

February 9, 2022 Patient Education Webinar- An Overview of AstraZeneca FJORD Trial for Bullous Pemphigoid

Amethyst: Welcome, everyone. Thank you for joining us for our Patient Education webinar to discuss an overview of AstraZeneca, Fjord Trial for Bullous Pemphigoid. This call is now being recorded. I'd like to thank you all for being on the call with us and to our sponsors, Genentech, argex, and Cabaletta Bio for making today's call possible. "Information is a key factor in treating and living with any condition. However, every patient's situation is unique. The IPPF reminds you that any information found on the internet or during presentations should be discussed with your own healthcare team and doctor to determine if it applies to your specific situation." Before we begin, I'd like to take a quick poll to see how many of you on the call with us today have participated in a clinical trial? You'll see that pop up on your screen right now, and while you're answering that, I'd like to introduce you to our speakers for today's webinar.

Amethyst: Dr. Fairley is the 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 130 articles and book chapters. Dr. Fairley is a diplomate of the American Board of Dermatology and a member of the American Academy of Dermatology and 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 completed an NIH-sponsored research fellowship in cell physiology at the University of Michigan, Ann Arbor.

Skylar Sever is a Registered Nurse and Clinical Trial Educator at IQVIA. Skylar has a deep passion for clinical research, particularly for rare diseases. She is currently supporting the AstraZeneca Fjord study, helping to build trial awareness and support to the study doctors participating in this trial. Her background includes Bachelor's degrees in both biochemistry and nursing, Parkinson's and Huntington's Disease research, critical care nursing and over 7 years combined of clinical research coordination, project management and education experience. Skylar is committed to supporting new and better treatments for rare diseases through her work as a Clinical Trial Educator. She is focused on connecting with patient and provider communities to engage in a discussion of clinical trial participation and what it means for them. Thank you both for being on the

call. I'd like to share the result of today's poll. So it looks like a good majority of you have not participated in a clinical trial. So thank you for joining us today, to learn a little bit more about today's clinical trial. Before we begin, I would like to go over a few housekeeping slides... (Reviews Housekeeping slides).

Amethyst: Now, it is my pleasure to introduce Dr. Fairly and Skylar to discuss the AstraZeneca, FJORD trial for bullous Pemphigoid. Thank you both for being on the call with us today, and I will turn it over to you guys.

Skylar: Thank you so much. I'm so glad to see that many of you have not participated in a clinical trial because I hope this is an opportunity to learn more about what clinical trial participation in general means as well as information about this particular trial. So, you can go to the next slide. As part of our presentation today, I'd like to give a quick overview of clinical research and why it's so important. Talk about bullous pemphigoid and why this study is pertaining to bullous pemphigoid and what the study drug, Benralizumab is, the type of drug, it is a monoclonal antibody and discuss what that means. I'll give an overview of the study, talk briefly about some of the criteria of who can take part in the study, give an overview of the periods of the study, the study medication, and some of the assessment's required as part of this study. I'll also take some time to talk about the responsibilities and rights. So really, what does it mean to participate in a clinical trial and if you're considering participation what you should think about and consider prior to participating, when making that decision. So we can go to the next slide.

Skylar: So what is clinical research? Clinical research is the division of health science that looks at health outcomes in humans. So as part of clinical research, we have clinical research studies or clinical trials and they're a somewhat interchangeable term. But clinical research studies are designed to answer important questions about potential new medications, or treatments, or devices. So, in this situation, in this case, we're looking at a potential new medication. So some of the questions that we ask in clinical research studies are: Is this new treatment, is it safe? Does it work as it's intended? How effective is it in comparison to whatever is usually given for that disease? Or how effective is it in comparison to not receiving that treatment? So looking to kind of get some of that information to determine and answer these questions. More and more in clinical research, we ask additional questions about how this impacts the quality of life? Asking some of those more open-ended questions about the experiences that patients are having with the potential use of this treatment and also how it affects their health care? Are they having to go to the doctor less or

more or admission to the hospital? So, we see research asking more and more about the patient experience in the healthcare needs of patients. To sum it up, we really wouldn't have any new treatment options without clinical research studies and to further that, we would not have new treatments without clinical research participants. So people volunteering to enroll in these clinical trials, and understand more about potential new medications or treatments for diseases. You can go to the next slide.

