

Welcome everyone! This call is now being recorded. I would like to thank you for being on the call this evening. ***Genentech is graciously sponsoring our call this evening and our Speaker this evening, IPPF Physician Ambassador, Dr. Razzaque Ahmed, Director of the Center for Blistering Diseases in Boston, is provided compliments of KabaFusion Patient-Focused Specialty Infusion. Thank you for joining us today!*** The call today will focus on the immunology of pemphigus and pemphigoid.

Abdul Razzaque Ahmed is a Professor of Dermatology at the Tufts University School of Medicine and the Director of the Center for Blistering Disease in Boston. It is the only Center of its kind in North America. He graduated from the All-India Institute of Medical Sciences, New Delhi, India. He immediately migrated to the US where he was trained in internal medicine, dermatology, and clinical allergy & immunology. He received a Doctorate of Science degree in molecular immunology from the Faculty of Medicine of Harvard University. He has a Master's Degree in Public Administration from the prestigious Kennedy School of Government at Harvard University.

He identified beta4 and alpha6 integrins as pathogenic autoantigens in mucous membrane pemphigoid and was the first clinician scientist to describe pathogenic IgG4 and nonpathogenic IgG1 autoantibodies in pemphigus vulgaris patients. Amongst his many clinical contributions, the most important, relevant and universally beneficial are the use of intravenous immunoglobulin (IVIg) and the combination of IVIg and Rituximab in treating patients with recalcitrant autoimmune blistering diseases. For these contributions he received the Walter Lever Memorial Lecture Award. It is given once in 25 years, because the contributions needs to be confirmed and its benefit verified.

In 1988 he established the Boston Blistering Diseases Support Group that meets on an annual basis for the last 29 years. Dr. Ahmed's commitment to patients with pemphigus

and pemphigoid is evidenced by his 400 publications but more importantly his unique, personalized way of treating each patient based on their individual needs and concerns.

Now, it is my pleasure to take introduce **Dr. Ahmed** to discuss a bit about **immunology** and to answer your questions.

Becky: Welcome Sir!

Dr. Ahmed: Thank you very much, good evening to everybody. I am delighted to be here and very happy and honored to participate in this webinar. Under the International Pemphigus and Pemphigoid Foundation. I would like to express my gratitude to Becky for guiding this program and to take upon the responsibility of this outreach program to our community of patient and to our sponsors Genentech and Kabafusion for making this evening possible. I would like to welcome all of you to this webinar and tell all of you that not only am I delighted to be here but more than willing to answer any questions you may have. Becky, please go ahead and begin the program.....

Becky: Thank you Dr. Ahmed. We have some questions that were pre-submitted, do you mind if we go ahead and jump right into those?

Dr. Ahmed: Yes, Please.

Becky: The first one is from Diane and she says “The article in the journal Immunity in 2016 talked of increased oxidative stress in Pemphigus Vulgaris is related to disease activity in HLA association. How does a patient reduce oxidative stress in their diet and other ways?” Perhaps maybe we should briefly in layman's terms describe what oxidative stress is.

Dr. Ahmed: What it really means is that a lot of the foods that we eat are genetically modified and are produced in ways that are beyond the abnormal natural production. The consequence of eating foods with this releases a chemical that can have a damaging effect and particularly a damaging effect on the immune system. That is why the whole concept of oxidative stress in our food system is very critical. Foods to our community and certainly in this particular manuscript or publication in Pemphigus. But in general to our community and many inflammatory diseases. It really has more to do with the fact that the foods that we have are produced in certain dietary benefits to us

and also in the same process produces stress because many of the products and foods can be damaging to us.

Becky: Thank you. Are there any foods that causes a flare for patients with Pemphigus that generally cause a flare?

