Becky: Hello. Welcome everyone. This call is now being recorded. I would like to thank you for being on the call this afternoon. Our speaker today is Dr Margaret Michalska, Medical Director of immunology, US medical affairs at Genentech. Thank you for joining us today. The call today will focus on Rituxan and Genentech Access Solutions. Thank you doctor. Welcome to today's call.

Dr. Michalska: Hello everyone. Thank you for joining in. The only technical question I have is which icon do I click to show my screen.

Becky: Sure. I'm going to change it over to you right now. If that is okay?

Dr. Michalska: Please do.

Becky: Okay. And we are now sharing your screen.

Dr. Michalska: Can you see my screen?

Becky: Yes. It says Genentech Patient Access Overview.

Dr. Michalska: Excellent. Well as you can tell, I'm not a technology wizards so I'm very glad this is working. Now that we have the technical details out of the way, I want to extend a warm welcome of, of Becky's to everybody on the call. Please know that we here at Genentech truly appreciate all patients but especially patients with rare diseases who are very vocal, very well informed and willing to make sure that right treatment is available to everybody with these rare diseases. We appreciate your efforts and we are certainly very pleased to offer our partnership in all that you do. What I thought I would do is I briefly go over what the company has to offer it to patients with rare diseases and then, I will address some of the questions that already came in or will be coming in as we proceed with a teleconference.

Dr. Michalska: Very briefly, the company Genentech was originated by a gentleman whose name is Herb Boyer, with the financial support of Stanley Cohen. The legend has it that the two sat over some beers during a conference, and that's how the company was born. And the novelty of the technology that Genentech has to offer was called recombinant DNA technology. Again, the legend has it that Herb Boyer had his son with pituitary insufficiency. He was lacking something called growth hormone that we need in order to grow. And he was dissatisfied with currently at the time available medications. So he proceeded to develop medication for his son. And now we are all benefiting from the technology that was thus originated. The company as I said was founded in 1976. So we just celebrated our 40th anniversary just a couple of years ago. In 2009, we became a part of Roche group and the company's headquartered in South San Francisco, California. There's some, 15,000 plus employees in the United States. And we have some 40 plus medicines approved for people with very serious or life threatening diseases. Our mission is to pursue science. And we say that patients come first and it's not just what we say, but what we practice. Lastly, we also like to enjoy what we're doing. So Genentech creates a very friendly environment for its employees. This actually addresses one of the questions that was asked in the questions that I've already seen. We tend to stand by our word. So we understand that in the system that's currently in the United States, there are pretty serious difficulties for people to get medications

that they need. So in 2017, over almost a quarter million people, we're actually helped by the assistance that Genentech offers through various access to care programs. Over 40,000 people received free Genentech medicines in 2017. So we, we tend to really make sure that if we can the patients access to medication is available. More to the topic of this call. As I'm pretty sure pretty much everybody on this call is aware, Rituximab was approved for a Pemphigus Vulgaris in June of 2018. It's approved for treatment of adult patients with moderate to severe Pemphigus Vulgaris. If you wondering what Rituxan is, it is a biologic medication which has a certain specificities for the underlying process in Pemphigus Vulgaris. It's called the biologic medicine, which means that the medication was developed using biological processes, which are similar to what happens in our bodies. So that's different from chemicals which are synthesized in the lab. Biological compounds are obtained through biological processes and result in obtaining a medication that very closely mimics the natural molecules that we all have in our systems.