Skylar: So why are we studying bullous pemphigoid in this study? I'm going to go over a few highlights of bullous pemphigoid. I'm sure many of you are familiar with these, but I think it's important to point some of these out to understand why we really do need new treatments for BP. I'll refer to it sometimes as BP. So bullous pemphigoid, we know it's a rare skin disease that causes damage to the skin layers to where the epidermal and dermal skin layers meet and that results in blistering, itching, redness, all the symptoms that we see in bullous pemphigoid. We see it most commonly in our older population and we see that it can come back even with treatment. We see that it can kind of come and go for 2 to 5 years and can kind of linger and have a lot of relapse where it's coming and going. The frontline treatments, the treatments that we give standardly for BP are steroids. So those topical steroids, the creams that are prescribed then the oral corticosteroids, the pills steroids that are taken by mouth. We know that those steroids, especially the ones that are taken by mouth, the oral corticosteroids have quite a bit of side effects, especially when we're considering that we have an older population and that they may have to kind of go on the steroids and then come off. Other treatments that are prescribed for bullous pemphigoid are immunosuppressants, medicines that calm down the body's immune system. There's not a lot of evidence how well these work in patients with BP. There's a lot of variability from patient to patient. The side effects, we have significant side effects with the use of immunosuppressants in patients with BP. This kind of shows us that we really do need new medication and new treatment options that could reduce the use of those oral corticosteroids, the pill steroids, and those immunosuppressants to help reduce all those side effects. So that is why AstraZeneca is considering this drug in patients with bullous pemphigoid. Next slide.

Skylar: So, let's talk about the study drug. We call the medicine that's being tested, the study drug in clinical research. Benralizumab is a monoclonal antibody and I'll explain what that means in the next slide. But it's currently approved as a treatment for patients with asthma, and it's approved by the Food and Drug Administration in the United States, it's approved in the European Union, Japan, and other countries. It's been through quite a bit of research already so we have a pretty good general safety profile

and we know that it's generally safe in patients. We also found that it's effective in reducing eosinophils. Eosinophils are a type of white blood cell that we see in patients with bullous pemphigoid. That's kind of an important point and I'll touch on that a lot throughout this, really why this study is being conducted and what it aims to do is to find out if Benralizumab can reduce the symptoms of bullous pemphigoid? So the itching, blister formation, et cetera, and find out how safe the study drug is in patients with bullous pemphigoid? I want to clarify that Benralizumab is not currently approved by the FDA for use in the general public for bullous pemphigoid so we consider it an investigational drug or investigational product. So it's under investigation and if you can advance to the next slide.

Skylar: I talked about Benralizumab being a monoclonal antibody. Some of you may feel that that's a familiar term because we've heard it a lot in the news about COVID-19 because monoclonal antibodies have been authorized for use to help prevent or treat infections with COVID-19. We see this more and more as potential treatment in various diseases. To understand what a monoclonal antibody is, let's first consider what an antibody is. Antibodies are part of our body's natural defense system. If we're introduced to a virus or bacteria or something infecting us, our body says that's not supposed to be here, that's something foreign and it makes a little protein that sticks to that pathogen or that virus whatever it may be, it sticks to it and it says to the rest of the cells and tells our bodies, this isn't supposed to be here. It signals other cells to come in and destroy whatever that pathogen or the virus. It uses our body's defense system to come and destroy those foreign bodies. So drug developers take this concept in looking at new treatments by saying, especially in an autoimmune disease where our bodies are attacking themselves and we have inflammation as a result of that and that inflammation is causing some symptoms. In the case of bullous pemphigoid where there is blistering and itching The concept we have in a monoclonal antibodies, if we introduce an artificial antibody into the body, you can design it to find specific cells that we could potentially reduce symptoms by eliminating them. We can introduce artificial antibodies that target specific cells, in this case eosinophils, that white blood cell that we see that correlates to symptoms of bullous pemphigoid and we can use the body's natural immune system to come and remove those extra cells. Just to highlight and to back up here, because I know I'm kind of diving in. The thought is to use a monoclonal antibody, Benralizumab, we know that it binds to and uses the body's natural defense system to deplete or reduce eosinophils in our tissue. So if we also see a high correlation of eosinophils with symptoms of bullous pemphigoid, itching, blistering, et cetera, by using Benralizumab, hope is that we can reduce the symptoms. Dr. Fairley feel free to jump in if you want to add any elucidation to my analogies here.

Dr. Fairley, I think you've got it. The Benralizumab's goal is to get rid of those increased numbers of eosinophils that we see in the skin of patients with bullous pemphigoid.