Dr. Ahmed: Yes, there is little doubt in my mind that especially for patients who have auto disease, and as many of the patients already know- in approximately 60%-70% of the patients the disease begins in the mouth and in almost 100% of the patients it will involve in the mouth at some point in time and off course with the disease Pemphigus Vulgaris. Obviously Pemphigus Foliaceus involves only the skin. I think the foods that are really of concern fall into two categories- first is food that are hard, crunchy and food that are going to cause trauma in the mouth only because of the texture of the food or the consistency of the food. A good example is potato chips. When people bite into a potato chip they use the front teeth which are the incisors. But to grind it they are using their molars, and then the potato chips become tiny pieces and act almost like tiny pieces of blades and cut into the lining of the mouth and giving people lesions. Particularly where the gum line joins the lining of the cheek. These areas are often referred to as gutters and you get lots of patients with lesions in the gutters because they've eaten this kind of food. The second category of food is more closer to the oxidative process because the biochemical content of the food can be in many ways damaging. And the easiest and simplest ways that almost every patient can identify with is tomatoes because tomatoes are acidic. Orange juice, grapefruit juice, pineapple juice. Again, this is because of the acidic nature. What most people don't realize is that chocolate falls into the same category and can do exactly the same thing. Certain berries can do it and many other fruits. The two things that fall into factors that can cause or enhance disease process in the mouth are the consistency of the food and sometimes the bio characteristics within the food. So that is very important for both in causing the disease and the healing process. Because when one avoids these foods they will discover that the mouth will heal much faster and the patients will be far more comfortable eating and will gain back what they lost because they were unable to eat before. If there is anything else someone thinks, then I am happy to address. That is in broad terms or broad strokes that one can best the issue of food and Pemphigus in the mouth.

Becky: Great, thank you so much. Are there any vitamin regimes that you recommend for patients or for patients to take?

Dr. Ahmed: I think that to a large extent the use of vitamins will depend on the food one eats. Generally patients with Pemphigus do have difficulty eating if their mouth is involved. Yes, I do think it's a good idea to take vitamins. Just speak to your primary care and see what vitamin they recommend. The vitamins you really need are for patients who are on prednisone and effects on the bones such as osteoporosis. Having vitamin D and calcium is very vital and for other patients are well the vitamins in the B group are generally useful and certainly minerals iron, magnesium. A good multivitamin would be more than sufficient. If people have difficulty swallowing a pill, then all of these vitamins are available in liquid form and you can certainly use it as drops and add it to any soup, food substance, milk. I think that taking multivitamins is not a bad idea and I certainly would encourage people to take it during the active phases of the disease and I think it will enhance their healing process.

Becky: Thank you so much. We have a patient who's asking "Is a skin sample enough for a diagnoses or is an direct immunofluorescence a must?"

Dr. Ahmed: I think that in 2017, a direct immunofluorescence is the golden standard. For two reasons- one, it becomes a uniform way in which physicians can communicate with each other and form standard of care. If you are going to say that someone has Pemphigus, I think that in today's day and age you have to do a direct immunofluorescence to be able to prove that the direct immunofluorescence was positive from a piece of skin that was taken next to a lesion but not the lesion itself. So that is a must. The second important issue was that many insurance companies with people who have private insurance and are being paid for or their treatments are being paid for by insurance. Many insurance companies now mandate that the diagnosis of Pemphigus be validated by a biopsy and by a immunopathologist. For those reasons also, it's essential to have a direct immunofluorescence. Indirect immunofluorescence is not absolutely necessary to make it a mandatory criteria, but here's the benefit from it. If the titles are high and the titles coordinate with the activity of the disease in other words if somebody has extensive disease and the titles are high then one knows that this is a severe disease. If the titles are low and the disease is low, in other words if there is a correlation between the title of the antibody and the severity of the disease then that's great. You can follow the patient as they recover and hopefully the title decreases and eventually becomes zero and undetectable. There are some patients whom the titles do not coordinate and therefore it's not really useful to them. The point I'd like to remake is that any sensible doctor does not treat a laboratory, they treat a patient. You don't always have to go or should not go by the title of the antibody and the indirect immunofluorescence. But treat a patient based on how they are doing and how well they are responding to therapy. The only benefit of the titles would be decision making

process. The decision making process can be clinical and should be based off of how the patient is doing. The antibody titles can be an additional benefit but is not mandatory. The direct immunofluorescent I believe is absolutely essential and to their advantage.