Dr. Michalska: The proposed mechanism of action of Rituximab is that it targets a type of lymphocyte a white sell, which has a variety of function in autoimmunity and immunity in general. Those are called B cells. And one of the roles of the B cell is to make antibodies, which, some of them are good. For instance, antibodies that we generate against different vaccines that protect us, some of them, in the heart of various inflammatory processes. For instance, in Pemphigus, the antibodies that attack proteins that hold the elements of the epithelium together, are also produced by the B cells. So if you curtail the overactivity of B cells, you can expect some beneficial effect to occur. Importantly, it's not a steroid. And my background is in rheumatology. I practiced rheumatology in Chicago for 25 years. So yes, steroids are very useful medications for a variety of conditions, but also we are very well aware of the consequences of long term exposure to steroids. The basis of approval of Rituximab for Pemphigus Vulgaris was a clinical trial that was conducted in France by professors Joly and his colleagues and what they did, they included 74 adult patients with moderate to severe pemphigus vulgaris. They were either taking the combination of Rituximab and lower and shorter course of prednisone or the other group were taking just only steroids. As you see in this slide, the duration of treatment of steroids differed in the Rituximab group, it was much shorter than the steroid only group. The study lasted for two years and the objective was to see how many people were in complete remission. In other words, had no new lesions, no old lesions and were off treatment for at least two months at the two year time point. The important finding in this study and the reason why FDA actually use professor Joly's data to approve Rituximab for pemphigus, was a dramatic difference between the two group. At two years, almost nine out of 10 people, 89% to be precise, were in complete remission as opposed to just about 28% of people taking only steroids. And as I said, they were in full remission, no new lesions no old lesions and off steroids for at least two months, at the two year time point. I am obligated to share the safety information with you. So, some of the important safety concerns are infusions reactions. As you know Rituximab is a medication given in the IV, intravenous infusion, and infusion reactions have been described. The definition is usually that of any adverse event happening within 24 hours after the infusion. There has been some skin and mouth reactions, which are listed on this slide.
So if any such thing occurs, that needs to be reported to your physicians. There have been cases of reactivation of hepatitis B virus, which causes inflammatory process and deliver. And sometimes it may be questioned and there have been cases of reactivation of that process in patients who had been treated with Rituximab. And there's also a rare condition called progressive multifocal

leukoencephalopathy, PML for friends, a condition which also has to do with reactivation of certain virus that many of us carry and it's normally quite innocuous except when treated with medications that affect immunity. There are some other side effects listed here including tumor lysis syndrome that's applicable, usually two patients who are treated with Rituximab for malignancies. There are serious infections that have been described. It may cause some cardiac problems such as chest pain, irregular heartbeat and heart attack. The kidney problems have been described in patients with non Hodgkin's lymphoma, again, that's a malignancy and that actually was usually the consequence of the tumor lysis syndrome. And some of the other issues such as stomach pain and bowel problems. However, probably most pertinent item here to patients who may receive Rituximab for Pemphigus is that the infusion reactions, which may include chills, fever some body aches and tiredness, et cetera.
This may be actually something that you may want to write down or kind of take notice of how to receive patients support. So there is a Rituxan patients support line. We have real people there answering the phone calls and the number is listed here and which it's (877)474-8892. And if any of you have any question about patient support there is somebody there who will answer your call and direct you to the appropriate group who deals with patients depending on the insurance eligibility and so on. There is also financial assistance that offers copay coverage. There are ways to get additional medical information if you so desire. Again, if you call that number and request medical information, you will be directed to people who can offer it. And then the coverage navigation services, they pretty much direct you to where you need to go or connect you with the person who can address a particular issue you may have.

Dr. Michalska: This shows you the copay card. And, I actually have to say that from my old days when I was a rheumatologist in Chicago, I had quite a number of patients who were quite delighted to use the system because it offered a significant financial benefit to them, meaning they could afford the treatment, which otherwise wouldn't be available to them. So by all means, you may want to utilize this in the coverage that you need. And again, the number here, the number is listed on this slide. And for the Copay card you call (855)722-6729. And this is essentially a diagram which shows you how this works. Between you and I, I would just write down the number, call the number, tell them what you need and you will receive your assistance. We ask you to continue what you're doing, meaning to learn about your disease, to talk to others, to offer support to friends. And this slide essentially summarizes all these activities that I know you're already engaged in and we appreciate and respect you for all that you do in that domain. Becky, I stop here because I think, our interaction will be most productive if I start answering some questions that I already have and then address the questions that will be coming in.

