CAR T in Pemphigus Vulgaris: An Update on the RESET-PV Clinical Trial

Marc Yale - IPPF: Welcome, everyone!

I'm Marc Yale, IPPF Research and Policy Advisor, and I'm so glad you're joining us! Before we start, just a quick reminder that this webinar is being recorded.

We also want to remind you, "Information is essential when it comes to managing and living with any condition. But, remember - everyone's journey is unique. The IPPF encourages you to always check with your doctor or healthcare team to make sure the information you hear today - or found online- applies specifically to you and your situation."

We know that many people in our community are interested in the research being done, so today we are excited to have Cabaletta Bio, a valued member of the IPPF corporate Council here with us today discussing the CAR T and Pemphigus Vulgaris (PV).

Before we get started, a quick reminder that everyone will be in listen-only mode during today's webinar. If you're joining us on a computer, you can listen in either through your computer speakers or by calling in on your phone. To choose your audio option, just click the little upward arrow next to "Audio Settings" in the bottom left corner of your screen. From there, you can select your preferred method - computer audio or telephone. Make sure to pick the one that works best for you.

If you'd like to ask a question today, just click the Q&A button at the bottom of your screen and type your question into the text box. You're welcome to submit questions at any time during the webinar and we'll do our best to answer as many as possible within the hour.

Please remember on today's webinar we will be discussing CAR-T in Pemphigus Vulgaris and the RESET Clinical Trial. If your question falls outside the focus of today's session, I will ask you to reach out to me by email after the webinar so we can follow up. Also, for those of you only listening in by phone, please note that you won't be able to submit questions live. To take part in the Q&A, simply click the link in your confirmation email to join via your computer or device.

Now, I would like to introduce you to our guest speaker today, Dr. Kresa-Reahl, Dr. Kresa-Reahl is a neurologist with over 20 years of experience in caring for patients with autoimmune diseases affecting the nervous system. Since joining the pharmaceutical industry 6 years ago, she has led clinical development programs spanning a number of autoimmune diseases. She is a Senior Medical Director at Cabaletta Bio and physician lead for their RESET programs in myositis and pemphigus vulgaris.

Jake Chung is also joining us to help moderate the Q&A session. Jake is a Senior Director on the Cabaletta Bio Medical Affairs team.

We are very excited to have you here today, thank you for joining. I will now hand it over to you.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: That's fantastic. Thank you so much, Marc. It's delightful to be here. And I'm going to tell you all a little bit about the Reset PV clinical trial. So, let's go to the next slide. All right, this is our disclaimer; we always have to have that because this is an industry-sponsored lecture today. Let's go to the next slide.

All right, so we've got a few things that we're going to cover today. So, one is a little overview of clinical trials, because everybody's always curious about that. Then we'll talk a little bit about the immune system and give you a cell therapy overview. And then, ultimately, we're going to dive deep into the RESET PV clinical trial, the design and some of the preliminary results. Let's go to the next slide.

Alright, let's talk a little bit about clinical trials. Let's go to the next slide. Okay, so some of this I covered last year, so if any of you were on the lecture that I gave last year, this may be a little bit repetitive, but it is important to understand. So, first of all, what is a clinical trial? So, clinical trial is really a study that's designed to evaluate if an investigational treatment is safe and effective for use in humans.

So, before a drug therapy can be FDA-approved, it has to go through multiple stages of rigorous testing, and there are actually 4 different stages that we have. The first stage is phase one, and that is just looking mostly at safety. It's got a small study with just a few patients that either have the disease or even sometimes healthy participants, and it's looking at the safety, but also the dosage. Sometimes we call that a dose-finding study.

Phase 2 is also a small study of patients that have the disease, and again, it's looking at safety and tolerability, but it can get a little early peek at early efficacy, so effectiveness of drug, and sometimes sponsors will combine these two phases into a Phase 1-2 trial. So, start out with just looking at a very small group of patients, and then some preliminary data. They can move into looking at a little bit of efficacy.

Once those are complete, if they look favorable, then companies that are developing therapies will go into Phase 3. Sometimes it can be known as Phase 2B, but it's definitely always higher than number 2. This would be a pivotal study, and when we say pivotal, this is the one where the FDA is paying the closest attention to make the final decision about whether or not the therapy can come to market. And this is looking not only at safety, it's always looking at safety. Looking at tolerability also, but looks at efficacy, so the effectiveness in the group of patients that has that disease. Once that phase is over, and that's typically a much bigger trial.

Then there can be something called post-marketing, or Phase 4 trials. And in Phase 4 trials, the drug has already been approved for the market, but there may be some extra aspects that are looked at, like maybe there would be a broader indication, maybe a wider range of ages that the drug could be used at, or a different disease state that's kind of related to the first one. So, Phase 4 can have multiple different aspects, but is kind of an afterthought, an epilogue, to that Phase 3 trial. The Phase 3 trial is the most important.

And sponsors along this journey can collaborate with the FDA to decide together about which patients would be most appropriate to look at, which types of outcomes should be measured, and what tests we should use to monitor safety, for instance. So this is very much a dialogue between the FDA and the sponsors, so that we get it right the first time, because we would never want to have to do it twice. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Okay, so what do clinical trials measure? So, in general, the clinical trials are looking to answer several different questions about an investigational drug or therapy. Probably, most importantly, you want to know, is it safe, right? So this is assessed by, it's answered by assessing the number, the type, and severity and duration of the adverse events that are happening in the trial. And adverse events are, untoward experiences that are happening to the, you know, during the trial. So it could be, any side effects, some symptoms that patients might be having, but also it could be changes in lab work, because we'll be monitoring things like blood counts, or liver function tests, or kidney function tests.

Next thing we need to know is, is it effective? And this is answered by assessing the clinical outcomes, and this will all differ by the disease state. So if you think about it, like a neurology trial might be measuring strength, or a dermatology trial might be looking at skin outcomes. So, another trial may be looking at just purely blood outcomes. So, that's all having to do with the design of the trial.