Becky: There is a patient who submitted a question : When a Pemphigoid patient had no flares for four years or so, is there a test to determine remission to see if my body has stopped recognizing itself as foreign?

Dr. Ahmed: It depends on if its Bullous Pemphigoid or Mucous Pemphigoid. In either of them I believe that if there is no disease, no antibody in the blood and that is assuming that there were antibodies detected in the blood before. Then, I think that one is in remission especially if for four years there is no disease. However, the key question I would have to ask- Is this patient still on treatment and could this remission be only because the patient is on treatment. If the patient is on no treatment and doesn't have the disease for four years, then, in my opinion the patient is in a complete remission and there is no reason to evaluate anymore.

Becky: Our next question is- She was diagnosed with BP in the sixties and she usually gets symptoms on her lower extremities. But after 2014 when she got a lumpectomy for cancer, she noticed that it is happening on her upper extremities. Is there a reason why her immune system would change the focus on where she gets the lesions?

Dr. Ahmed: In the strictest sense of the word "no". The immune system itself is not recognizing regions or spots on the body. In other words, the immune system doesn't say that "I'm gonna choose to have the disease on the scalp, back, chest or on the upper or lower extremities." What happens is the following- the ability to develop a blister in Bullous Pemphigoid, whether the blister is on the leg, or upper arm is entirely based on how much antigens are available at that sight. It is quite possible and is generally accepted that the antigens are far more present on the distance areas of the bodies which is the arms, forearms, wrist, legs and soles of the human body. People with Pemphigoid tend to get blisters very frequently on their hands or arms, feet, or on the soles of their feet. If there has been a certain change from one area to another, the only good answer one would be able to give is the antigen the portion of the human skin which the antibody is made is becoming more available and accessible to the auto-antibody than it was before. There is no real scientific reason. The only instance where you could speak about such a change is when people get radiation. Radiation is given to the body often because of cancer and the changes that occur to the skin secondary to the radiation. And that radiation process can change or alter the density of the molecule that are responsible in causing the disease to which the auto-antibodies

bind. The patients which receive radiation, particularly breast cancer patients have been reported in this case. There are many case reports in which patients that have had radiation and then developed Bullous Pemphigoid in that particular area. That particular reason that these molecules to which the antibodies are produced are altered in the skin where the radiation was produced. If this particular patient did not get radiation and did not have radiation exposure from cancer treatment and the fact that the lesions were more on the feet and now on the upper extremities is purely because the availability of the antigen and no other reason. At such, the treatment would be no different, the approach would be no different and it's purely a matter of the disease traveling from one region to another and no other significance can be attached to it. Certainly no significance in the diagnoses of the disease and certainly no significance in how it would be treated. How it will be treated on the upper extremity will certainly not be different than how it would be treated on the lower extremity.

Becky: A patient has said that they were diagnosed in February with Pemphigus Vulgaris oral limited. They've been treated with azathioprine and Prednisone. The biopsies were mixed IgG and IgA Antibodies. Is there a better treatment this patient can be using?

Dr. Ahmed: I think that there are better treatments and newer treatments but in the event that the prednisone and imuran are working then I think that one should give it a chance to work. The fact that the patient has antibodies to two different immunoglobulins and I want to make sure sure that the message is clearly understood. One part of the message could be that in the direct immunofluorescence when looked under the fluorescence microscope for biopsy diagnoses the staining of the skin could show IgG and IgA. The second part of the story could be that the antibodies produced by the body could also be IgG and IgA. To either event it doesn't become tremendously significant unless one talks of therapy and when talks of prednisone and Imuran are working If they are working I would certainly give them a chance and let them work their way out and have the patient go into remission. On the other hand, if the response is not satisfactory, if the response is not long lasting and if the patient has breakthrough or relapse of the disease in spite of the prednisone and Imuran then I think it's time to think of other avenues and certainly newer and better treatments of either Rituximab or IVIG or combining Rituximab with IVIG would be a very good way to go. My opinion would be if the Imuran and prednisone does not work, then one looks for alternatives. But if it is working then I would stick with it and make sure that the patient is going into remission with a combination and not simply jump ships because other things are available.