Becky: Great. That sounds wonderful. So Margaret, we had a whole bunch of questions that came in prior to the call. Do you want to start answering some of those and I'll start collecting some of the questions that are still coming in, live during the call?

Dr. Michalska: That certainly works for me, so without further ado, because there are quite a few of them and I have to tell everybody on the line did I did my due diligence, I did my homework, last light things that I needed to look up. I looked up. So I hope the information I have to offer will be useful to you. So let's get going. The question here is, “How many times, does one take treatment for Pemphigus?” And the answer is according to the doctor's release trial, the medication was given in a

thousand milligram infusion two weeks apart, so day zero and day 15. And then at months 12, there was every repeat infusion of 500 milligrams with the intention of getting it every six months as judged by the clinician. Again, I am going to be saying this over and over again, the decision to treat and the decision how to treat is a decision made jointly by your physician and yourself. So I can share with you what's been published, what's known and what's available in the prescribing information for Rituximab. But ultimately the decision is that that you make with your physician.

Dr. Michalska: There was a question about a joint pain following the infusion of Rituximab and this severity of that reaction, we call it musculoskeletal pain, is what determines the course of action. If it's transitory, if it's transient, if it's say a couple of days and it's manageable with something like I said Acetaminophen, it is a well known adverse event of Rituximab and you needn't worry about it. If it's more severe, if it's associated with fever, it's associated associated with rash swelling, that may be something called serum sickness reaction and you need to bring it up to the attention of your doctor immediately. Patients who develop the latter should not be treated with Rituximab because another exposure to Rituximab may even cause more severe effects. Importantly, before any infusion of Rituximab, you are given premedicate patients. So you receive Acetaminophen, you receive and antihistamine usually Benadryl, and we recommend that a hundred milligrams of methylprednisolone is also given about half an hour before the infusion. This is actually to prevent those undesirable effects of infusion of Rituximab.

Dr. Michalska: Next question,how long does it take for remission to occur? In Joly's trial, in the trial that I'm referring to here, the delay to complete remission in the prednisone group, prednisone along group was 22 months. The delay to complete remission in Rituximab was nine months. So we talking about patients who had no lesions, who achieved full remission. So it's about nine months for Rituximab, I mean, again, that's the median values. So some people will have more, some people, longer time, some people will have a shorter time, but as far as how soon the effect of Rituximab can be seen that again varies. But it's been described with being weeks to months after the first infusion.
I have a question here on patients with Pemphigus vegetans and in Joly's trial there were no patients with Pemphigus vegetans. There are however reports in the literature, the reason why we don't usually use this in to make broad statements, is that those are very few patients who were exposed to Rituximab with Pemphigus vegetans. From what I've read, the response was good and people do use it even though it's an off label. In other words, it doesn't have the official approval, for that condition.

Dr. Michalska: There was a question about the sort of incongruent idea that mouth lesions can be seen as a result of Rituximab therapy. And the question was, well, doesn't that make Pemphigus worse? But I wanted to say here is this, that if you look at the safety profile and the drug, it looks at adverse events in all indications. And many of you realize that Rituximab was first approved in November of 1997 to treat lymphoid malignancies, specifically non Hodgkin's lymphoma. Some of these conditions actually come with oral lesions at such. So sometime it's very difficult to say, well, you know, it was the underlying disease or it was the consequences of treatment. Based on experience relayed by professors Joly and his colleagues it appears that effectiveness of Rituximab in Pemphigus vulgaris is such that no oral lesions were reported as adverse events in that trial.

Dr. Michalska: Right, I think I told you about how it's administered. I mean some of these questions ask about similar issues, so, I'm not ignoring them. I'm hoping that I'm answering them and sort of omitting the repetitions. Now there was a question about this safe rate of infusion and the recommended rate of infusion in Pemphigus is 50 milligrams per hour, which is roughly four hours of infusion. The question is can it be given faster? It has been in lymphomas and leukemia. It's not recommended for pemphigus because we have no data to support that it's safe. I want to add that if a patient experiences some discomfort early in the infusion despite the premedication, it's a common practice to slow the drip to kind of, to slow down the process of infusion. It is sometimes done and it's often sufficient to alleviate the discomfort.

