it as much as we dislike it

**Becky:** It's a double edge sword but it has some side effects. So Rhonda says that I've been recently diagnosed with MMP which is currently localized to my mouth. The dermatologist has prescribed Mycophenolate Mofetil. Is this an effective treatment for MMP?

**Dr. Fairley:** It certainly can be. MMP I would say, different people respond in very different ways to it and there's under a lot of different options, particularly if it is just localized to the mouth. But Mycophenolate is certainly a tried and true and a good one to try. If it doesn't work there's a lot of other options, but I think that's a very reasonable place to start.

**Becky:** Great. Sammy is asking, medical information about Rituximab shows a high rate of mortality in the first 24 hours after infusion. How common is this?

**Dr. Fairley:** I have never seen it in any of my patients ever. I've never heard of a autoimmune blistering patient having mortality from Rituximab. I think when you look at that data, you have to understand Rituximab was originally developed as a cancer agent for treating lymphomas and it was utilized in conjunction with a lot of high powered anti-cancer agents. So I think that's where

this sort of information is coming from. It's not coming from patients with pemphigus who are being treated with it. And we always, you know, treat Rituximab with respect. It's doing things to your immune system, but I'm not aware of any autoimmune blistering disease patient having fatality from Rituximab in 24 hours.

**Becky:** Well that's great information. It's a little comforting to hear as well. Lisa wants to know, is monitoring through the desmoglein 1 and 3 tests a helpful baseline to see if a patient has remission. I don't have blisters but my gums have some ruffling and my scalp itch. My doctor does this test every 6 to 9 months and that is how we decide if I should go for a Rituxan maintenance dose.

**Dr. Fairley:** I think that can be helpful. The desmoglein levels oftentimes move pretty slowly. I find it fascinating because somebody will feel a lot better and look a lot better and you measured their desmoglein levels and they're kind of sloping down but they're not exactly dropping like a stone. So I think every 6 to 9 months is plenty. And but it's very important to do them for each person because what I found is there are some patients whose desmoglein levels may still be weakly positive but they are really clear, they're fine and they don't need any more Rituximab. But then if that's their kind of baseline, which is still sort of a low level positive and if you see the levels start to climb again, that's when they're going to need another treatment. So I think that if you're going to monitor desmoglein levels, that's a way to do it. Do it for this individual person and not just cut some arbitrary line where you're going to start to treat again, but look and see where that patient's levels go after treatment, when they're doing fine, and then watch for if they start to rise again. And I would also say this, the only ones that are pretty reliable are the ones for pemphigus. The pemphigoid levels aren't quite as reliable because there can be a lot of them that have antibodies that aren't particularly active, so they don't travel with the disease quite as reliably as the pemphigus ones do.

**Becky:** Okay, that's great information. Our next question, Laura Lynn says, my 85 year old mom has had Rituximab for 6 months, then IVIG monthly for 3 times. Neither seem to make a difference. Prednisone helps her but she has medication induced dementia. What else can she do? And then says that the CellCept has also made her a little crazy.

**Dr. Fairley:** And does she have pemphigus or pemphigoid? Do you know?

**Becky:** Oh I am sorry, MMP.

**Dr. Fairley:** MMP, okay so 6 months of Rituxan and IVIG. So I do think MMP sometimes can be a little more resistant than pemphigus to Rituximab. Some people respond very well others not so much. And part of how aggressive I would be with your mom at 85 would depend on what surfaces she has involved. If it's just in her mouth and she's able to eat everything I might back off and not be quite so aggressive with her if she's having dementia and things like that as a response to some of her medications. Methotrexate can work for MMP as can mycophenolate

and those would be options for her as well. Mycophenolate and actually neither of those would be likely to get her into trouble with dementia or making that worse. So there are other options you can use for that, but a lot of it just depends on which surfaces she has involved. We tend to be much more aggressive with the eyes or the larynx because obviously if you get scarring with the eyes, you can end up with blindness. Or the larynx of course you need that for breathing. So those, those are pretty critical.

**Becky:** Great. No great information there. Our last question comes from Bonnie, who wants to know how long is it safe to stay on Dapsone? She's been taking it for 18 months at a 0.25 milligrams and the blistering in her mouth is under control and she also rubs fluocinonide on the gums 3 to 5 times per week. She also has a follow up questions. Do you know if breast implant illness can cause MMP?

**Dr. Fairley:** Okay. So first of all I would say if you're on 25 milligrams of Dapsone and the fluocinonide had just a couple of times a week that's a very safe regimen. Dapsone has been used for a different disorder called dermatitis or piriformis and some of those patients stayed on it for years at considerably higher doses. So that's a pretty low dose and probably safe as long as you knew that. As far as breast implants go, we don't know of any link with them to autoimmune diseases. The big thing that of course has been described with them more recently is the breast implant related lymphomas, but true auto immunity. There's been a lot of discussion of it and a lot of looking at it, but it certainly hasn't panned out for things like mucus membrane pemphigoid.

**Becky:** Okay, great. Well, Dr. Fairley, that was a very, very quick hour. Thank you for being on the call with me today. I think we could probably keep you here for another two hours with all the questions that have come in, but I just sincerely appreciate your time and it was extremely educational having you on our call.

**Dr. Fairley:** I'm happy to be here and answer as many questions as I could.

**Becky:** Thank you and thank you for everyone who called in today for joining us on the call and of course thank you to Genentech for making today's call possible. In closing, I just have a few announcements I would like to remind you that this month we're raising funds for the IPPF research and advocacy programs with a goal of raising \$15,000. Your tax deductible donation enables the IPPF to advocate for patients and collaborate with stakeholders for the development of research of pemphigus and pemphigoid. We provide the most current information to clinicians treating these diseases, researchers investigating potential carers and patients. With your support we maintain relationships with congressional representatives and other rare disease support organizations who provide the IPPF with the opportunity to advocate for favorable state and federal legislation, research funding and policies that benefit those affected by pemphigus and pemphigoid. Your tax deductible donation will help the IPPF to continue to provide the promise of new therapies, improved access to treatments, and a better

understanding of these diseases through advocacy efforts, research grant program, clinical trial support, natural history study, and biobank. I'm very excited to announce that the 2020 IPPF annual patient education conference will be held at the Treasure Island to hotel in fabulous Las Vegas from August 21st to the 23rd our hosts this year will be Dr Janet Fairley who is on the call with us today and Dr. David Woodley. We are so excited to have you host the meeting with us this year in the Las Vegas Dr. Fairley!

**Dr. Fairley:** More questions to be answered.

**Becky:** That's right. Registration will be opening soon and we hope that you'll join us for an educational and fun weekend. And if you haven't heard the IPPF has a natural history study. If you haven't registered with the IPPF natural history study, we sincerely encourage you to do so. The IPPF natural history study is a patient registry sponsored by the National Organization for Rare Disorders or NORD and U.S. Food and Drug Administration, the FDA. You can register today at <https://pemphigus.iamrare.org> this online data system collects, stores and retrieves patient data for analysis and 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, even a cure. Lastly, if you have a question that didn't get answered on today's call or have additional questions, you can email me Becky Strong at [becky@pemphigus.org](mailto:becky@pemphigus.org) or call (916) 922-1298 extension 105 and I'd be more than happy to help. This call recording will be sent out after, with a survey following this call. Good night, everyone.

**Dr. Fariley:** Good night.