Becky: How long does it normally take our immune system to react to Cellcept, Imuran, the immunosuppressant group of medications that are offered?

Dr. Ahmed: One needs to understand one basic fact, very importantly in addressing this issue of providing a balanced level headed answer. These drugs are lumped and grouped together under the dialogue of immunosuppressive agents. Each drug is different and how it's different. It's different chemically, the molecular structure of the drug is different and most importantly how it acts and why it acts is different. That is the most important dynamics of this therapy. If you take a drug like Imuran, we know for sure that Imuran is not going to be very effective almost for two months. There is a long lag period from the time you begin Imuran and Imuran begins to work. On the other hand if you take a drug like methotrexate it begins to work in a shorter period, perhaps in 2-3 weeks. But if you take a drug like Rituximab, it is a very severe immunosuppression, in fact the most severe of all the ones we have available, then you will see that Rituximab works within weeks. Many patients have complete clearance of disease in about two weeks or so. Each drug is different, each drug acts differently, and therefore take a different amount of time. I think the message I want to get across to our listeners is- It is very critical that you speak to the doctor that's treating you and ask the doctor in really specific terms when you should expect the drug to kick in or when do you expect the drug to begin to act. Needless to say, you also need to realize that how soon a drug will kick in will also depend on the dose of the drug. Not all drugs, not any of these immunosuppressive agents that we talk about have one specific standard dose. The dose is going to be calculated either on the weight of the patient, or it will be based on the severity of the disease and in a drug like azathioprine it's based on the level of an enzyme called TPMT. If patients have low amount of that enzyme they will need lower amounts, or if they have high amounts then they will need larger amounts. There are multiple factors that go into determining how soon a drug will be able to kick in. I would strongly suggest to a patient that you have a very candid conversation with the doctor treating you and pointedly ask the question- When do you think this drug will kick in and when do you think it will begin to act because it's going to be different from drug to drug.

Becky: A patient is asking, she has bullous pemphigoid. She says that getting the flu shot and other vaccines stimulate the immune system. Should patients with pemphigus or pemphigoid get a flu shot and what are the chances of increasing the immune system that it will attack our skin?

Dr. Ahmed: I don't think that these vaccines that people get are in any way going to advance the autogenic effects of the immune system. In other words if someone went

and got a flu shot, a flu shot is going to protect you or hopefully protect you from getting a bad virus to enter. It is not in any way going to increase the amount of pemphigus or pemphigoid antibodies or antibody. There are two different roads, two completely different branches of the immune system and rarely intercept one with the other. Here are some of the important issues that need to be remembered- the key question you want to ask the person giving the vaccination is it a live virus, live vaccine, or a dead vaccine. Dead vaccines have lesser problems and less side effects to worry about. Live vaccines, particularly live viruses have far greater influences on the body and immune system. I would suggest for patients to talk to their doctors, talk to the person giving the vaccine. It's not a bad idea to avoid live vaccines, but certainly dead vaccines are less likely to cause any damage. Certainly it is less likely to make the pemphigus or pemphigoid worse. Having said that, I should tell you only for purposes of completion. That there are approved physicians and scientist in the world that believe that these vaccinations are not good because they can cause autoimmune disease. I can tell you that the belief is not universally held with those that disagree, but again in the basic question of that as well a live vaccine versus a not live vaccine. I don't think that anybody needs to worry that if they are getting a vaccine from a dead virus or only a part of the virus if they have pemphigus or pemphigoid. I don't believe that it can get any worse from getting the flu shot. The decision to get the flu shot should be something that they and their primary care doctor should make it in joined consultation. I don't think that you should just go to any pharmacy because you should make sure that you go to someone who can give a valid explanation of what is happening and you certainly want to avoid live.