So the next one is, we want to know, how is the drug or therapy working in the body? So, a lot of times, the translational team in a different company will be looking specifically at how the drug is, in the bloodstream, how is it metabolized? How long does it take for the drug to, you know, come into a level in the bloodstream, and then go away in the bloodstream. So how long does it last. In cell therapy, we're actually kind of counting the cells that we can detect over time.

So, on the right-hand side here, you can see at a clinical trial the different things that we measure. So, at the top there, we have safety, which we're looking at adverse events, and we're looking at trends over the course of time. We're also looking at the clinical outcomes that are looking at efficacy. There are biomarkers, which would be typically blood tests or even imaging, to see if the therapy's doing what it was supposed to. And we look at pharmacokinetics, which is the metabolism of the therapy in the body. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Okay, so comparators and blinding. So, clinical trials can be designed with or without comparators. So, I don't know if you've ever heard of something called a placebo, where a person gets a pill, and then they also get a pill that looks identical to it that doesn't have the active ingredient in it. That's the one that a lot of people have heard about, a placebo-controlled trial, but not all trials have comparators like that. In fact, certain trials, especially if they're early-stage trials, or if they involve rare diseases, if they have breakthrough therapies, you know, something that would be really rare that's desperate for a new treatment, those could all be trials that wouldn't necessarily have to have a comparator. Also, if there's a high unmet need, that might be a trial that doesn't have a comparator.

So information about whether a comparator is being used in a clinical study is provided as part of the informed consent, and we're going to talk a little bit about informed consent a little later. But it's really important that patients know up front whether or not there's going to be an inactive product that's given to them, or what comparator is being used.

When a comparator is used, the trials could be used, could use blinding to minimize bias. Because sometimes, if a person would know that they're on the therapy, they may be so excited about the therapy that that would, that would, influence the way that they're performing in the trial. And it could also influence the physician who is performing the assessments of the trial. So, single blinding is where the patient doesn't know which therapy they're on, the placebo or not, or the active comparator or not. And a double-blinded trial is where the participant and the site team as well don't know which therapy a patient is on. So, over on the right-hand side here, we can see the different types of comparators.

So, we have active comparators, which would be a standard of care therapy. We have the placebo, which I mentioned is an inactive product. We also have things like historical comparators, so if there's a lot of history in databases about how patients do over time, you could compare your trial to how patients would do historically. There could be a different dosage that's used, so sometimes clinical trials will use kind of a very small dose, and then compare that to a much higher dose. So, that's just a different way of comparing. So there's a bunch of different ways that design, that trials can be designed. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Okay, so monitoring safety. Clinical trials are very carefully monitored to ensure participant safety. There are actually multiple layers of this. It's really important that before a drug would come to market, that we make sure that it's been rigorously tested, for safety.

So there are different layers of safety monitoring. The first would be the research site, the local physician that would be directly caring for the patient. Then kind of on top of that would be the trial sponsor, Medical Monitor, and that happens to be my role at Cabaletta. So, I'm looking at all the data that would be coming in from the different sites to make sure that there's no trends, no changes in blood work that would make

me concerned that there was any kind of a side effect that hadn't been identified already in an individual patient.

Then, institutions, like hospitals, have something called the Institutional Review Board, or an IRB. That is an independent group of professionals who's tasked with reviewing the trial design, making sure that it's, you know, ethically made. And that the consent process is done correctly, so that it makes sense that the patients going into the trial understand the risks and the benefits.

Then, over all of this is, of course, the FDA, that they are tasked with approving the initial request to start a trial, and then they also review regular filings of safety updates. So, you know, typically once a year, all the safety information is given to them, and they review that. to make sure that, you know, that there isn't an issue where they would feel the need to stop a trial. And ultimately, they're the ones that decide whether or not the risk-benefit is acceptable for final approval. And once they give their stamp, that's when it can come to market and be used in patients in general. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Okay, let's talk a little bit about the consent process. So, all clinical trials require the participants be fully informed about the key aspects of the study before they join, and this consent process has multiple different parts. So, usually, the physician is sitting with the patient and explaining these concepts, but the list here is showing all of the different aspects that would typically be in an informed consent form.

First, you want to know the explanation of why the research is being done. What gap is this filling that, or what need is this filling to do the clinical trial? Then, how long will it take? So, if a person commits to the trial, are they going to be in the trial for a few weeks, or are they going to be in for years? They also need to know what procedures are going to be done. Is it just blood draws? Is it just clinical assessments? Or are there imaging? These all will be listed, and sometimes they'll put them in a table so that you know, based on the visit, what would be coming.

There has to be a discussion of the risks and the benefits, so you want to make sure that you have heard in the consent form about what side effects would be potentially happening. Even if it's never been tried before, is the therapy similar enough to something else that's already out there that there might be something called a class effect? And so, you would be aware of that. Or, just based on the mechanism of action of the drug, would there be side effects that we would need to be looking for? So all of those would be listed.

Also, the benefits. So hopefully improving the patient's disease will be listed in there, too, and in what ways they may improve. There also needs to be a list of treatment alternatives, because there are some conditions that already have several medications that would be on the market, and you want to make sure that a person doesn't just come into a clinical trial without knowing that they have other alternatives. So, you

want to make sure that they have an informed decision, that maybe they've tried these other things and they haven't worked for the patient, and that's why they're coming into the clinical trial.

We want to also know about how your data is being protected, right? Because we'd be collecting information about your general health, and maybe some lab work, so the ICF is going to tell how are we going to collect this information, and how are we going to store the information, and how are we going to keep it protected, and how long does it need to be kept, and who has access to that medical information. We also have, in a clinical trial ICF, who to contact if you have questions. So if you have this discussion with the physician and you've gone through everything, but there's something that you got home and you forgot, you can have a number so that you can call up and get answers that you need.

Then, there's also always a reminder that the participation in the study is voluntary, and that you can stop participating at any time. And after a detailed discussion with the site staff, if you've gone through all of these different things, the final wrap-up of that is to sign the consent form, and that's usually the kickoff to the person being in the clinical trial. And there's actually a nice summary of that on the NIH website, and I'd encourage you to check that out. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Okay, so why do people participate in clinical trials? So, one would be to gain access to investigational treatments that are not yet available to the public. So, especially for rare diseases or serious conditions, the medications that are already available may not be doing what they need to, and so this would allow a person to have access to something that is on the horizon.