Skylar: All right, thank you. I think we can go to the next slide now. Now I'm going to talk about specifically what this Fjord trial is. Just so you know, companies like AstraZeneca and other pharmaceutical companies, they like to give nicknames to clinical trials. It just makes it easier than having to say a bunch of numbers and letters. So, they've nicknamed this trial, The Fjord Study and so this study is going to take place in multiple countries and it will include about 120 adults. We call this trial a placebo controlled trial. That means this study will use a placebo compared to Benralizumab. A placebo looks just like a study medication or, you've heard the term sugar pill, in this case it's an injection so it will look just like the Benralizumab injection but it doesn't contain any active medicine, it's kind of like a dummy drug. Participants that enroll in this study will have an equal chance of receiving either the Benralizumab or that placebo, the fake Benralizumab that doesn't have any active medicine. The total duration of the participation is at least 11 months, and I say the least because there is an optional extension period where all participants in the extension portion would receive the Benralizumab. For participants that complete this study, the initial part, where they may be receiving Benralizumab or they may be receiving placebo could carry on into another part of the study where all participants, despite whether they were receiving placebo the fake medicine, the look alike, all participants would receive the Benralizumab on an ongoing basis. There's also an optional interview substudy in this clinical trial. This would be a series of interviews to understand more about patient experience, to answer some of those questions on how could this potentially impact a patient's life? How does it impact their need for health care? What are their experiences? How does it impact ability to work or spend time with family, or do the day-to-day things? So really, looking to understand Benralizumab compared to the placebo and how that could impact a patient's life day to day.

Dr. Fairley: You better tell them quickly Skylar, that they are getting something besides the placebo though. I can see them out there thinking, I'm not going to keep itching for six months.

Skylar: Yes, we'll get to that here in the next 1 or 2 slides. If you can advance one slide, please.

Skylar: So I'll quickly go over some of the criteria for participation. So participants have to be adults, must have active signs and symptoms of BP, active irritation, blistering itching, et cetera. There needs to be a confirmed diagnosis or willing to have a confirmed diagnosis with a skin biopsy. Patients that are considering this trial have to have a certain level of severity. We use the Bullous Pemphigoid Disease Area Index Activity Score, this is an assessment that the study doctor would do when considering eligibility at certain visits at the study. There would have to be a certain level of severity and as Dr. Fairley mentioned, patients on placebo will not be going without anything. There are oral corticosteroids that are prescribed as part of this clinical trial so patients would have to be candidates to take those corticosteroids. Next slide please.

Skylar: Some reasons that participants could not take part in this trial would be having a form of bullous pemphigoid other than the classic predominantly skin bullous pemphigoid. So it would have to be classic predominantly cutaneous versus mucosal bullous pemphigoid. There can't be any other major health condition that could make it not safe for an individual to enroll or that could impair their ability to complete assessments on a little handheld phone. Individuals could not be HIV positive or have a severe allergic reaction to another monoclonal antibody. Sometimes we refer to those as biologics so that's what you see there in the slides. No history of a severe allergic reaction to another monoclonal antibody or vaccine, and no planned major surgical procedures that are anticipated during the course of this study.

Skylar: Let's talk about the different periods in this slide. There's four periods, the first is a screening period and you'll see a screening period in pretty much every clinical trial. This is the portion of the study where you're being evaluated to see if you could potentially participate in a trial. A number of tests and assessments are conducted during this portion of the study and we make it pretty short in this study period so that if participants are just having blisters, they can start those oral corticosteroids and get some treatment right away. Then there's the treatment period. If an individual is found to be interested, they agree to take part, they're found to qualify, they would enter into the treatment period. There's 36 weeks in the treatment period for this trial, about 12 visits to the study center or the clinic where the study is going on. During this period, any participants would take the steady medication, either the Benralizumab or the placebo, receiving either one of those two, and that would be by an injection every four weeks and then also taking the oral corticosteroids. Starting on a treatment regimen of those and then those would be reduced over the course of that treatment period to hopefully being able to come off completely. After the treatment period, those participants would be offered to go into the extension period, and that's where

everybody's getting the Benralizumab. At that point a lot of the criteria lifts and it's really just administration of the Benralizumab every four weeks to all participants that are enrolled in that portion of the study. There is also a 12 week follow-up period, so there would just need to be a visit 12 weeks after receiving the last dose of medication, whether it be placebo or Benralizumab. Alright, you can advance to the next slide please.