Dr. Michalska: Another question, how long does this drug stay in your system? Yes, there are studies to show how long Rituximab stays in your system. What we clinically use is sort of a surrogate measure, namely the levels of B cells, something called CD positive, 19 CD positive and B cells because the attempt here is to lower the population of these cells and it's usually apparent within the first two weeks after the infusion with the levels of these cells go down if you do a cell count. They stay suppressed for about six months and they start repopulating around month six. Thus very often Rituximab is we reinfused at month six. If the perception is that patient would benefit from this additional infusion, again, in Joly's trial, the reinfusion was at months 12.

Becky: Margaret, can I just ask a question and I don't know if there is an answer for this. Do you know how many B cells are knocked out with each infusion?

Dr. Michalska: The intention is to actually bring the population almost to nondetectable so the intention is actually to, I don't want to say wipeout but to actually bring the cell count so as close to nonexistent as possible. So yes, and you know, different individuals will respond in different ways but you know, if you look at the graphs, the cell counts very often come pretty much to do almost zero.

Becky: Oh, great, thank you.

Dr. Michalska: Does that answer your question?

Becky: Yeah, absolutely.

Dr. Michalska: Next question here is regarding infections. Specifically somebody asked, "So many people around me coming down with colds this time of the year any instruction about this before Rituxan?" Yes, if one reduces the population of immune competence cells, specifically the B cells, the likelihood of getting infected, in fact it goes up. So, you know, common sense, avoiding large gatherings of people, many of whom may be coughing and sneezing is a good idea. If you're traveling, it's not a bad idea to use a face mask just to make sure that the likelihood of exposure is much less. But then other thing that is fairly important is the immunizations. And I'll talk about it a little bit more in a moment, but keeping up to date with your flu vaccines and some of the others is probably a very good idea.

Dr. Michalska: Another question, “Do I need to stop any medicines before getting infusions?” The answer is no. There is no evidence that there is an interaction of Rituximab with any other medications. And the question follows, “I've heard that some people needed to stop cellcept before getting rituximab.” Again, the combination of Cellcept and Rituximab has been anecdotally reported by physicians, is used in some of the other autoimmune conditions. For instance, systemic sclerosis. And a doctor may decide that the combination of immunosuppressive agents is needed to control the disease, but no, there is no indication that one should stop cellcept before taking Rituximab. There are some questions about bio similars and I believe they come from outside of the United States. So I'm not sure that I can offer that much expertise but many of you who need to get your medications are aware that the biosimilars are coming. In the U.S., Rituximab biosimilar has been approved for one condition only and it's a non Hodgkin's lymphoma. The FDA requires that if a biosimilar where to get another indication that it would be studied in that condition. So there isn't a blanket approval for everything and anything that Rituximab is approved for, each of the indications need to or in other words, requests for each of the indication needs to be supported by clinical data that a biosimilar is bio equivalent to the originator Rituximab. The question is how much cheaper the biosimilars are. Usually the discount is on the order of about 15 to 30%. And the rules vary state to state and country to country. So I really cannot give you any general information. Generally, however, there is a position that, again he should be based on the discussion of the patient and the physician before a switch to a biosimilar is made. Again, it's different in some of the European countries. My understanding is the national health service in Britain as well as the national health services in Germany and the Netherlands favor biosimilars. Currently there are no data to support bio equivalency of Rituximab and Rituximab biosimilar in Pemphigus vulgaris.