It also allows patients to receive study-related care, tests, and procedures from doctors that have expertise in rare conditions, and especially their disease in specific, you know, specifically. So, a lot of times, clinical trials are run at very, you know, prominent centers that have people that have spent their whole careers learning about that particular disease state. So, you get the opportunity to work with a person that is an absolute expert in the field. And also, there is the option to contribute to the understanding of the disease and develop possible treatment options which would help everyone with the disease. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Okay, so why are clinical trials important? So, there's a bunch of different reasons for this. So, clinical trials are really critical to determine whether investigational therapies are both safe and effective. Clinical trials can also be designed to investigate whether a therapy is better than what's already out there, you know, better than standard of care.

Now, without clinical trials, medical advances really can't move forward. It would all just be hearsay, you know? And back in the day, there was people that put forward, you know, snake oil and just had ideas about, oh, well, here, try this, and they didn't have

any science to back it up. So clinical trials are really important to establish that we all agree, that the medication works.

So before joining a clinical trial, in addition to weighing the benefits and risks, you really should consider whether you have the time to commit to the trial all the way through. Like, for instance, some trials go for a long period of time. You want to make sure that you have the wherewithal that you can come back for all the clinical visits.

Also, do you have the support that you need to attend the appointments and go through the trial assessments? So, for instance, if the trial center would be, you know, 8 hours away, and there's no access to a car or any way to get there, you might want to think twice about doing that. But fortunately, a lot of sponsors they work with companies that help make travel really easy if you have to.

You also want to make sure that you feel that you could stick with the treatment. Even understanding that there could be some side effects, you want to make sure that you can go all the way through. If there are serious side effects, obviously you can stop at any time, but there may be some other side effects that would be mild or, you know, a minor annoyance, and you want to make sure you don't necessarily want to throw in the towel right away, because otherwise, all of that important data would be lost. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Alright, let's talk a little bit about the immune system and give a cell therapy overview. Let's do the next slide.

All right, so what is the immune system? So, the immune system is designed to protect us, mostly from, you know, cell invaders, like bacteria, but also viruses and funguses. Pretty much even foreign proteins can be attacked by the immune system. It helps our body fight infections, and it's made up of the organs and special cells that all work together to help protect you.

In this picture, you can see there's a bacteria at the top, and then there are different cells that are working to eliminate that bacteria. So there's B cell, which is in blue here, and T cell, which is in yellow here. And that B cell is making these little Y-shaped things. Those are called antibodies, and B cells are specialists at making antibodies that can go after these foreign invaders and destroy them.

So, the T cells and the B cells have complicated interactions where they can sort of educate each other about what a foreign invader is, and then, depending on the cells, especially T cells, can have memory cells, which actually can remember an invader that they've fought in the past, and if they see that invader again, can quickly train up all of the other cells and expand and grow to fight off that infection if they see it more than once.

So, the next question would be, what happens with autoimmune diseases? So, in autoimmune diseases, things can go wrong with this system. I mean, normally, it's out

there trying to help you, you know, fight off foreign invaders, but occasionally, the immune system gets misdirected to go after normal tissues in your body, and that's what we call an autoimmune disease.

So, this can have effects in the body, like inflammation, can cause damage to different organs, and it can cause day-to-day symptoms, sometimes fatigue, or depending on the organ that's being affected, it can cause dysfunction, like in pemphigus vulgaris, it can cause problems with the skin, causing blisters. The symptoms can be long-standing, and sometimes they can be really severe. And so patients may need long-term immunomodulatory treatment, because what we have to do in an autoimmune disease is we typically need to dial down the immune system's response, because for whatever reason, the immune system, in trying to take out foreign invaders, has gotten this mistaken idea that is going after your own tissues. S you need to dial that down, and immunomodulators can do that. But there is a downside to doing that, too. Because if you dial down the immune system too much, then its normal function, which is fighting off invaders, could be blunted. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Okay, this is just a general overview, blood cells one-on-one, and you can see on the right-hand side here that, there are cells that are in the bone marrow that can become a myeloid cell or a lymphoid cell, and then depending on how they mature, they can end up as, different types of cells, and the different cells are listed on the upper left-hand corner here.

So on the bottom, you can see in the middle there, the red one is the erythrocyte, which you guys are very familiar with. That's what makes the redness in your blood. There's platelets down there that help your blood clot, and there's macrophages, which are cleaning up debris in the immune system's attacks. Then there's also a series of blood cells that are really important for immunity, and these are in the adaptive immune system. These are the ones that have the chance to, remember previous pathogens that they've seen, and rev up the immune system if those pathogens are seen again. So, lymphocytes are some of those, and they can be divided into B lymphocytes or T lymphocytes, and the Bs are the ones that make the antibodies, and antibodies are really important in pemphigus vulgaris because they are directed against DSG3 and DSG1, which are causing the disease itself, and we'll go into that in just a little bit. Let's go to the next slide.

Okay, and it turns out that B cells, the ones that make the antibodies, can play a key role in autoimmune diseases like pemphigus vulgaris. The B cells contribute to autoimmunity through a variety of different mechanisms. So one is these autoantibody production, so they can make antibodies that are directed against normal tissues that they shouldn't be doing. These antibodies should be going against pathogens, but in autoimmune diseases, they're going after normal tissue.