Skylar: If we have an individual that agrees to take part, they qualify to take part, they would be assigned into 1 of 2 groups. This is completely at random because this is a placebo controlled and patients would be randomly assigned into either receiving Benralizumab or the placebo. For this trial, it's a 1 to 1 ratio, meaning that there would be a 50% chance that a patient would either receive the Benralizumab or the placebo. It's kind of, by chance, it's like rolling the dice of who's going to get one. That's important to understand but in addition to that, this is a double blind study. What that means is that neither the participants nor the study team, so the study doctor and the study staff and a lot of the clinical team at IQVIA where I work, don't know who's receiving which treatment. So, whether they're receiving the placebo or the Benralizumab and having that blinded component is really important to getting objective information. So, if a participant knows that they're receiving Benralizumab, our mind is very powerful, and they could report having less symptoms thinking they're receiving treatment. Versus a person who's receiving placebo, they could think, oh I'm not improving because I'm not receiving this study medication. So, it's important to really make the information that is collected as objective as possible and that's why we do a double blind study. I will add though, should there be any safety concerns, it's very easy to quote, unquote, break the blind. So, if there's any safety concerns with a participant and we need to find out if they received either the Benralizumab or placebo with a quick phone call, that study doctor can find out who has received what. And like I said, this is an injection, it's a subcutaneous injection under the skin and that's for both the placebo and the Benralizumab. To highlight again, all participants during the treatment period will be prescribed the oral corticosteroids with the goal to taper off once the symptoms are resolved that they are experiencing.

Skylar: So here's just a quick overview of some of the assessments that are part of the participation in this clinical trial. We have some general questions about medications and medical history and it is really important to understand about the bigger picture of a person's health in general, a physical exam and those assessments on the severity of their bullous pemphigoid symptoms so doing a skin assessment, height and weight, looking at vital signs and ECG, looking at heart rate and rhythm. Pregnancy tests would

be required for all women who are able to have children. There are also blood and urine tests that would be collected as part of participating in the trial as well as skin biopsies and taking pictures of different portions of the skin where there's blistering, et cetera. Then completion of assessments on how you're feeling such as itch and things like that on a handheld device that would be taken home.

Skylar: So that's kind of the quick overview of clinical research, clinical trials. Like I've shared in my biography, I'm very passionate about educating people about clinical research. I just want to touch on a couple points about what are some other things to consider if you or someone you know is considering participating in a trial. So what are some of the expectations or the things that you'd be asked to commit to if you are considering a trial? That's to understand that safety is the most important thing in clinical trials. So protecting an individual's safety or participant safety is the most important thing. The way that a study doctor can do that and the way that companies like Astra Zeneca can ensure safety of those participants is to have a lot of measure assessments built into those study visits such as looking at blood work, looking at vital signs. So, it's really important if you're considering a clinical trial, to feel like you can attend all the scheduled study visits. It's also really important to be in communication with the study team and the study doctor. Sharing any changes in your health, changes in any medications, any side effects, or any new experiences that you're having because all of that information is really important to understand about this medication and to protect everyone's health. Again, if you are participating and you need to change a study visit, definitely keep in touch with the study team and the study doctor about that.

Skylar: While there are expectations, there are rights of participants that I think need to always be made very clear, and will always be covered with an individual before they agree to take part in a study. But participating in any clinical trial is always voluntary. So, for whatever reason, a participant can withdraw or stop taking part in that clinical trial. I think it's very important to formulate questions if you're considering a trial, or someone you know, to talk with their providers, talk with physicians that they trust and know, talk with their friends and family, and formulate some questions so that if you do agree to take part in trial, you can get all the information you need to make a really confident decision for yourself. It's important to understand that current and future medical care is not affected by participation in clinical trials. If you were to agree to participate or are considering it, all the risks and benefits of a clinical trial are discussed prior to agreeing to take part. Then also all the information that is collected, so anything that could identify you is removed. So when all this information is sent to Astra Zeneca

for this trial, all that information is de-identified. All that personal information does not go to Astra Zeneca. That's kept only with the study doctor. Just so everyone is aware, if you haven't participated, that information is all protected. I don't know if there is anything you want to add, Dr. Fairley?

Dr. Fairley: Yeah, a couple of things. First of all, when I deal with IPPF members, I find there's some of the best informed patients around, so probably you all know this but in the 30 years I've been studying the blistering diseases, the vast majority of that time the treatment's never changed. We just suppressed the immune system until the immune system was so suppressed it couldn't attack the skin anymore but there are lots and lots of side effects of that. I think in the last five years, it's become really exciting that there are some things being developed specifically for these disorders and also, like the study here, the Fjord Study, repurpose the medicines we already have that we know a fair bit about that because of its actions, how it works, we think could work in pemphigoid. To me, as a physician, trying to help patients, this is really an exciting time. The other thing is we talk about standard of care, which are things like steroids and other medications, none of those have been through the FDA process. None of them are actually approved for use. That's quite different. Being approved for use means there's enough data that they're safe and they're effective, that the FDA has put a stamp of approval on them. And why do you care about that as a patient? Number one, it's a certain amount of information that you know they must have to allow this to happen. But the other thing is, that helps us greatly when we're trying to get your insurance company to cover the medication for you. Right now a lot of times, my patients will tell you, I'm always saying, we're gonna go after your insurance, we're going to try to make them cover this for you. But when it's not an approved medication, sometimes it's very hard to get the medication we might think is the best for you and the one you'd most like to take. So when you get some of these medications over that hump of FDA approval, it becomes a lot easier for patients to access the ones they need. So I think those are some of the reasons, if I were a patient, I would want to help these things move forward because if they work well, it will be a benefit to all the patients as far as access and assurance of safety and efficacy.

