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Jasper Therapeutics

Investor Event at AAAAI to Discuss BEACON Study of Briquilimab in Chronic Spontaneous Urticaria

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PRESENTATION

Ed Tucker

It's Ed Tucker. I'm the Chief Medical Officer for Jasper. It's my pleasure to open this session this evening where we'll discuss briquilimab and the BEACON data which we presented earlier today in both a poster and also Tom Casale's presentation at the podium earlier today.

With regards to the presentation this evening, we will be presenting some forward-looking statements. The details of those can be provided in our SEC documents and those can be found on our website, on the jasper.com website.

Without further ado, the agenda for this evening, I will just give some opening remarks and then I'll pass to Professor Martin Metz from Berlin who will discuss the BEACON study results in summary, and then he will

pass to our CEO Ron Martell who will discuss up and coming milestones and then some closing remarks and then we'll be ready for some questions and answers.

With regards to BEACON, as we showed earlier today, from a top line perspective we're very, very pleased with the BEACON data. This is preliminary data from our CSU study. The results demonstrate a differentiated efficacy and safety from the product when administrated subcutaneously. We demonstrated there rapid onset of efficacy with deep clinical responses and those responses occurred within one week of administration, which is quite remarkable for a subcutaneous administered medicine. We also saw complete response as early as two weeks at our higher doses.

We drove those clinical responses with UAS7 reductions as high as 29 points and we saw multiple cohorts with UAS7 reductions of greater than 25. Those reductions were also durable. We saw complete responses out of four weeks for our 120 mg cohort to six weeks for the 180 mg cohort and to eight weeks for the 240 mg cohort.

With regard to safety, this drug is well tolerated. We can demonstrate a very favorable safety profile, and this is demonstrated both in terms of its PK and PD attributes. What I mean by that is this is a drug which has a half-life of about 9 days, a Tmax which occurs within about 4 days from administration, and what that means is it's driving the mast cells very potently and very actively into apoptosis and that leads to those early clinical responses.

So, at Jasper we believe that this data brings together the safety and efficacy of briquilimab as demonstrated in this study, but also our early study of SPOTLIGHT which is in our CIndU data which was our preliminary data which was released late last year. We believe that this is a really good readthrough from both of these studies. We'll have further data in midyear from BEACON that continues to enroll patients at the higher doses and we can discuss that later in the Q&A. But all of this data together, we believe creates a very strong package and a good rationale for us to move into registrational studies in the second half of 2025.

It is my pleasure to introduce Professor Martin Metz. He is the professor of dermatology and deputy director, head of Translational Research and Clinical Studies at the Institute of Allergology at Charité in Berlin. He is the lead EU investigator for our BEACON trial. He's also the lead investigator for our SPOTLIGHT study, that's the CIndU study, and he's also a member of Jasper's Scientific Advice Board as well.

Welcome, Martin. I'll hand over. Thank you.

Martin Metz

Thank you, Ed, very much.

I'm afraid that you said everything, right? So there is no need for me to present anything here. But maybe some of you haven't seen—I guess all of you, basically, have seen the data, so it's more the chance of recapitulating everything and maybe for you to get more—into the discussion, then. It's also nice to see some of the faces that I know from Teams in real life. That's really nice.

All right, so it's about the BEACON study. As he said, it's the CSU study that we're looking at, Phase 1b/2a dose escalation study.

A few words on chronic spontaneous urticaria. I don't need much. It's maybe the most important aspect of this disease is that these patients suffer and these patients require effective, really effective treatment. As Marcus Muller always said, treat the disease until it is gone and complete symptom control until this has happened.

What the patients suffer from are itchy hives and more than half of these patients with chronic spontaneous urticaria also have angioedema. Now, here we're talking about Kit, mainly CD117. This is the receptor for the stem cell sector. It is expressed by various cells but the mast cells is the one cell that constantly requires SCF to survive. In the absence of SCF, over time the cell starves and goes into apoptosis.

Briquilimab, Ed already mentioned, is one of the antibodies that prevents SCF combining to Kit and therefore in the end is inducing apoptosis.