They can also do antigen presentation. They can take antigens from foreign pathogens and show them to other immune cells to kind of train them up in a way. They can do this by T-cell co-stimulation. Then they can also secrete pro-inflammatory cytokines,

and cytokines are chemicals which help the immune system communicate among the branches of a cell. So, pro-inflammatory means increasing inflammation, and that can be good when you are trying to fight off an infection, but not necessarily a good thing if your immune cells are going after normal tissues in your body. So targeting B cells could be an effective way to manage diseases that are driven by B cells and T cells. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: This is a little bit about B cell maturation. So we talked about B cells, we talked about T cells. This is a little more drilling down on B cells in general. So B cells have different phases of life that they can have, or phases of development. And each stage of development, they have these little proteins that can stick up from the cell surface, which I like to think of as kind of like flags, and they all have numbers that are associated with them because they've all been characterized by scientists. So, all of them have in common that they have CD19, which is a protein that's like a flag, like I said, on the outer surface of the cell. But then, depending on the level of maturity of the B cell, they have other markers. And as you can see, these little boxes on this slide, there have been therapies that have been developed to go after these other little flag. So, like, anti-CD20 would be, like, rituximab, for instance. And there's anti-BAF, which is, BAF is one of the cytokines. There's also, you know, there are all sorts of things that would be going against plasma cells. So, in CD19 CAR T therapy, which we're going to talk about in a minute, we are directing our attack, or removal, of the… all the cells that are showing this flag, CD19. And so by doing so, we're selectively removing the B cells, a subpopulation of which is causing the disease, pemphigus vulgaris. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: All right, let's talk a little bit about cell therapy. So, what is cell therapy? Cell therapy is the transplantation of human cells to replace or repair damaged tissue or cells.

So, an example of cell therapy that most people are familiar with would be a blood transfusion. So, in a blood transfusion, taking blood cells from one person, a donor, and giving them to a recipient, that would be an allogeneic transfer of cells. But patients can also do autologous cells. So, like, sometimes you may know somebody that was having a surgery, an elective surgery, that was coming up. And they banked their own red cells. That would be an autologous, you know, autologous cell therapy. All right, let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: And this is a little bit about what a chimeric antigen receptor is. What are CAR T cells? So, this is a complicated slide, but just to break it down for you, on the left-hand side, it's showing, the interaction between a T cell and its target cell. So, it has a complicated T cell receptor, and that's represented in red over here, and the orange is representing the target antigen. That is the protein that it's going after. The HLA that's in blue over there is kind of the card-carrying part of the cell that it's interacting with that's showing you self.

And on the right-hand side, what we can see is a chimeric antigen receptor, which has a lot of similarities to a natural T cell receptor, but it's kind of all compact in one spine, one part of it, which is all represented in green here.

It has a receptor that is looking at the same target antigen, but it doesn't need the HLA to interact within the target cell. And it has built into it, kind of the ways to stimulate the cell to multiply and to kind of turn on that immune response. And that's what the 41BB and the CD3-Zeta are doing. So that's all built into the car, to interact with the target antigen, and then also to stimulate the cells to multiply and go after other cells that have that target antigen. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Okay, and how are these manufactured? So, this is a multi-step process, starting out with one over here, which is getting the T cells that are coming from the patient's own blood, and we collect these by a process called leukapheresis, where the T cells are selectively removed from the blood. These T cells are then brought into the lab, where they're reprogrammed. They are given the delivery of a gene encoding the CAR, and the CAR, remember, was that green aspect that I showed you. And once they are given this car, they express that on their surface, and so they are then directed against any cell that would show, in this case, CD19, which would be like the B cells.

Once those cells are produced, they are then simulated to reproduce, so we make many copies of that cell, and then they are stored in, you know, they're kind of frozen, and they are stored, and then they're ready for shipping. So the next step would be either with preconditioning, which is a form of chemotherapy, which prepares the bloodstream to receive the cells or sometimes without preconditioning, and the PV RESET trial is using no preconditioning. The cells are ultimately given back to the patient, so these are their own cells that have just been reprogrammed, and those cells now are trained to find CD19, which is the protein flag, I like to call it a flag, that's on those B cells. So those cells can recognize B cells and eliminate them. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Okay, CD19 CAR T cells have already been approved to treat some types of cancers, and that's actually where this began. So, the CD19 CAR T was developed to eliminate leukemia cells, which are a B cells that have grown out of control. So, the CD19 finds those cancerous B cells and eliminates them. And fortunately, it has had really good response, for the oncology patients. There have been 53% to 81% complete remission, and up to 57% long-term remission. And there's a list of about 5 different medications that are on this slide, all of which are FDA approved for these cancer indications. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: All right, so CD19 CAR C cells, they target B cells, including those that could cause symptoms of pemphigus vulgaris. So, in this case, the CAR T cell is directed against the CD19, which is expressed on the B cell, so they have an interaction, and as soon as the CAR T cell finds its target, it will cause a cascade, which will cause elimination of that cell. And because it's specifically directed

to only go after CD19, in theory, it should not really be going after other cells in the body.

So, one of the reasons why we do the clinical trial is to make sure that that is not happening. But in theory, the way it's been designed, it should be going after only CD19. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Okay, so whenever there's a therapy, we always look at the benefits of it and the mechanism of action, but we also look at potential side effects. And CAR-T, CD19, in the oncology space has been associated, and also in the autoimmune space, has been associated with some specific symptoms, which could be, and these are, you know, not happening in every patient.
Actually, it could be pretty rare, but one of them is cytokine release syndrome, which is where there are cytokines that are released, which, remember, I told you is the, certain chemicals that have to do with the immune system that can cause fevers, and sometimes low oxygen, and sometimes even changes in blood pressure. So that would be one. There's another one called immune effector cell-associated neurotoxicity Syndrome, or ICANS, and in that scenario, there are cytokines that are elucidated that have to do with the blood vessel that actually can impact the central nervous system and cause symptoms that could anywhere be from changes in language function, or sleepiness, or changes in consciousness, and could, at very severe cases, cause things like seizures.

Those are extremely rare. Also, there could be a risk of infections, because any time we would be eliminating the B cells, and the B cells are normally tasked with patrolling for infections, there could be, if they were eliminated, a risk of infections until the B cells have the opportunity to return. There is also, in the oncology literature, some very, very rare cases of secondary cancers, including T-cell lymphomas, where the T cells are growing beyond what they should and causing cancers. But again, that's extremely rare. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: All right, so let's tell you a little bit about, Rese-cel, CABA201, and the RESET PV study. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: I'll give you a little bit of an overview of pemphigus vulgaris. You guys are very familiar with this. It's based on autoantibodies and clinical features, and there are two different types. We have mucosal PV, which is about 25% of the population, and mucocutaneous PV, which is 75% of the population, much more common.