Skylar: Yes, thank you. Then that is a perfect caveat into, I have a 1-800 or a toll free here, 1 (855) 233-1701. This number goes to me, I'm Skylar, the clinical trial educator supporting this study. If you have questions about this trial and you're interested in getting in touch with one of the study doctors and to learn more about it, please give me a call here and I will get you in touch with Dr. Fairley who is one of our investigators on this trial, or one of our study doctors. We may have a trial center near you that is

participating. So please give me a call, and I'm happy to get you in touch with one of those centers or clinics. Additionally, there's clinicaltrials.gov, you can search for this study under the condition of bullous pemphigoid and other terms Fjord.

[Clinicaltrials.gov](https://clinicaltrials.gov) is a website that houses all the clinical trials going on, the ones in the past, present and future. That's a really great resource to understand about different trials for different conditions and diseases. So I think we're ready to open up for some questions.

Amethyst: Great. Thank you for that great overview. We've had a lot of questions come into the question box and a few that were submitted beforehand, so we're going to jump on into those. I'm gonna just pull that slide back up so everyone can write that number down. Fred asks, has this drug been trialed in older adults? He is 81 years old.

Dr. Fairley: I think that's one of the things I'm really thrilled about with the newer studies, they do include patients up to age 90. This is going to be representative of the group that is most frequently plagued with bullous pemphigoid. The average age of onset is 65 to 68 and the older you get the higher your risk for it. So this study will allow us to look at older patients as well.

Amethyst: Great. Thank you. I know you discussed that to participate in the trial one has to travel or at least be seen 12 times at the clinical trial site.

Skylar: Yes, that's correct. During the treatment period, there's 12 visits. Then if someone was to continue into the extension period there would be additional visits. There in terms of travel, if there is some travel support that's needed, we're definitely able to help support that.

Amethyst: Is that in terms of housing such as hotels and or flights?

Skylar: Yeah, it's kind of on a case by case basis and it's dependent upon the different center or the site where they would be participating. It's definitely a possibility. I think there could be some situations where flying across the continent might not be in the best interests of that participant. I can say for sure, that it's definitely something we can

accommodate, and it would be meals, travel, planes, if necessary, depending on the situation, hotel, et cetera, and mileage.

Amethyst: Great, Thank you. What if the patient isn't able to travel? Are they able to have the option to do any remote or telehealth appointments?

Skylar: That's a great question. That is something AstraZeneca is working on right now. So as of now, we don't have that in place but it is something that could be coming in the near future.

Amethyst: Great. Thank you. Once a patient contacts you or contacts a site, how long until they're actually enrolled in the trial, as long as they meet all the criteria? What's the timeline for that?

Dr. Fairley: Well, it can be quite rapid if they've already had a biopsy and have supporting documentation that they have bullous pemphigoid, that would meet the criteria for the study. It also depends a little bit on whether they're currently on medications. Some of the medications require a wash out period. So, it's a little variable, but if you're a brand new patient or your patient who's been off medication and suddenly flares, you could go into it I think maybe as quickly as four days.

Skylar: Yeah, it could actually be the same day if you have a previous biopsy. It's set up so that a participant could be found eligible the same day but in reality, it could be more like four days.

Amethyst: Okay, great. So, if they do have a previous confirmed diagnosis with a biopsy, they will not need to receive another one through you guys?

Skylar: Actually, we would, part of the study is a series of biopsies. So even if you have that first confirmed diagnosis biopsy, it would need to be validated in terms of data collection and analysis. So, there would need to be additional biopsies, even if you've had a single biopsy.

Dr. Fairley: I think the single biopsy, the initial biopsy I was speaking about, was confirming that you are a bullous pemphigoid patient and you don't have one of these weird variants that wouldn't be eligible.