Let's go into the trial. You can see all the details here. It is a lot of different data that we're looking at here, because here's we're looking at multiple ascending dose, so you're looking at these various and different dosing schemes. You see here starting from open label with very low doses to placebo-controlled phase. You can see it here, yes, placebo-controlled phase where you have different doses but also different dosing. So, Q8, Q12, single dose for the highest one, and you see the ratio between the briq treated and placebo treated ones.

Notably you see the inadequate response to omalizumab was a prerequisite, but that's not true for all of the dosing schemes. You see especially also future patients that are included here also include patients that are oma-naïve.

Other than that, key assessments, of course, UAS7 and urticaria control test safety. This is also a Phase 1b so safety is the primary interest, and which I think is important to also look at the rate of mast cell depletion by looking at serum tryptase. This is the data that we also have at hand at the moment, and skin biopsies where we don't have any data yet (inaudible). Jasper has also work to do. But it's important that we have this information.

The tryptase alone will only give us certain amount of information. We can discuss this later as I think that looking really at what is happening in the skin is also important.

Baseline demographics, this is pooled. It makes sense because we're not looking at super high numbers here. From the overall baseline, the pooled demographics, there's nothing super special. It's the age which we usually see in trials, but also if we look at (inaudible) population. Is it that exciting and good? It's good.

Seriously? I look at the people at the door. Is there something that we follow? Keep going? I'll keep going. Okay, yes. You're business people, I know. If you don't mind, I'll keep going. I'll keep going. All right. Okay.

Severity, UAS7, all good? All good. All right. There was a very, very, very brief emergency. There. All right.

As I said, we look at severity. This is also what you see from other trials, so these are severely affected patients. UCT, no control at all. You see the serum tryptase levels, which is interesting, would be even more interesting if we were to add good numbers on normal healthy controls because the numbers that we usually have is more like probably around 5, so then maybe a little bit higher tryptase in CSU, but surprisingly we don't really have good data.

Start with first data here. This is looking at the PK data and the Tmax, and what you can see—and this is the first really important information I think that there's a very rapid Tmax. If you look at the 240 mg, this is the number of patients here with 3 but this is very robust data, so we're looking at something just before a week, so 4 to 7 days Tmax, very rapid onset. Then clearance over time and by Week 8 even with the highest dose it's certainly gone, so predictable clearance even in the highest dose, after two months, and we will come back to that maybe when we talk about potential effects on not only efficacy but also on safety.

What does it do? In the end what we want to achieve is mast cell depletion, so the one easy thing to look at is tryptase. I said that tryptase is not the super excellent good biomarker because it doesn't necessarily directly translate into absolute mast cell numbers in the skin, so if we get 50% reduction in tryptase like we do here with the 80 mg, which is most likely not sufficient, it does not necessarily mean that we also have 50% reduction of skin mast cells. But where it is extremely helpful is when we see tryptase levels going below the detection limit because then we can actually say, "Yes, of course. Then we don't have relevant mast cell numbers—any mast cell numbers in the skin." This is really what we want to see and where we can be sure of what it means in patients and for our patients – the in-between is a little bit more difficult.

What you can see here is that the single dose, 240, you have up until Week 4, maybe Week 6, a complete reduction and with 180 you are also getting down here and the others are somewhere up there. But again, this is really what we want to see, as robust as possible, very deep depletion of mast cells.

All right, efficacy. You see here the Q8 dosing. Remember it's different, some are Q12 and some are Q8 dosing for 80, 120 and 180 mg. You see that the numbers are still low, of course. Therefore, you'll also have spread here and this will look different when we have larger numbers, but what we can clearly see is the efficacy of the drug. We see this by the UAS7, the mean UAS7, the 80 really do much, but everything above that has a robust reduction in the urticaria activities or an immense reduction in the mean UAS7 score at Week 12 and of course compared to placebo.

If you look at the well controlled rates, the well controlled (inaudible) UCT score of 12 and above, it's up to 75% of the patients where this is achieved. But most importantly, also complete response rate already at a dose that is lower than what we're looking for, what I showed with the 240 where we have the complete reduction of tryptase.

Here are the same data for Q12. Always looking at 4 weeks post the last dose, right? Therefore, this is the data for 16 weeks and here before you saw the data for Week 12. Always looking at four weeks post last dose or post second dose.