The mucosal PV is associated with lesions in the mucous membranes, and that means all the inner linings of places like the mouth and inside the eyes. There are multiple different mucosal membranes that could develop blisters, and this has to do with antibodies against DSG3.

Then, there's also mucocutaneous, which could involve lesions on the skin, pretty much anywhere on the skin, the scalp, or anywhere on the body. And that has to do with antibodies against DSG-1.

So, pemphigus vulgaris is a B-cell-driven disease, really with a high unmet need, and the current therapies that are out there are modestly effective, but unfortunately, some of them can be poorly tolerated. And our current therapies can be associated with health risks long-term, especially infections, which can sometimes be serious. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: So, what is Rese-cel CABA-201? So, CABA-201 is the investigational treatment used in our RESET PV study. The clinical trials looking at the safety, tolerability, and effectiveness of CABA-201 in the treatment of pemphigus vulgaris.

It's an investigational chimeric antigen receptor CAR-T therapy that's designed to treat pemphigus vulgaris by targeting the B cells that could be causing the disease. Remember, I mentioned on the last slide that the B cells are directly secreting antibodies that are causing the disease. CABA-201 is made from your own T cells. I showed the process: they're harvested by leukapheresis, manufactured in the lab, and then given back to the patient.

It's T cells are a type of white blood cell, and it's using your own immune system to get rid of the disease-causing B cells and restore, hopefully, the healthy B cells in your body, because once the cells are eliminated, then the bone marrow, reproduces new B cells, and hopefully they would not be as pathologic as the ones previously.

An overview of the process. We have actually mentioned some of this already. It's very similar to what I already showed you, which is that the white blood cells are harvested, the T cells are harvested, and then in the lab, they're modified to express the CD19 CAR. Then the cells are multiplied so that we, you know, we collect many of them, and then they are given back to the patient. And in the PV study, there's no preconditioning given to the patients. Just the cells. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: And this is a little bit of the interaction, which you've seen already in one of the earlier slides. It's Rese-cel is designed specifically for patients with autoimmune disease, and one of the reasons is because it's made with all human CD19 binding domain and 41BB co-stimulatory domain, which is just saying that all the different components of it are fully humanized.

Some of the products that were made for oncology have, murine proteins, which are derived originally from mouse proteins. So ours is just purely human. And one of the reasons is, was we want to, especially in autoimmune disease, try and, you know, minimize the chance of your own immune system recognizing the CAR as a foreign protein. Let's go to the next slide.

So this is an overview of how the trials go. The RESET PV trial is one of several different RESET trials for other autoimmune diseases, but in the RESET PV clinical trial, it starts out with screening, which is making sure that the patient is appropriate for the clinical trial. Then, patients have leukapheresis, where their cells are collected, then they're brought to the lab, and they are manufactured into Rese-cel. Then, on day one, there's a single infusion of Rese-cel, where the cells are given back through the vein, and this is given in weight-based dosing, which is 1 million cells per kilo. So it's based on weight.

Then we're watching very closely in the first 29 days to look for any adverse events, so specifically side effects, so it will be collecting adverse events for the clinical trial. And then we're looking also at other endpoints, which include clinical effocacy. So we're looking to see how do the antibodies do. Are they reduced? Because higher antibodies would be associated with worse disease. And how are the cells, maturing, how are they growing in the body? How long can we detect them? These are all important questions that we need to ask. So it's not only safety, but it's also PK and PD, meaning how the cells are multiplying, and how long they stay, and then how the effectiveness is for the clinical condition, and how long that benefit lasts. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: So this is a little bit about, what we've seen so far with three of our first patients, that were in the trial, and this data was already presented at the ESGCT meeting that was last fall, but we wanted to make sure that we got it in front of you guys, because I'm sure this would be of interest to you. So, this is looking at the baseline characteristics of the first three patients in the RESET PV trial.

So, we have ages ranging anywhere from 48 to 64. There was a mixture of the different types of PV, so we had one that had purely mucosal disease, and we had the other two that had various combinations of mucocutaneous disease. The antibodies were DSG3 for all of them, but two of the patients also had DSG1.

Then we had, patients were measured for the amount of disease that they had, whether it was mild, moderate, or severe, and all of them had at least moderate or severe disease that was measured by a scale that we call the PDAI score. They'd all been exposed to prior agents, and that had broke through, or had not had tolerability to those agents, and these included things like rituximab, or MMF, methotrexate, glucocorticoids. And so, these patients had all been tried on medications, and for whatever reason, had not gotten the response that they were looking for. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: This is looking at the side effects from the medication. So, we have listed the side effects that we would be specifically looking at for CAR-T therapy. And remember, I mentioned CRS, and I also mentioned ICANS, and serious infections is something we always monitor for also. And what you can see here is, of these three patients, we had only one incidence of CRS, and there are

different grades of CRS, 4 being the worst, so it was a grade 1, which is the lowest that you can have. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: This is looking a little bit more of the efficacy data, so I'll walk you through this one. So, we had early clinical activity in rese-cel without preconditioning, with some near-complete resolution of the clinical symptoms and rapid reduction in the autoantibodies in two of the three patients.

So, taking you through this left-hand side, this is the PDAI. These are the clinical scores where we're rating the different lesions over the skin and inside the mouth. And what you can see here is that we have, sort of the green, yellow, and red is showing, you know, mild, moderate, or severe disease. You can see where the patient started, and you can see that over time, by week 8 or week 12, the scores had reduced, which is a nice thing to see.

Then, looking in the middle column here, we're looking at the anti-DSG3 and anti-DHG1 titers, meaning that we're measuring the antibodies in the bloodstream. And remember, higher titers would mean more disease, so what we're hoping for is a reduction in these antibody titers. And you can see that, for at least 2 of the 3 patients, those titers did decrease in the early data. And then on the right-hand side, sometimes a picture is worth a thousand words. You can see that there's a patient that was in the clinical trial that had pretty severe disease at the very beginning, and by week 12, had some clearing of the lesions, which was really nice.