Amethyst: Great. Thank you. Speaking of variants, Gaynel messaged earlier, she has an involvement in her trachea. Would that disqualify her?

Dr. Fairley: If she has involvement in her trachea, she almost certainly has mucous membrane pemphigoid and that sort of internal involvement is not part of this trial at this point.

Amethyst: Great. Thank you. I know you spoke about the different wash out periods, what would be the wash out period for something like Rituximab or IVIg?

Dr. Fairley: Rituximab I believe is 12 months but I know there was just a modification so Skylar could answer that.

Skylar: Yeah so with the updates that we've had, Rituximab is a monoclonal antibody so it would be four months and then IVIg is I believe 30 days.

Amethyst: Are there any other medications that are definitely not allowed for the patient to be taking while they're enrolled in this trial?

Dr. Fairley: Other immunosuppressants that are used to treat bullous pemphigoid aren't allowed in the trial. So if you had rheumatoid arthritis and they had you on medication for that, that's an immunosuppressant, you probably wouldn't be eligible.

Amethyst: What side effects of the investigational medication?

Dr. Fairley: Like any other medication, you can have an allergic reaction to it, any medicine can give you that. Some people have infusion reactions when they first get

the shot, like a local reaction. Other things, eosinophils, your body uses them to fight parasitic infections. So I think theoretically people are wondering, could it make you more prone to those? Here in the U.S. we don't worry about that as much as in some portions of the world where parasites are very frequent. Here, they're very infrequent so I don't think that has been a significant issue with our patients who take this medication. Skylar did I miss any?

Skylar: This drug is marketed and approved for asthma. What we see on the label for Benralizumab in prescription for asthma is the common side effects being headache and sore throat. And, again, like Dr. Fairley said any medication can give you a potential severe allergic reaction. From the previous research AstraZeneca has done on it, it's fairly safe. There were some reports of some things like sinusitis, sinus infection, increased asthma that were found in the previous studies but all of those would be reviewed in detail. I also wanted to comment, any potential medications that that wouldn't be allowed on the study would be reviewed in detail with you if you're considering the study.

Dr. Fairley: I think also, the thing to point out is that all the data that's out there is pretty much in asthmatics who may be quite different from pemphigoid patients. That's one reason we do the study. But worsening asthma, unless you're a preexisting asthmatic is probably the big one.

Amethyst: Great, thank you. Somebody asked, what is the standard dosage of the steroids that you would receive while you're either in the placebo arm? And did you say you also would get the steroids, if you are in the arm that you received the drug in?

Dr. Fairley: Yes, so basically what's happening is you've got two groups of folks, some are getting the Benralizumab, some are getting placebo and everybody is getting a weight based dosing of steroids. Then the goal is to taper those steroids down and to see, are the folks who get placebo unable to do that taper as well as the people who get the Benralizumab? And are the Benralizumab folks going to be able to totally get off steroids versus the placebo? So that's how it's designed, but it's a weight based dosing of the steroids. If you're bigger, you'll get more, you're smaller, you'll get less.

Skylar: And there's a lot of discretion with the study doctor, so for instance if Dr. Fairley, she could adjust it as needed for patient to patient.

Dr. Fairley: And the goal is to keep people comfortable and without the blisters. No matter which arm you're in, that's our goal. And the way we figure out if the drug is working, is to look and see how much steroid it's taking in those groups. Hopefully we find that the Benralizumab takes a lot less steroids than the placebo. But again, that's why we're doing the trial, is to see if that's true.

Amethyst: Great, thank you. Harry wanted to know, in regards to a current treatment that a patient is on, is there coordination with the study site and the person's current treatments for any other condition, and do the physicians help advise on that?

Dr. Fairley: Absolutely. The physician you see when you are considering enrollment, they wouldn't terminate any of your medications for other disorders, the only thing they would probably talk to you about is wash out of your pemphigoid medications. Other than that, I'm not going to stop somebody's cardiac medicines if they need them, that won't happen.

Amethyst: Great, thank you. Kristin said that her mother is a little bit older and it looks like she would be more interested if there was a tablet. Is there future thoughts about maybe using this, or having this as a tablet form as well? Or, just the injection?

Dr. Fairley: I think everybody would prefer a tablet there. It's just not available at this point. Monoclonal antibodies, if you try to take them by mouth, all the acids and things in your stomach kind of chew them up and not enough of them get in. That's why a lot of the biologics are injectable. Though, once things come to market a lot of them become what we call auto injectors. I think that was really forged with psoriasis research. They're medications that come in a syringe, and you cock them and then they release and it just injects it. Those sorts of things maybe in the future but right now, it has to be given in an injectable form, unless you're aware Skylar that there's a pill on in the future?