Becky: Excellent advice sir! A patient is asking- how does prednisone and cellcept and IVIG work together? This patient has been on IVIG before and are currently taking prednisone and cellcept for a flare after two years and will be getting IVIG's on one week a month to get the disease under control.

Dr. Ahmed: I don't really doubt in my mind that they will all complement each other. This is how they will compliment- IVIG has two major benefits. It's one major benefit is that it is an anti inflammatory drug. Very similar to what prednisone is. IVIG will help augment and enhance the effect of prednisone by helping create an anti inflammatory which will help recover from pemphigus. The second aspect of IVIG, is that it tends to reset the immune clock. In other words if the immune circuits have gone kaputz then it will reset the thermostat or bring it back closer to normal. What immunosuppressant does like Imuran or whatever the drug will be, it decreases the amount of autoantibody produced by the bone marrow. Yes, in another way IVIG would be enhancing those effects. So, if one needs or wants to get s combination of prednisone, Azathioprine, and IVIG

together, I think that it would make a lot of sense and there is no reason not to get it. The only question I would have is that you would like to minimize the amount of prednisone for the long term side effects of prednisone are very hazardous and would be best to not take it. That has greater concerns to me when using all three of them. Mainly when you use prednisone it should be in small doses, azathioprine, which can also be in a smaller dose along with IVIG. I think it should be an effective combination.

Becky: Along the same lines, a patient is asking- after two Rituxan infusions, how should one wean down on the prednisone and the Azo Thio Cream?

Dr. Ahmed: I think that once one gets Rituximab, the science become very important. Rituximab has both the effects of the immunosuppressive agent as well as the effects of prednisone. It has a powerful anti inflammatory effect, which is why most patients that get rituximab, clear of blisters within two weeks or a maximum of three or four weeks and dont have any blisters left. That's the powerful anti inflammatory effect of the rituximab itself. The second thing is that the rituximab makes the B cells zero. The B cells are the cells that made the autoantibody. If there are no B cells around, the ability for the body or autoantibody may significantly reduce or not help, not always but in many cases. Anybody who begins rituximab may therefore in the distant future get off of the prednisone and the Imuran or Cellcept. I think that Rituximab is wonderful also if it allows you to get off of the other medication.

Becky: Another question, both related to the Rituxan and Imuran. Asking- Which has a greater side effect and which one is more invasive. It sounds like Rituxan is the one to have a little more greater side-effects is that correct?

Dr. Ahmed: Yes, it certainly does. It certainly is not a drug to be taken lightly or a drug that should be used without caution and without monitoring and close monitoring. So, yes, it's not a drug that's not toxic. I think it's a drug with significant issues and that the person using it should be aware of, and in my own opinion the patient should be completely aware of. Because at the end of the day, it's a patient's body and it's a patient's life. The doctor is simply a delivering agent, but the patients are the ones whose life is at stake. So, I think that they should be very much aware of the side effects as well.

Becky: A patient is saying that many inflammatory autoimmune disorders have been correlated in recent years to gut dysbiosis and they have discovered that he has a low gut microbiota diversity and severe imbalances with over abundance of several

candidiasis bacteria. Is it known if this is a common feature in pemphigus patients and if so are there any effective treatment?

Dr. Ahmed: The treatments that are used for Pemphigus are prednisone and some immunosuppressive agents and then of course more recently people are jumping on Rituximab. Neither of these should have an impact on the flow of the bacteria in the colon. In other words, we all have certain amount of e coli and certain amount of bacteria and fungi growing in our colon. It really should not be affected in any dramatic way. If a patient is experiencing a lot of changes in the floor of their gut, changes that are not pleasant or are uncomfortable or causing problems of any kind, I would strongly suggest that they speak to their primary care doctor because there are ways to provide more bacteria and elements to the gastrointestinal tract. But they have to be done with caution, they have to be done judiciously and they have to be done with planning execution, and finally they have to be done with a certain goal in mind. Before anybody begins to do anything, they should know exactly what they want to achieve. What their goals are and how they are going to arrive at those goals. Doing it randomly with taking certain supplements or by adding certain bacteria to one's diet always carries the risk of several other issues. It should be done with physician's supervision, understanding and advice. I would definitely not do it without that.