So, we had PDAI improvements that were most significant in the two patients that had a peripheral B cell elimination, and that makes sense, that with the reduction of the B cells is also the reduced ability to make those pathologic antibodies. All three patients were able to stop their previous immunomodulators as of the data cutoff. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: So, in summary, the clinical and translational data for the initial dose cohort, we had clear evidence of biologic and clinical activity in all three PV patients in the initial dose cohort. We had PDAI improvements that were present in all three. That was most compelling, though, in two of the three patients. And all patients at the time of the data cutoff were off their immunomodulators, and glucocorticoids, like prednisone, were being tapered from low doses.

The rese-cel was well-tolerated in PV patients, and this was given without preconditioning, so no chemotherapy was given to these patients. And based on limited data without preconditioning, the CRS rate was very similar to what rese-cel patients with preconditioning were experiencing. So it wasn't anything any worse than what rese-cel with preconditioning, is showing.

Then, we're also looking at higher doses, so this is what we call a dose-finding study. Remember, I was talking about Phase 1-2, so that's what this particular trial is, is a

Phase 1-2 trial. So, we're looking at what dose is most appropriate, and we're looking at side effects over time. So, let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: So, if this is something that is of interest to you, what would you expect if you happen to be a participant in the RESET PV study? So, by participating in the RESET PV study, you would be playing an important role in understanding pemphigus vulgaris, and receive study-related care, tests, and procedures from a study doctor, and no cost to you. That's really important. We make sure that, you know, it's not, inconvenient to you.

There's also some compensation for your time during certain study visits and reimbursement for reasonable travel expenses, so I want to make sure that, you know, it's not a massive hassle to be involved in the clinical trial.

So, the trial consists of screening, which is where the physician is checking each patient to make sure that they're appropriate for the trial. Then there's apresis, as I mentioned, where they're collecting those T cells. Then there's manufacturing, CAR T-cell production, where the cells are converted into rese-cel. Then there's treatment preparation, which could be preconditioning, but in the RESET PV study, it's mostly no preconditioning that we're giving. Then there's the infusion of the CABA-201, and then there's monitoring, and we're going to watch especially those key 29 days where those side effects from CAR-T therapy are most likely to manifest, CRS or ITANS, but we'll be looking long-term also, not only at side effects, but at the effectiveness of the therapy. And there will be follow-up, and it could be, you know, it's going to be over multiple years to see how the drug is working long-term in the body.

So, therapy with CAR T cells could cause serious and potentially life-threatening side effects, as I mentioned. You know, it's not all, you know, just roses, right? We have to weigh the risks and the benefits, and that's the whole point to going through a very detailed, informed consent process. The potential benefits and risks of participating in the clinical trial need to be explained to you by your physician, and you need to figure out, based on your particular disease, whether or not the trial is right for you. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Okay, so if it turns out that, based on all you've learned today, this is something that would be of interest to you, we have 10 different clinical sites. They're poised all over the all over the country, and there is the capability to help with transportation if you live somewhere that's not anywhere near these purple dots. The locations are all recruiting right now, and so there is a link here on this slide to the clinicaltrials.gov site, which lists the specific sites, where they are, and who to contact, if that was something of interest to you. And, if the patient, as I mentioned, doesn't live near a trial site, travel can be arranged.

All right, there's also a QR code here to visit the trial's clinicaltrial.gov website. Let's go to the next slide.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: All right, so if you're interested in participating in the REST PV study, you definitely want to talk to your doctor, because only your doctor, and you can figure out if this is appropriate for you. You can also contact the Cabaletto Bio study team. There's an address here, clinicaltrials at Cabaletobio.com, and we also have a website that explains a little bit about the trial. And there's a QR code for that.

Alright, I think we're pretty much wrapping up. So we'll leave this QR code in caseyou need it. Great, thank you, Marc, for the opportunity to speak with all of the patients today.

Marc Yale - IPPF: Yeah, thank you so much, Dr. Kresa-Reahl, for a wonderful presentation. I gotta tell you, I actually learned a lot. I thought I knew it all, but I learned some stuff here.

Yeah, so just a reminder, everyone, you can put your questions into the Q&A. We've got a lot of good questions coming up, so I'm going to start with some of those, and hopefully you'll be able to answer them. We also had some pre-submitted questions. We may not end up getting to those, because we've got some really great, great questions in the Q&A.

The first question is from Steven, and Steven wants to know if there is a one-to-one comparison with rituximab yet. And does it work faster, better, longer for remission? Or is it too early to compare the efficacy?

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Yeah, it's definitely too early to compare, right? Because this does not have a comparator arm. So it's just being given for looking at safety right now. But you're correct that in the future, it may, be compared, or it may be compared to placebo. I mean, that trial would need to be designed, but we need to get the Phase 3 trial done first.

Marc Yale - IPPF: Right, absolutely. Yeah, that makes total sense. So, you know, maybe some comparative effectiveness research will have to be done down the road, absolutely. Jacqueline would like to know, what is the length of time from last, the last rituximab therapy, so if you've had it before to being eligible for the trial.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Yeah, so that is actually on clinicaltrials.gov, and Jake, you'll have to chime in if what I'm allowed to say, what I'm not allowed to say, but it's a number of months, but it depends on whether or not the B cells are back yet, right? So, if the symptoms are clearly breaking through, and the B cells have all returned, then that potentially, could be a candidate for the trial.

Marc Yale - IPPF: Right, and that sort of thing is, from what I understand, is typical. They call it, like, a washout period, where, you know, if you're on previous therapies, you have to wash those out of your system before you can start a clinical trial. Is that correct?

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Yep, that's how it usually works.

Marc Yale - IPPF: Okay, great. And then Janet's got a question, if CAR T cells attack B cells, why might this be better than just using, you know, a therapy like Rituxan, or rituximab?