Skylar: No, but just for the purpose of this trial, if the concern is having to do self-injections, the study staff actually will be doing the injections unless we move towards a remote home health type of situation. But for the sake of the study, if the concern is injecting oneself, that would be done by the study staff.

Amethyst: That's good to know, because I don't know if I could muster the courage to self-inject.

Dr. Fairley: I'm always amazed because when all the medicines started to come out for psoriasis that had to be injected. I thought these are going nowhere, nobody's going to want to do this but I find patients are just fine. They're pretty bold. Once you teach them how to do it, most of them can do it just fine but as Skyler said, that's not a worry right now for this study.

Amethyst: Great, thank you. So I was reading a little bit about the clinical trial on clinicaltrials.gov prior to the webinar, learning more and I saw that for patients to be in the trial they have to have a BPDAI activity score of 24 or more. What does that mean in terms of severity, so that a patient at home kind of understands how severe their disease needs to be?

Dr. Fairley: With the BPDAI you basically look at someone's skin and you figure out how extensive the involvement is, both of the itchy plaques and blisters. The physician goes body part by body part and documents the involvement in those areas. It has a numeric that goes with each body part, and then it adds up to a number at the bottom. Now, 24 is probably a mild to moderate amount of activity, but if you have 2 small patches, that probably isn't going to make it to 24. But you don't have to be horribly bad either to qualify for the study.

Amethyst: Great, thank you. Somebody asked, what if I have a flare that I can't get under control during the trial, whether you're in either arm? Are there built-in rescue protocols for a flare?

Dr. Fairley: Yes, there definitely are. There are certainly protocols for how we would handle the corticosteroids and things to try to make sure the patients are really under control. If somebody is really getting bad, though, within the parameters of study and the physician feels this isn't good for the patient, they're offramps. As Skylar said, you can stop participation at any point if you're really doing poorly.

Amethyst: And if a person has a flare, will AstraZeneca or the investigator say, because you had a flare you're out or if they're flaring, like you said, try to get that back under control.

Dr. Fairley: Yeah, if we can work with them and get them back under control again, there's real criteria for what we can do and try to help the patient stay in the protocol if they want to stay in the protocol.

Amethyst: Great, Thank you. Mei Ling asked if a patient has a medical procedure such as a dental surgery involved. Would that make them not qualify for the study?

Dr. Fairley: They say no surgeries scheduled but a dental procedure?

Skylar: I think if it's known, we can find out, we can just ask AstraZeneca if it's of any concern and they can make a determination on a case by case basis. So it's not completely off the table in that type of situation.

Amethyst: Great. Thank you. One question is, what are the differences between the primary and secondary endpoints and how were these determined for the study?

Dr. Fairley: Somebody must have gone to clinicaltrials.gov, and was looking at that pretty carefully.

Amethyst: You said our patients are pretty educated.

Dr. Fairley: More proof that I'm right about that. The primary endpoint is the major question that is trying to be asked in this trial. So that'll be the primary endpoint but there's a lot of other things you might look at. When Skylar was talking about quality of life, that might be a secondary endpoint. It's not the very first thing you're looking at. The first thing you are looking at is, does this allow patients to get off steroids. But other questions that we're very interested in to help the patient feel better. If it lowers their corticosteroid dose by 20%, but people don't feel any better, then maybe it's not such a win. So that's what the secondary endpoints are for, to gather additional information on how well this medication works.

Amethyst: Great. Thank you. Was patient input sought when designing the trial?

Dr. Fairley: Good question. Skylar, you might know more than I.

Skylar: Actually, AstraZeneca did take a lot of consideration on patient input. They did some preliminary research, some subjective interview research and information about patients' experiences. They've really tried to consider the patient perspective. They are on an ongoing basis and even consulting with the IPPF as of now, to really understand and reduce the burden on patients. So really trying to consider, what their experiences are and what their experience would be in participating and ensuring that that's represented in the design of this study.

Amethyst: Great. That's very good to hear. We had several questions about the study locations. Currently, Isobel asks, are the trials being done in the UK at all?

Skylar: We are in the works currently to bring on the UK. So there will be, I'd say, maybe within the next year, there will be centers opening up in the UK.

Amethyst: Did you mention, how many current study sites do you have?

Skylar: Globally? I don't remember off the top of my head, wait 64, and we're actively opening additional sites. I think we'll have around 80 when it's all said and done. In the US, we currently have 5, and we're working on additional sites in the U.S. We could have up to 15 in the United States.