Becky: There are two questions that have been submitted and they kind of go together- "Is pemphigus genetic and what are the chances my offspring will have this disease?" and the other question is "When I get pregnant, how likely will the baby show signs of pemphigus or get a blistering disease?".

Dr. Ahmed: I'll answer them separately because they are similar yet a little separate. The statistical chance of any patient having a child or a sibling with pemphigus is 1 in a billion. That's the statistics. Now, it is not at all a genetic disease. At the IPPF meeting we have lectures that talk about the genetics of pemphigus, and really haven't had a talk on the genetics of pemphigoid but there is a tremendous amount of research on that as well. What these lectures really tell you is the gene play a role in the generation of the disease are the mechanisms in which the disease takes place. But by no stretch of the imagination is pemphigus or pemphigoid a genetic disorder. The simplest example I can give people is diabetes. If their grandfather and father had diabetes, there is a good likelihood that they will develop diabetes too. It is not that kind of a disease. It is not a disease which is passed from mother to son, mother to daughter and so forth. Pemphigus is not at all a genetic disorder. Anybody and everybody who are listening to this webinar should be very clear in their minds that their children, grandchildren, have no increase or susceptibility and no increase likelihood of getting

pemphigus at all. If they get it they are getting it randomly but it is not from a genetic process. First and foremost, it is not a genetic disease at all, neither should it be considered a genetic disease. The studies that are done, use the word genetic in an inappropriate way for the common person trying to understand. Where to use it in a medical lingual has a very different sense of meaning. With respect to pregnancy and pemphigus, there are two or three different diameters that need to be considered. When a woman develops pemphigus in pregnancy, there are one of two scenarios. The first scenarios is that somebody already has pemphigus and gets pregnant. The second scenario is that someone does not have pemphigus but develops pemphigus during the course of the pregnancy. But what is the key issue, the key factor? The key factor is what is the title of the autoantibody. If you look at the desmoglein 3 or 1 and the antibodies for desmoglein 1 and 3 are very high, these autoantibodies are very high, then they will cross the placenta. If they cross the placenta in high enough term and high enough titles then they will give the baby a few blisters. However, it needs to be emphasised that these blisters are transitory, and temporary and they will go away. And the child that was just born does not need to be treated. The only thing you need to make sure of is that the baby does not get infected because the blisters can get infected quickly. But the neonate does not need to be treated because in two or three months the antibodies stabilize and the blisters completely go away. The child is not born with pemphigus. The child may only develop blisters if your antibodies have crossed transplacentally. If it as crossed then it is coming into circulation with the newborn child. The answer to the question is that it will depend a large extent on weather the disease occurred before pregnancy or during and what was the title of the antibody and the time at which this has happened that will determine how much antibody goes into the unborn child. Even if the child does develop blisters they will rapidly go away and will not become a disease process. What also needs to be emphasised and understood in a regular way is that in many women after they develop the baby there can be a flare of the pemphigus and can get worse. There is well many reported case in which some had not as bad pemphigus when they were pregnant . But after the pregnancy, and after they deliver the baby the disease got worse. You'll need to be aware of that as well. Again, I need to emphasis that pemphigus is not a disease that is genetically transmitted and that the issues of pemphigus in pregnancy are not extremely complex or unknown. The one thing I do need to make sure that our audience understands is that if a woman has pemphigus during a pregnancy, she needs to be monitored at what is called high risk pregnancy. It is very important that she lets her doctors know or her OBGYN know that she has pemphigus and they need to watch out and be sure that it doesn't come back because it can be quite dangerous. (49:00)

Becky: There is a patient who is asking and said her husband had a knee injection and then started blistering in his mouth and then three months later he had another knee injection and started on his whole upper body. Do you think that there is a correlation of certain medications that can cause Pemphigus Vulgaris?