Fantastic data you see on the activity going down to really very, very low levels, and again, well controlled in up to 75% of the patients.

This is what we really want to see, right? This is 240 mg. This is a single dose and 100%, every patient that received this 240 had no more signs and symptoms, not one single itchy weal. This is for quite a time. So for eight weeks, not more signs and symptoms. Well controlled, we already see patients in Week 1 and even in later time after the eight weeks there's still patients that have well controlled disease. This is really absolutely fantastic and what we want to see.

Putting them together and looking at it over time, you have these different doses, 120, 180, 240, Q8 for the first and the single dose for the 240. Again, you see this 100%, complete control of symptoms staying down and then it comes back. Still, very good but different response when you go for the 120 and 180.

Interestingly, I want to point out this 120 which did very well, you know, in the reduction, but it comes back faster, right? Symptoms come back faster. When the second dose comes, it goes beyond that, what it did show before, so it goes down again, goes back up again. The 180 seems to be more like a constant going down.

Now, there's something special about the 180 because there's a lot of questions why does 120 and 180 (inaudible) the different? One explanation is indeed something you can see here. This is sensitivity analysis, meaning that two patients were excluded from this and there was a reason to do that. Because these two patients, they were in the 180, both were in the 180 mg Q8 cohort and they had—they did show a complete reduction in tryptase, so their mast cells were gone, but the symptoms were still there. So this tells us that

these patients were most likely not CSU patients because you can't have both signs and symptoms without having mast cells. We can discuss this also later. There are differential diagnoses, mostly likely urticaria vasculitis. Super rare possibility also of inflammatory disease. I doubt that this is the case but urticaria vasculitis is something that can be a confounder.

So, if you compare—I switch back and forth here. Between them you see the 180 then is more robust in the reduction as seen before. This makes sense to or is (inaudible) to look at this side in the way, and larger (inaudible) trials of course this will with a higher number of patients you have less confounding effect of these individual patients.

Safety. CSU, it's a tremendous burden for the patients but they don't die, right? That's why safety is key also for any drug in urticaria. It's comforting to see that briquilimab demonstrated really favorable safety profile here where there's nothing much coming up. There's one patient where there was a treatment related serious adverse event that, as always you can and have to discuss these individual cases. I wouldn't have put this patient into a hospital but it certainly did look like—no, not only did it look like but it was not anaphylaxis, which is always a topic that comes up and I discussed this with a few at the poster also. I mean, anaphylaxis is not an aspect that we necessarily have to deal with with any targeted treatment, because the best drug to treat anaphylaxis is getting rid of mast cells. So, it's just the potential of initially having some activity on mast cells that can lead to anaphylactoid reaction, which we didn't see here in these patients. And compared to the placebo, there wasn't really anything special.

But the one special thing that we have to look at—we know this from (inaudible) data is these Kit-mediated adverse events. The headings say safety. I don't see this as a safety aspect; it's more tolerability or something that you do see. Because this is hair color changes and skin discoloration, taste changes, and I have to say taste change always means less—it's not a true change in taste, so things that we know from COVID where it suddenly tasted horrible or different, this is not the case. It's just that it's less of a taste. And neutropenia.

So, you can see the numbers and this is high. Careful, it's still a number of patients overall treated, but we're looking at relatively small numbers where we see these hair color changes. Didn't see skin discoloration.

Something very interesting to look at, we see this in placebo. In one patient, I think it was the same patient with the hair and the skin discoloration. So whenever you ask patients—and this is actually especially true, even if we don't see this here, but we know this from our patients, when we ask them about did you experience taste changes, if you ask them then they are, "Yeah, maybe. You're right, yeah."

But, nevertheless, it does happen in a subset of patients, but the patients do usually not mind. That's why I would not consider this as a safety aspect. Where you could theoretically put it as safety is when you look at neutropenia, but here we're actually looking at neutrophil count decreased, not so much a true neutropenia. We'll go into detail on this slide where you see the number of neutrophils and something that you see similar also to other Kit-targeted approaches where you have in the higher doses, you have a reduction. This is the reduction in the neutrophil number, but it doesn't go in mean below the lower limit of norm. So it really depends on where you start out from.