Dr. Michalska: Question about the duration of remission with Rituximab. So in Joly’s trial, the median cumulative duration of remission was, 14 months, over a year with Rituximab and two months in the arm that included patients on prednisone alone. Again, very significant difference. A question here is, “I have a fatty liver disease with fibrosis, am I a candidate for Rituxan?” And again, that's a discussion you need to have with your doctor. There is no known hypertoxicity, no toxicity to the liver from Rituximab treatment. The only concern is that if you've been exposed or have occult meaning not clinically manifest infection with hepatitis B virus, that you be tested before Rituximab is ever considered. Are there any patients that cannot take Rituximab? No, there are no known contraindications to Rituximab. Obviously, if someone has an allergic reaction to Rituximab or a Rituximab-like product meaning another anti-CD 19 or anti-CD 20 molecule,in my best clinical judgment, shouldn't be exposed to a similar drug. There's a question that someone asks, “I was a patient who did not have the right enzymes to take Azathioprine, am I still a candidate for Rituxan?” Yes. The two are completely unrelated and what you’re asking about, is the enzyme called TPMT, which we have to metabolize Azathioprine, to get rid of it, to get rid of the toxic metabolites of Azathioprine. If your level of this enzyme is low, you don't get rid of these substances as you should and toxicity can ensue. But there is absolutely no cross reactivity with either the mechanism of action or the need to have a similar enzyme present when you taking Rituximab.

Dr. Michalska: “Can I be on prednisone all while taking Rituxan?” The answer is yes and very often high dose of steroids is initiated in patients who have especially severe symptoms of Rituximab because it make take a few days or sometimes a few weeks or even a couple of months for Rituximab to have its full effect. As I told you, the depletion of the B cell population is what we are after. So to control your

symptoms fast and better, prednisone is very often introduced first. The good news is that, at least in Joly's trial, patients in whom Rituximab was added to the prednisone, the prednisone dose achieve much better results as I have already told you. Alright, the question about immunizations. So, generally it's a very good idea to be immunized against common infectious complications such as influenza and pneumonia as well as herpes zoster before you start Rituximab infusions. If you have the luxury of holding off with Rituximab, I would encourage each and everyone of you to have your vaccinations up to date. Takes about, there should be a lag of roughly four weeks between the immunization and the initiation of Rituximab therapy so that the immune system can mount a response to these vaccines. People over 60 should be vaccinated with Pneumovax or whatever the current, vaccination against pneumonia is used. The flu vaccine should be given appropriately as well as in my, again, clinical opinion patients should be vaccinated against herpes zoster. That's the virus that causes shingles and very often, gets reactivated in patients who are on immunosuppressive therapy. You say, "All right, I'm already on Rituxan, how soon after the infusion should I get vaccinated, say against pneumonia?" Well, you should get vaccinated probably about two or three months after your last infusion because by that time there will be some immune response that your system, will be able to mount. And thus the reaction to the vaccine will be actually fruitful, productive. Live vaccines are not recommended to patients who are on Rituximab treatment. The majority of them apply to children such as the mumps vaccine, that the mumps, measles and rubella vaccine and some of the others, or its pertinent I think in adult population, especially now that people travel a lot. Yellow fever is a live vaccine so it should not be used in patients who are on Rituximab therapy.

Dr. Michalska: Moving on, there's a question about paraneoplastic pemphigus. And again, I can share with you what I know about this. Paraneoplastic pemphigus is a variety of pemphigus that's been associated with malignant diseases. So the key is to appreciate the diagnosis and to find the underlying malignancy which has led to the development of this particular clinical picture. So based on what I've read patients who do best are patients in whom the primary malignant problem is identified, treated, and they respond well. Yes, Rituximab is one of the agents that's being used to treat, paraneoplastic pemphigus. The problem is that, unlike pemphigus vulgaris, in which there are very specific antibodies present, in the paraneoplastic pemphigus the array, the variety of antibodies produced is much greater. So it's harder to eradicate the cells that are responsible for that particular process. But yes, it has been used and the patient that was submitted actually describes in detail the the clinical course of that patient, which was complicated by very low platelet count and very low white count. You know, the question that I would have is, what was the primary malignancy or what was the treatment for the primary malignancy? Because the profound depletion of white cells and platelets could have been caused by things other than Rituximab. But again, I don't know enough about this case to offer opinion. Let's see, oh, that's an interesting one, not the others aren't, but I'm sort of always fascinated as to how various physicians have a different clinical practices. So the question is, "I see that FDA approved two infusions two weeks apart, but my doctor has recommended that I take with Rituxan every four weeks." And that's actually a very interesting and sort of historically based issue. When Rituximab was first used for malignancies, the recommendation was that one uses 375 milligrams per meters square of body surface on four consecutive weeks. And that practice still is ongoing in some centers. There was actually a conference that we organize here at Genentech and invited a number of dermatologists to participate and we ask them which dose they prefer and how they feel about it. And interestingly, some of them