Dr. Kiren Kresa-Reahl - Cabaletta Bio: That's interesting. So, has a lot to do with where the rituximab is able to get to because it may be that there are some parts of the body where the rituximab can't go, and maybe the CAR-T could go. So it's all theoretical so far, but it's a good question. So, we definitely know that rituximab is really good at eliminating the B cells in the blood compartment.

But the question is, why do symptoms come back sometimes for people after rituximab? And I guess one of the theories is that maybe there are some places where the B cells are hiding out and not able to be attacked by the rituximab. So, one would hope that CAR-T therapy, because, you know, the cells have the ability to get all sorts of places in the body, it, in theory, might be different the way that it works than rituximab. But again, this is theoretical, and we can't make any claims based on that, but that's one of the reasons why we're doing the clinical trial.
In theory, the CAR T-cell is a lot more targeted.

Marc Yale - IPPF: In theory, the CAR T-cell is a lot more targeted as where perhaps rituximab is a little bit more broad and kills all of those B cells, and perhaps, as you mentioned, you know, the autoantibodies live in those memory cells, so it doesn't necessarily get everything. Is that correct?

Dr. Kiren Kresa-Reahl - Cabaletta Bio: I think it's a little bit, it's not exactly that it, that the rituximab is broader. They're both working on CD19, but it has to do with where the, where the B cells can be found by the product. So in the rituximab case, it can eliminate the B cells in the circulation. But it may be that there are other. The circulating antibodies, right.

Marc Yale - IPPF: Gotcha. I think another…

Jake Chung – Cabaletta Bio: Yeah, I was just going to say, another key thing that we're looking at in the trials, and a differential aspect of CAR T-cell therapy is we're evaluating a one-time dose of CAR T-cell therapy. Now, it may be, you know, years down the line, or what have you, that redosing could be considered with CAR T-cell therapy. That's an outstanding question that we don't know. But with rituximab therapy, it's pretty well established that whether it's every 3 months or every 6 months, you have to, you know, get re-infused with rituximab.

And just a quick, note that rituximab, Dr. Kresa-Reahl was talking about, some of the flags that are targeted by different therapies. So, rituximab, targets CD20, which is, sorry about that, that's right.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: CD20, exactly, because they're very, they're very close, but you're right. I'm so sorry, Jake, I was picturing it was CD19 as well. No, that… that's a good point that you make. It is… so it is a subset. It's remember that not all of those cells had CD20 on them. Right, so CD19 is much broader in terms of the number of the B cells that can be eliminated. Yeah, I always think of them as almost equivalent, but they are not.

Marc Yale - IPPF: Very different. Okay, yeah. Great. We're getting some great questions. You can tell our community is very interested and savvy. So Michael wants to know, do you know what percentage of the plasma cells are wiped out after a single infusion?

Dr. Kiren Kresa-Reahl - Cabaletta Bio: So that's something that we're we're gonna be looking at, and it's mostly plasma blasts that have CD19, but there are some long-lived plasma cells that don't express CD19.

Marc Yale - IPPF: Gotcha. And Rob wants to know, and I guess we kind of covered this already, theoretically, what's the advantage of this type of therapy over Rituxan? And again, it's more targeted. I think we kind of covered that already.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Well, it's targeting a broader number of B cells. It's got, yeah, and in theory, it can go deeper in terms of different tissues where it's eliminating, but remember that picture of the B cells where they had the different maturation of the B cells? The CD19 is present on many more of the stages of the B cells than even the CD20, which is rituximab's target.

Marc Yale - IPPF: Sandra wants to know if you need to be in active disease, not in remission, to be eligible for the trial?

Dr. Kiren Kresa-Reahl - Cabaletta Bio: The clinicaltrials.gov does say that you need to have active disease, so if you're in complete remission, it would be, you know, you would be asking yourself, why do you want to try something different? It sounds like whatever you would be using sounds like it's working, right? So we would want people in the trial who, for whatever reason, their current therapy is not working for them.

Marc Yale - IPPF: Great.

Question from Steven. And again, we're talking in theocraticals here. Steven wants to know, or at least, you know, their doctors seem to think that this therapy perhaps could eliminate PV forever. Like, we don't talk about cures in our disease, because we know it's not, there really isn't a cure for our disease, but theoretically, perhaps that could be true, I suppose. I don't know if you can answer that.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Well, I mean, that's the hope, right? Because if you could give the product, and it would get all of those B cells, the pathologic B

cells, and then your bone marrow brings out the B cells fresh. That would almost be like hitting a reset button. So now you've got the clue why we named the trial.

Marc Yale - IPPF: Why'd you call it reset.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: That trial, we were hoping that that would be the case, so that'sso we need to see how things go over the long term. So that's one of the reasons why we have the trial going on for the length of time that we do, is we're going to see how it works over time. But in theory, if you could, you know, dig deep and get all those B cells, which aren't necessarily targeted by rituximab, then you could truly reset. So, cross fingers that that would be the case.

Marc Yale - IPPF: Right, but, like, in your presentation, you shared, like, you know, all of the stages of clinical trials, and we know that, you know, these stages take a very long time, because we want to get it right, right? We want to make sure we're doing it right. So, you know, some of these trials can take up to 10 or 15 years, right? We certainly, we hope it doesn't, but we don't want to rush things. We want to make sure we get it right.

Marc Yale - IPPF: Renee wants to know if the biosimilars for Rituxan would be the same as far as being able to participate. I'm assuming they would, probably.

Dr. Kiren Kresa-Reahl - Cabaletta Bio: It would be B-cell therapy, right? So, yeah, it would be okay. It would be okay. It's not like rituximab only is the. It's a class effect.

Marc Yale - IPPF: Got it. Great, great, great question, great answer. And then we, looks like we've got maybe time for one more… two more questions, and then I'm gonna… I have a few announcements. So, we've got, an attendee who would like to know how long do the modified T cells continue to attack the B cells?