There was one patient that had a very low neutrophil count in the beginning who was one of those patients that then turned out to be neutropene, but this really depending on where start out from.

Overall, this is very much in the normal range of neutrophils and we really do not see this as a safety aspect, especially as there was no association with any infection or whatever.

This is something that I am doing here. I would not do at the scientific meeting because it's not 100% fair if you don't have a head-to-head trial to put them really into one, but nevertheless, it's interesting. Just be aware that this is not head-to-head, right? I mean, there are differences in (inaudible) and so on and so forth.

This is comparing briquilimab data with the various doses and the barzolvolimab 150 and 300 dose. You see that there is a pretty similar reduction in UAS7 if you compare it with some of the doses of briquilimab, and then you have this (inaudible) That's three patients, but I mean if this is going to be the case for the next 20 patients, I mean wow. Then, if it stays down here, this is superb and this is what I look for.

Getting even more difficult in the comparisons, because it's also looking at completely different times when the studies have been done, so looking at Xolair, the ASTERIA I and II trials, this is, I don't know, 15 years ago, right? Of course patients also change then if you have approved treatments and so on.

I think this is a little bit—it looks better. It's something that we know also from other trials in psoriasis and so on, so the early—the first trials was the ones looking best. Nevertheless, it's okay to get an idea, and Oma is a wonderful drug. I think we need it in urticaria. It's a good drug and you see this compared to the others that came or will come, like dupi and remi, this is around the same ballpark, what can be achieved in the reduction of UAS7.

It does change when we look into Kit-mediated approaches. This is true for barzolvolimab. This is better than the other, also a if you talk placebo, and it is even better with the briquilimab data that we have so far, especially as we're looking here also in the super difficult to treat patients only, so those with the most severe urticaria and those other ones that were previous Oma failures.

All right, so that brings me to, again, all the stuff that I had said in the beginning and I said a little bit more about. We have this early Tmax that fits to the rapid onset of the clinical response and the rapid decline in UAS7. The durability is dose-dependent but in the higher dose you have a very durable and sustained. Here, I was hoping for the beer, but yes, I'll wait for that.

Safety, tolerability is really favorable. This is really true. I am not only saying this here, but this is something that I also say in the scientific meetings.

It has the potential with dose optimization, so this is something to look closer into in future trials with potential loading dose, for example, and then there is the chance, especially with the short half-life to possibly play around and gain—I mean we can't gain much on the efficacy side if we look at the 240, but we can maybe get even better with the hair color changes and so on.

The mast cell depletion, I hope I don't have to say that mast cell depletion is the key and this is promising in CSU, in CIndU and beyond that. So we are also looking at other diseases. We've seen data for barzolvolimab in prurigo. I am convinced that we will see this in other indications in the future.

And certainly—and this is final sentence here—it supports advancing the program and I think this is what planned also from Jasper. So, thank you for the moment.

Ed Tucker

Thanks you, Martin.

Ronald Martell

Thank you very much, Dr. Metz. Really appreciate your insight and all of your experience in this space and your interpretation of our data.

As we all know, and as Dr. Metz just articulated, this data set that we just reviewed on BEACON is the initial data readout from the first cohorts in the study. Having said that, I think maybe for a moment and sort of a bridge from Dr. Metz's last slide is most of you in the room know that when we began this journey about a year and a half ago, we saw the promise here and we saw the promise from those that came before us, like barzo. But we believe that there was a better way to treat these patients, and by that we mean an optimal biologic dosing strategy.