Dr. Ahmed: Depending on the medication one got can be in direct correlation or not and it's difficult to determine what happened with the knee surgery, etc. So, I can't give a specific answer to that question because I would need to know a lot of specifics. However, with that said, there are certain drugs that are known to imitate pemphigus. In other words if one had the right background and is given these drugs. The common (50:13-) which is not the same as penicillin you would need in an antibiotic but a drug based on the same formula but develop into a different molecule. The second group of drugs are the drugs such as (50:31-33) all of them end in the word (50:35) These drugs have also been known to trigger pemphigus in patients both in Europe as well as in the United States. Then there are sporadically a whole long list of drugs because if one single drug causes pemphigus and the biopsy proves it, then the physician and the pharmacist and the hospital are obligated to report to the drug company and let them know that this happened. There is only one reported case in which a drug not caused but is associated with pemphigus and so it was reported and the list becomes extremely long. But I would only stick to these two medicines because they are well documented to be the cause of pemphigus in patients. There have been many drugs that have caused pemphigus and so they were reported to the FDA. In terms to real relationship to the disease process, the blood pressure pills are probably the best and certainly penicillamine which is often used in collagen vascular diseases or autoimmune diseases is the only other one known to be associated with. I want to make very sure that our audience realizes that I am very carefully using the word associated. The cause and effect relationship is very difficult to prove.

Becky: Is there any known risk factors for pemphigus or pemphigoid besides for the medications you just spoke about that can trigger?

Dr. Ahmed: I'm not so sure for the trigger process that brings it on. There are factors that one can see that are universal and present. Which makes sense because there are a lot of pemphigus in China, Brazil, in the U.S and Israel as well as in Canada. If you think about it, the temperature, the weather, the bacteria in the environment is so different from one country to another. It would be very difficult to say that there is one specific thing or one specific factor that triggered or brought on the pemphigus. The only thing we do know is that certain things can make it worse. For example, sunlight can. And there are people in Boston who in the middle of the winter when the UV lights are

near above 0. Go to Bermuda or Jamaica and lie in the sun where you get a tremendous amount of UV light and sure enough they will break out. So, yes, in those instances you can say that it triggered a relapse or triggered the disease to come back. Are anybody lying on the beaches in Bermuda, or Jamaica who are from New York or Boston going to develop pemphigus? The answer is no because there are million of other people doing it every day and are not developing pemphigus. The answer is- in patients who have the disease and go lie in the sun can sometimes have a relapse. But can the sun itself be a trigger factor, initiating the disease? The answer is no. When one has to differentiate between those two factors that begin the disease on day one are those factors that can make it come on or get worse when patients already have pemphigus and it's not a new thing for them. I don't think we really know anything specifically any trigger tat universal and worldwide that makes the disease happen. We simply know that there are factors that can make it worse when it's already there.

Becky: A patient is asking if the (55:26) or autoimmune diet is effective in treating pemphigus vulgaris?

Dr. Ahmed: Diets are a fat process. They come and they go and they have their own scientific basis or factor. I think that they key and most important thing you need to think about is that the food is soft, and especially not hurting the mouth and protein intake should be good. The reason I say that is because the blister fluid, both in pemphigus and in pemphigoid is identical to plasma it's identical to the water part of the blood which is full of protein. People lose a lot of protein when they get either pemphigus or pemphigoid. I would suggest that the key and most important thing is to make sure that you are getting enough protein so that you are replacing any protein that's been lost. Other than that there really would be no specific issue that would raise because it really would not be scientifically valid or universally accepted.

Becky: Is it possible to overcome pemphigus or pemphigoid without steroids or basic medication if it's not a full scale case but a lighter one. Have alternative treatments with blistering diseases been investigated enough in general?