Dr. Kiren Kresa-Reahl - Cabaletta Bio: Oh, that is a good question, Jake. How much am I allowed to say? I can I guess we could, we could talk about oncology. Well, we can't necessarily talk about our product, but…

Jake Chung – Cabaletta Bio: Yeah, I think, you know, so the data that Dr. Kresa-Reahl shared was with 3 patients from our PV study. We have, disclosed data on up to, really, at this point, at least 40 patients across some other diseases, and what we've seen, and I'm using the big “we” here in terms of folks who are studying this in autoimmune diseases, is that the CAR T cells expand, they go after those B cells, as we've talked about, and then, by and large, they seem to, go away within a few weeks to a few months.

And that's something that's been seen, as I said, in autoimmune diseases, like PV. Again, just 3 patients' worth of data that we've shared with PV. There is an interesting story in blood cancers, in hematology, where they seem to stay around longer, but I think that's another discussion for another day.

Marc Yale - IPPF: And a different, totally different indication disease, right? Yeah, so, no. But, I mean, that's kind of where the whole theory came from, was from, you know, treating cancer and that thing. So, great, good question.

Last question is, how severe would the disease have to be in order for you to get into the trial? So, I guess, is it moderate to severe?

Dr. Kiren Kresa-Reahl - Cabaletta Bio: That's a good, that's a good. Yeah, a good indicator, but it's, once you talk to your doctor, you know, they'll go over, because they can assess with that PDAI and figure out, because there's different thresholds, for the PDAI that would… that would meet it.

Marc Yale - IPPF: Right, PDAI is a measure that the doctors use to determine, you know, how, what, you know, how severe your disease is.

Marc Yale - IPPF: Great. Well, that hour went very fast. I want to thank you, Dr. Kresa-Reahl and Jake, for answering all of these great questions that our community had. If you do have a question that pops up in your mind, if you think you know, after the webinar, please feel free to reach out to the IPPF. You can email info@pemphigus.org or send a question to me. It's Marc, M-A-R-C, at pemphigus.org, and we'll certainly try to get all the questions answered.

I do want to thank you so much again for joining us today, both of you, and for all of the people in the audience who joined us. You know, the information that you share for our community is so important, and we really value, you taking the time to do that today.

Before we go, I just do have a couple of announcements.

Marc Yale - IPPF: You know, a diagnosis for pemphigus and pemphigoid can leave people feeling very scared, isolated, and overwhelmed. So once they find the IPPF, everything changes. And you can find answers, support, and a community that understands that support is only possible because of all of you. And so your gift helps the IPPF reach patients at their most vulnerable moment, providing trust in education and peer support, advocate for access to life-changing treatments, and remind every patient that they are not alone. So, with your help, the Pemphigus and Pemphigoid Foundation just, doesn't just survive, we thrive as patients. So, please, if you have an opportunity, donate today. You can scan the QR code on the screen, and together, we are changing what is possible in our disease.

We are excited to share that the IPPF has added six new research questionnaires! The IPPF hopes that these new surveys will help us answer many more unanswered questions about pemphigus and pemphigoid through your help. Join the IPPF Natural History Registry Study today at: https://pemphigus.iamrare.org

We recognize that these surveys take time and understand that your time is valuable. This critical research however is needed to identify gaps in our understanding of these diseases and only your participation will truly make a difference.

The IPPF Natural History Registry Study is now even easier — there's now a mobile app available for you! The IAMRARE app, which is free to download, gives you a more convenient way to stay involved with our registry, wherever you are. With the app, you can manage your participation, complete surveys, receive updates, and more — all from your phone or tablet. Download the IAMRARE mobile app today from the Apple App Store or Google Play.

I'm so excited to share that registration for the 2026 IPPF Patient Education Conference is now open! The conference will be hosted from August 28-30th in Chicago at the voco Downtown Riverwalk Hotel! This is more than just a conference, it's a powerful weekend of learning, connection, and community. Whether you're newly diagnosed or have been living with pemphigus or pemphigoid for years, this event is for you. You'll hear directly from world-renowned experts, get practical tips you can use right away, and most importantly, connect with people who truly understand what you're going through. Early registration ends June 15th so don't forget to register. We can't wait to see you in Chicago!

Stay in the know about what is going on in our community by signing up for our email list! You'll get exclusive updates on this year's Patient Education Conference, upcoming webinars, events, and the latest news in the pemphigus and pemphigoid community. Joining is easy: just scan the code or visit www.pemphigus.org, click the menu bars on the upper right hand corner and click "Join Our Email List", then enter your info in the pop-up box. Sign up today to stay informed!

Have you had a chance to explore the IPPF's Patient Resource page? If not, now's the perfect time! Whether you've just been diagnosed or are seeking trusted guidance on managing and treating pemphigus and pemphigoid, our Guide to Pemphigus and Pemphigoid is an essential resource. It's filled with medically reviewed answers, practical tips, and expert insights to help you navigate your journey with confidence. We've made the guide available in multiple languages, so it's accessible to as many people as possible. In addition to the guide, our Patient Resource page offers a wide range of educational materials to support you.
We hope these resources empower you with the knowledge you need to live more comfortably with pemphigus and pemphigoid. Visit the Patient Resource page today and explore all the information we offer.

If you are looking for a doctor who understands pemphigus and pemphigoid, be sure to check out the IPPF Find a Doctor Directory. This tool allows you to search for doctors in your area - or anywhere in the world - who are experienced with these rare diseases. Scan the QR code on the screen or visit our website to get started!

The IPPF has several upcoming support group meetings. If you'd like to join a meeting, visit our Support Group page to find an event and to register. We are also looking to expand our support network so if you're interested in starting a support group in your area, please contact Becky Strong, at becky@pemphigus.org. It's easier than you think and a great way to give back and help others find the support they need.

Join us for our next Educational Webinar on Thursday, May 7th, where Dr. Victoria Werth, Professor and Chief of Dermatology at the University Hospital of Pennsylvania and the Veteran's Administration. Scan the QR code on your screen or visit our event page to register for the webinar. We hope to see you there.

Thank you again to everyone that joined us today. A recording of today's presentation, along with a survey, will be sent out after the webinar. Good-bye.