feel that in their population, their preference is to use the four weekly dose, given either six months or every 12 months depending on the severity of the disease. Also, which I thought was quite interesting depending on the infusion center, if the patient is referred to a rheumatology infusion center or the freestanding infusion center, that's usually the dose that I mentioned to you, which is 1,000 milligrams two weeks apart. If one is referred to the oncology centers and they are usually using the four, once a week for consecutive weeks infusion. That really depends where one goes and what the protocol and that center is. But the caller, the person who submitted this question says, well, would this be a problem with my insurance? And yes, it may be. I think that's where you actually may be well assisted by our patient assistance program because they can help you kind of ease this out. Again, I would encourage you to utilize this service because they're quite knowledgeable how to maneuver through insurance issues and coverage issues. I hope I answered that question.

Becky: I think you did good. Thank you.

Dr. Michalska: Right, I talked about vaccines because there was a question, I talked about live vaccines, yes. “Is there any reason to have any type of blood work before you start Rituximab?” Yes, we usually recommend, we meaning physicians who prescribe it, that one gets a baseline CBC, complete blood count to make sure that you’re not anemic, that you’re not thrombocytopenic, that all these cell lines are in place. So that's usually done as well as the sort of basic metabolic panel to make sure that the kidney function, liver function, everything is okay. And we usually do this as baselines, so he doesn't mean that we anticipate something to be abnormal, but that's just to make sure that we know what it is before starting the therapy.

Becky: Margaret?

Dr. Michalska: Yes, go ahead please. Cause I'm looking if there's something I left untouched here, but go on please.

Becky: There was a question about asking, is there any update on the use of Rituxan in children? Ben is saying that he has a nine year old, approaching two years since their first infusion. And just wondering if there's been an update or any research on Rituxan being used in children.

Dr. Michalska: To my knowledge, there are not any currently ongoing trials in autoimmune skin disease and Rituximab of childhood. Rituximab has been used in a pediatric patients with a completely different condition called vasculitis. So please stay tuned because those data may be available in pediatric patients. And again, the issue isn't so much that it's not effective, the issue is we need to know that it's safe to use in children. So I can't offer any further information because it's not yet available, to my knowledge it shouldn't be before this year is over.

Becky: Great. Thank you.

Dr. Michalska: Any other questions? I've had four pages of questions I printed out, so I hope I addressed most of them. But there is a question here that I would like to address. It is, “Is there any progress to

approve Rituximab for other forms of Pemphigus?" So, a brief response is, no. But if you, if you're familiar with professor Joly's trial, he included some patients in his trial that were diagnosed with pemphigus foliaceus. No, it has not been approved by the FDA because they were just 17 patients in that cohort with pemphigus foliaceus. But, you know, I did a literature search last night just to look what people are using for different forms of pemphigus, you know, there were many, many reports on Rituximab in various other forms of pemphigus. So, even though it's not approved in the U.S. it's again a decision of a dermatologist who makes sure that the patient gets the best treatment for the condition at the particular point in time. And for all of them for foliaceus, for vegetans, and for paraneoplastic pemphigus there are reports of Rituximab being used. Any other questions, Becky, that you got?