Dr.Ahmed: I don't think that there has been a huge amount of research in alternative methods and here are the reasons. Which alternative medicines are we going to think about, herbs, roots, Chinese, or Japanese or which country are we going to choose for alternative methods to see whether it will work or not. And you can not afford to take a patient legally with very widespread disease involving 70% of the body and the patient is very sick and toxic. You really can not put them in a study in which one group gets prednisone or other immunosuppressive agent and someone else gets some sort of

herbs. Those experiments would be very hard to pass by which is called Institutional Review Board (IRM) which is a committee of people that would let someone do such an experiment or not because it is hazardous to the patients health and they certainly would not want it to be taking place under their roof. There really isn't a real strong body of knowledge available to us. Even in languages such as China or Hindi, Arabic or Hebrew or any other ancient language that we can use to see if those tests helped patients with pemphigus. In today's day and age there are certain Chinese products available, but the sad part of it is that there are plants that can make similar to prednisone, cellcept or Azathioprine or anything similar. For many of these herbs that are coming overseas actually contain agents or contain drugs that have these pharmacological effects. So, if one has to take prednisone it is better to take it by the mouth instead of in a branch, a leaf or a seed. There is really no good alternative medicine and no good real studies to document that it can be of any benefit. So I think that maybe there are good herbs and alternatives, but they just haven't been studied in a controlled environment. One has to come to a legitimate and sensible conclusion. The answer is that these studies haven't been done and we really don't know so we can't condemn it and we can't say that they don't work because we haven't really used them in a way which they should be used in order to create a positive outcome.

Becky: A patient says that she has bradycardia and is asking if Rituximab treatment is safe for a patient with Bradycardia and if there are other treatments that are safe as well.

Dr. Ahmed: Yes, I think that this is a very important question because many people who are using Rituximab don't always realize that Rituximab can have serious cardiovascular effects. I think that what she needs to do is see a cardiologist, and have this cardiologist evaluate her very thoroughly and most importantly find out why she has this Bradycardia or low heart count. Is it because there is some conduction defect in the heart or is there some other reason in the heart that is causing this. And determine and very well document because that will tell us if it's safe to use Rituximab or not. Simply hearing that somebody has a low heart rate, would I give them Rituximab? The answer is no. I would make sure that a cardiologist has evaluated the patient, done a very thorough work up and is telling me that this is the reason that the heart rate is low. In my opinion and in my experience I've treated 35 with this disease and having to need Rituximab and given it to them and it's been safe. Till that event occurs, one has to be very cautious and very careful in the kind of medication one gets.

Becky: A patient is asking if there is any risk in taking Rituximab if one is TB positive but there is no active infection shown on chest X-Ray?

Dr. Ahmed: This is again a very gray area and most people actually prefer if they are certain that there is nothing on the chest X-Ray but tests positive or some other evidence of TB, then one wants to give antitubercular therapy simultaneously and perhaps begin it a month or two before and then begin the Rituximab. The patient needs to have treatment that's appropriate for Tuberculosis before Rituximab is given that's for sure.

Becky: Well thank you, that was a very fast hour Dr. Ahmed.

Dr. Ahmed: Yes, it was. I hope that I was able to answer the questions to the satisfaction of those who asked them and was able to provide them with practical information. I think that providing people with information that's practical, something that they can deliver and something that they can ask someone else to provide them with further information is much better than just giving answers that people may not be able to benefit from

Becky: Absolutely! Once again I just want to thank **KabaFusion for having IPPF Physician Ambassador, Dr. Ahmed speak with us and Genentech for sponsoring this call** very much for being on the call with us today. It was extremely educational having you on our call. I would like to give a huge thank you to everyone on the call for joining us today!

Our next webinar is tentatively scheduled for February 2018 on Mental Health with Chronic Disease. Don't forget to register for the IPPF Natural History Study, a new patient registry sponsored by the National Organization for Rare Disorders (NORD) and the US Food and Drug Administration (FDA). Register today on the IPPF Website under the research tab. And a reminder the IPPF is still looking for Awareness Ambassadors to visit local dental offices. Please click on the Awareness Ambassador link for more information.

Lastly, If you have a question that didn't get answered on the call, or have additional questions please e-mail me at becky@pemphigus.org, or call me at (916) 922-1298 x:105, and I would be more than happy to help.