We know that as Dr. Metz just articulated and finished there by saying it's about the mast cell and it's about depleting mast cells. Having said that, there's a couple of strategies. You can just bomb the mast cell and keep dosing and dosing more of an AUC type of a strategy, or you can lean into the properties of your antibody like we are. Our shorter half-life, our rapid Tmax, our high Cmax, hit that so that you're depleting or engaging with the c-Kit receptor so that SCF can't bind, you initiate the apoptosis. If you were in Dr. Casale's presentation earlier, he was talking about that whole biologic mechanism. And if that is true and if you look at our 240 data, our 120 data, all you have to do is look at the tryptase data that Dr. Metz just presented, even at the 80, the 80 doesn't deplete the mast cells the way the others do, but it has that same biologic effect, that same rapid onset. So why not lean into those properties, hit the mast cell, get that high Cmax, then lean into the shorter half-life, and we think that's now starting to play itself out in the safety profile, that we see some of these c-Kit AEs, but our patient journey is significantly different. We're clearing the antibody out, and all those AEs that Dr. Metz just showed you, they all resolved before the next dose. So we think that there's a better way to give this drug, a better way to treat CSU patients, a better patient experience.

What we're doing here is the next cohorts of data. So around mid-year, you'll see all of this additional data that will be coming that will then enable us to pick that optimal biologic dose or doses to take into our registrational study, our Phase 2 adaptive design that you've heard Ed talk about.

With that, 2025 is really setting up to be a transformational year for Jasper. In the mid-year timeframe, we'll have more than double the amount of patients that we read-out in January, and those will be coming from both CSU and CIndU, and across those we'll have more than 100 total patients at a variety of dose levels, and for an extended length of time for repeat dosing that will really help us make sure that the doses we're taking into that adaptive clinical design enable us to then to pick a registrational dose and move rapidly into our Phase 3 clinical trial. That's what you're seeing here, is that second half of this year we'll be into that adaptive study and by the middle of '26 we'll be into our Phase 3 clinical trial.

So, a lot going on at Jasper this year. Significant read-outs in the middle of the year in both CSU and CIndU, and as we've guided previously for the asthma data, in the second half of this year as well.

A number of data real-outs, as well as you'll see the medical conferences and scientific meetings. I have to put a plug in for a couple of the posters that were up today and are coming, and the work that we continue to do on the preclinical side, really understanding of the biology of the diseases we're going into such as asthma and maybe others in the future. But 2025 is really stacking up to be a transformational year for us and that data read-out in the middle of the year will enable the data that we know—as Dr. Metz said, that 240 is real. Yes, it's a n of 3, we get it. But when we have multiple doses at that level and when we have repeat doses, and when we also look going back to the previous slide, remember, we're doing a 240 followed by a 180. Maybe the best thing to do is you hit those mast cells hard, but do we have to follow with that same dose level in order to maintain it? We want to explore that, and by the mid-year timeframe, with all of that data and in consultation with experts like Dr. Metz, we'll be able to design our Phase 2b adaptive study where we know we have a couple of really active doses, but what's the best way to treat these patients?

With that, I'll stop talking and we'll open it up for questions. We're also joined up here by Herb Cross, Chief Financial Officer. So for those in the room or those online, we'll open it up to questions.

Ben?

Ben Burnett

A question for maybe….

Ronald Martell

Grab a microphone so maybe the others online can hear.

Ben Burnett

This is Ben Burnett from Stifel. A question for Dr. Metz. Looking at the briquilimab PK data that you showed, we see the drug concentrations, they peak quickly and then come down. I guess at what point would you expect to start to see relief on target Kit tox in that curve? Any estimate there?

Martin Metz

Difficult to say actually. This is something that we also have to learn now from future trials that is looking at that. My take always was that you need to—and this is what you said, hit hard maybe in the beginning because if you get rid of the mast cell and if it's a good thing to have this Tmax with very high doses where you then start starvation of the mast cells, and if you achieve this you don't require the constant—that's at least the idea, right? Stays up, the concentration, because if the mast cell goes into apoptosis they are gone and it takes a while until they are coming back.

I'm not sure whether this answers your question.

Ben Burnett

Yes, maybe you were speaking to the maintenance dose that you were just talking about.

Ronald Martell

I think that's right, yes. It's the difference between a strategy of a Cmax dosing strategy versus an AU strategy, AUC dosing strategy where you're constantly maintaining some level of let's call it therapeutic inhibition, but if you're desiring to deplete, that's a different strategy.