Becky: Sure. There have been a few questions that have came in that asked about the long term effects of Rituximab, either from multiple series of infusions. I know like with some medications can increase the risk of lymphoma and different other conditions. Is there any research being done that you know to discuss the long term effects of Rituxan?

Dr. Michalska: Yes. I mean, first of all, the company is absolutely diligent about collecting safety information. And I'm just not saying this as a kind of a boasting aspect here. We are obligated to collect this information diligently for all medicines that Genentech or Roche has. So you will recall that Rituximab was first approved in '97. It is a pretty long track record for a medication on the market. And again, it was approved to treat lymphoid malignancies, so lymphomas, leukemias, et cetera. There hasn't been any signal of adverse events or untoward occurrences with long term exposure. So, you know, '97, it's over 20 years now that the drug has been on the market and these reports are compiled every 12 months to report the incidences of untoward occurrences of Rituximab. So I'm pleased to say that to date we have no such information, which makes one content. Right? Parenthetically, let me mention a patient of mine from my Chicago days who started Rituximab for rheumatoid arthritis in 2006, which was when the drug was first approved. To this day, he is on it. So you know the frequency of infusions may change because if the condition is better controlled patients tend to try to persuade the physician that there'll be okay, even though the infusions are less frequent, which, you know, it's negotiable. But no, there have been no additional events or the number of incidences for instance of the, PML progressive multifocal leukoencephalopathy have not gone up either. So they are steady numbers steady, there hasn't been any significant increase of those.

Becky: So the longer your on,I just want to clarify just for my own knowledge. The longer that you're on Rituxan, so it doesn't increase your risk of PML, like your risk remains pretty consistent no matter how long you're on it then.
Dr. Michalska: That's correct. There hasn't been any information to support the risk goes up with the duration of treatment.

Becky: Great. Thank you. There was a question that came in too, I know that Rituximab has been approved for moderate to severe pemphigus vulgaris. And this question I think is kind of a good one that kind of addresses like what that really means. This patient says that they were on prednisone and then they got down to five milligrams of Prednisone, like about 95% of the ulcers were gone and then her

allergies have flared it up again. Her voice has gone, she has a lot of oral lesions and she's wondering if she would be considered a moderate or severe case or would this be mild or how is that measured?

Dr. Michalska: There is something called PDAI score, which is the pemphigus disease activity score. Which is usually using clinical trials. My suggestion to the patient is to see a dermatologist familiar with treatment of pemphigus. If your oral lesions are such that they interfere with your ability to eat or drink or speak. Again, as a former clinician, I would consider it at least moderate, if not severe. So I would like to encourage you to be referred or to find, possibly through the help of IPPF a dermatologist who is familiar with Pemphigus in your geographic location because this needs to be addressed promptly.

Becky: Great. Thank you. Another question and you might have already said it and I could've missed it too. You had talked about a test about a baseline test, before the first infusion to measure the B cells. What is the name of that test that would be run?

Dr. Michalska: It's called just complete blood count with differential. The differential part is what gives one the breakdown for different populations of white cells. So you have the B cells, the t cells, the monocytes, the eosinophils and everything else. The percentages are given. And as I said, very often the levels of B cells I use to judge both the efficiency with which Rituximab works and the time when the physician chooses to reinfuse the patients as the number increase and thus the risk of the consequences of the, you know, nasty work that these cells can do, i.e. producing antibodies goes up. So, that is a complete blood count with differential, one of the routine tests that can be done everywhere.

Becky: Great. Thank you. There was another question, in your initial presentation with the slides you were talking about, there was a thing about muscle and joint pain. Does that typically happen right away? And there's a few patients that have sent in questions that said that they've had a delayed muscle and joint aches about three weeks out. Is that something that's common?