Amethyst: Great. Fred wants to know if there's any currently in Southern California?

Skylar: I'm working on it. Currently, no, I think Arizona would be the closest. But I think that Southern California is a big need, so I'm working on that as we speak.

Amethyst: Great. Thank you. Based on all these questions about the study sites, where can patients find out more about where the current sites are there? Is there a website or is that listed on clinicaltrials.gov?

Skylar: Yes, it's listed on clinicaltrials.gov and you can call me if you feel comfortable giving me a call, I'm happy to get you more information about where the sites are and provide the contact information. So, again, that number in case anyone's on the phone, it's 1-855-233-1701.

Amethyst: Great, thank you.

Dr. Fairley: If you are close to Iowa, Iowa is one.

Amethyst: How many patients are needed for the total enrollment of the trial?

Skylar: 120.

Amethyst: Great, thank you. And real quick, I know you also mentioned it towards the beginning, what's the time commitment again for somebody who might be interested in the trial?

Skylar: So, for the treatment period alone, the portion of this study where you could be receiving either the placebo or the Benralizumab, that's at least 11 months. Then the extension period, so you could rollover onto the extension period if you completed the treatment period. That's a minimum of a year so that really could go on for a while. It kind of depends upon when this drug would be applied for if all goes well, if it's submitted for use to the FDA. But at least a year for that extension period.

Dr. Fairley: That's optional. The extension is optional. If somebody doesn't want to participate anymore, they don't have to.

Skylar: Yes. Thank you.

Amethyst: Great. Thank you. Well, that was a very quick hour. We had lots of great questions. Is there anything either of you would care to add before we wrap up?

Skylar: I just want to add that all the study procedures and the study medications or the Benralizumab, that is at no cost to patients. So, all those assessments, the visits, I just want to make it clear that there would be no cost to the patients for any of the clinical study related assessments and the Benralizumab.

Amethyst: Wonderful. Thank you both very much for joining us today and thank you for everybody on the call with us. I'd also like to give a huge thank you to our sponsors, Genentech, argenx and Cabaletta Bio for making today's call possible. Before we go, I

do have a few quick announcements. Our next patient education webinar will be next week, February 15th, to discuss Research in the Real World: COVID Vaccines and Pemphigus/Pemphigoid. Dr. Michael Kasperkiewicz- Associate Professor of Dermatology at Keck School of Medicine, University of Southern California will discuss his recently published articles, "COVID-19 vaccine acceptance and hesitancy in patients with immunobullous diseases: a cross-sectional study of the International Pemphigus and Pemphigoid Foundation" and "A Case Report: Circulating Anti-SARS-CoV-2 Antibodies Do Not Cross-React With Pemphigus or Pemphigoid Autoantigens". We will also have patient panelists Carolyn Fota, Dave Baron, Rudy Soto, Becky Strong, and Marc Yale. They will be discussing their experiences with Covid and the vaccine. We hope that you will join us for this amazing webinar. Register online today.

Amethyst: The IPPF has a number of upcoming virtual support groups across the country. If you are interested in attending a meeting, please check the IPPF's Event Page to register for a meeting. Also, we are always looking to expand our support network. If you are interested in starting a support group in your region please contact Becky Strong at becky@pemphigus.org. It's easier than it sounds to start a support group and you can help connect others in your area with other patients. If you are interested in continuing to help support the IPPF you can become a healing hero. Healing Heroes fund the future of the IPPF community by making sustaining, monthly gifts to support our mission of improving the quality of life for all those affected by pemphigus and pemphigoid. No amount is too small, even a \$5 or \$10 monthly donation goes a long way and continues to allow us to provide for the greater good of our community.

Amethyst: Do you wish there was a better understanding of our diseases by doctors and researchers? Do you wish there were more FDA-approved treatments and better treatments available? Well here's your chance to get involved and make these goals a reality - Join the IPPF Natural History Study today! The Natural History Study is a patient registry sponsored by the National Organization for Rare Disorders (NORD) and the US Food and Drug Administration (FDA). Your information is private, the IPPF Natural History Study follows strict government guidelines to assure patient information is protected. Your participation and the data will be used by the IPPF to help advance research, better understand the patient journey, find better treatments, and hopefully one day a cure. By sharing your journey and answering some questions, you directly have an effect on the future of all people affected by pemphigus and pemphigoid. So get

involved today! You can find the Natural History Study by visiting www.pemphigus.iamrare.org

This call was recorded and a recording will be sent out with the survey following this call. Thank you all for joining us.

Skylar: Thank you everyone.

Dr. Fairley: Yes, thank you.