Dr. Michalska: The delayed one is less common, but those has been reported. About 2% of patients who received Rituximab infusion across all indications will report some degree of musculoskeletal pain. Again, the important distinction to make is if it's sort of reasonably manageable and can be controlled with mild analgesics. It needs to be made known to the prescribing physician, but it's nothing to be particularly concerned about and it does happen, we acknowledge it. It's unfortunate, but it doesn't have any serious consequences. This is in contradistinction to Rituximab induced serum sickness in which the joint pain and more importantly, joint swelling is significant and that is often associated with fever or skin rash and that is a completely different entity altogether. So that is a medical emergency and needs to be brought to the attention of your doctor right away.

Becky: Margaret, and if they're experiencing these side effects that are that far out, should they, they obviously need to contact their physician first, but would Genentech like to be contacted as well or is that not necessary? What would it be reported by the doctor?

Dr. Michalska: Well, either way we encourage everybody, just to tell you how obsessive compulsive we are about this. If I'm sitting in a restaurant and at the next table there was a discussion that somebody

on Rituximab developed joint pain, I am obligated to report it through our reporting system. So we encourage you to discuss it with your doctor because you may need the assistance right there and then and the appropriate behavior is required. And either you the patient or the doctor need to report this to us, within 24 hours if possible because we want to know.

Becky: Great. That's a true commitment and we as the patient community definitely appreciate that. Well Dr. Michalska that was a very, very quick hour and I apologize to some who, there's still a few questions that didn't get answered and I do apologize for that. But if you would like to email me, Becky, becky@pemphigus.org., I will try and be sure to help get some of your questions answered. And Dr. Michalska I want to thank you for being on the call with us today. This was an extraordinarily, extremely educational, having you on our call and I sincerely appreciate it and I want to give everybody listening a big thank you for joining us as well. A few parting announcements.

Dr. Michalska: May I say my thank yous. Primarily to the patients, thank you for engagement. We appreciate and respect you very much. Thank you to the IPPF for doing a great job. It was a pleasure to be invited.

Becky: Great. Thank you. Just a few parting announcements. The IPPF awareness program has launched a new awareness campaign that stresses the importance of a biopsy when diagnosing pemphigus and pemphigoid to help accelerate diagnostic times. Your tax deductible donation will support our biopsy saves lives campaign that will educate and encourage dental professionals to consider a biopsy sooner in order to diagnose patients faster. We're counting on you to make a difference in the lives of Pemphigus and pemphigoid patients and their families by helping us accelerate diagnostic times. Donate today and help us reach our goal of $15,000. If you haven't heard the IPPF has a natural history study, if you haven't registered for the IPPF natural history study, we encourage you to do so. The IPPF natural history studies is a patient registry sponsored by the National Organization for Rare Disorders (NORD) and the U.S. Food and Drug Administration, the FDA.
You can register today at www.pemphigus.iamrare.org. This online data system collects, stores, and retrieves patient data for analysis in research studies. The more data we can collect, the better the information we can give to researchers, the sooner they can find better treatments, earlier diagnosis, and one day – **A CURE**!

The IPPF is also pleased to announce the date and place of the 2019 IPPF Annual Patient Education Conference. The 2019 conference will take place in Philadelphia from October 11-13th. This is our 25th year as an organization and we hope that you will join us this year for an educational and fun weekend in the city of brotherly love! More registration details to come in the next few months. Mark your calendars, We hope to see you there!

Our next Patient Education Call will be Thursday, June 27th from 8:00 - 9:00 am PST with Dr. Joel Laudenbach, Doctor of Dental Medicine. Dr. Laudenbach practices Oral Medicine at the Carolinas Center

for Oral Health, within the Atrium Health hospital system in Charlotte, North Carolina, this call will discuss treatment of oral pemphigus and pemphigoid. Registration details for the June call will be on our website.

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

This call recording will be posted on our website and sent out with the survey following this call. A great big thank you to Genentech and Cellgene for helping to make today's call possible. Thank you again Dr. Michalska, we really appreciate you being on the call.

Dr. Michalska: My pleasure, good bye.

Becky: Thank you, good bye.