Martin Metz

It's really a completely different strategy, right? This is why we have to rethink this. If you're looking at, let's say remibrutinib, which just presented later today, of course you need this constant. You need your dose up the whole time because when it's gone then the effect is gone and you get the mast cell activation. But since here you're looking at the depletion of mast cells, you don't require this over time, slightly, right? Because when it's gone, it's gone. And at some point they come back and this is also what we see, but you see from the single dosing of the 240 that it takes a long time until they come back.

Ben Burnett

I'll buy that, Dr. Metz, by extension if the antibody is creating these on-target c-Kit effects, if you're dosing in concert with that mast cell depletion and return, you could in theory then give patients a drug-free interval where those c-Kit related cells can regain function, restore signalling, whatever that might be, so that you're avoiding those effects.

Martin Metz

Absolutely, especially as I said in the beginning, the mast cell behaves differently than the other Kit-bearing cells. So, they really require the SCF otherwise they go into apoptosis. This is different also from the melanocytes. This is why we don't see—we have worked for many decades with mast cell deficient mice and they are mutant in Kits, so they don't have Kit from the beginning and therefore they are completely white. But the melanocyte as such doesn't need SCF constantly, right? This is true for also the other cells. So, unlike the mast cell, this is really specific here and therefore a good opportunity for a good safety aspect that by at least theoretically going this approach that you have the effect on the one cell that you're really targeting, that you want to target that is the mast cell, and this lower exposure too than the other Kit-bearing cells.

Ben Burnett

Thank you.

Ronald Martell

Thank you, Ben.

Ben Burnett

Great. If I could just ask one more, just for the management team. Regarding the Phase 2b adaptive into the Phase 3, I was wondering if you could maybe speak to some of the logistics you have to go through, once you select the dose, like, what you'll have to do to start the Phase 3 and maybe kind of rough timelines around how long that could take.

Ed Tucker

Thanks. First of all, the advantage of the operational adaptive is that it actually gets us into the Phase 3 quicker. It reduces essentially the down time between completion of the Phase 2 and into the Phase 3.

We will obviously need to agree with the agency around some of the premises for dose selection moving into the Phase 3, so we will take our dose selections from BEACON and the other data, the totality of the information that we've gathered from our program to date, and then we'll make decisions around dose selection for that adaptive 2b. It's an operationally adaptive, so the patients that are enrolled into the first part of the 2b into 3 will not be used in the primary analysis for the Phase 3. They will be unique patients that remain in the Phase 2. They will contribute to the safety database, and as you might guess from the (inaudible) efficacy here, creating the safety database is the limitation for the BLA package as opposed to having enough patients to demonstrate the efficacy. We will demonstrate efficacy, as Martin has explained today. So, the Phase 2b will certainly accumulate and help us with the creation of the safety database.

With regards to how we move from the 2 into the 3, there will be prespecified requirements in terms of the assessment of the doses, how they behave, and that will be based upon both efficacy and safety. If both doses are acceptable with regards to efficacy and safety, then we'll look wider across the program to make an informed decision about the final dose that we take into the two Phase 3s.

Andreas Argyrides

Andreas Argyrides, Oppenheimer on behalf of Jay Olson. Just two questions on safety here.

Based on the current safety data and PK profile of briquilimab, which seems to have some advantages versus barzo, what is your prediction on the long-term safety profile and how that may compare to barzo? For those c-Kit on-target AEs, which ones are particularly hard manage? Then one more follow-up.

Martin Metz

Well, always difficult to answer if you have different stages of the clinical trials. In the end, the Kit-targeted approach, if it is highly effective it also affects Kit on other cells. So I think in that respect the type of adverse events are similar. There will be no difference between barzo and briquilimab. But we have discussed about the possibility and the potential, and this is due to the half-life, which is different between barzolvolimab and briquilimab, that there is a chance of using this window to improve the safety profile. This is the hypothesis and there is, I believe, a good possibility that this is the case, but I also have to say we have to wait for the data to come in, to be able to say that.

This was the one part. The other?

Andreas Argyrides

The second one is I guess for the management team.

Martin Metz

Okay.

Andreas Argyrides

And maybe you can also chime in. If you could talk about what types of AEs are more likely to be driven by Cmax and what type of AEs are more likely to be driven by drug overall exposure? Are there any particular AEs where you think briquilimab can show clear differentiation against barzo?

Ed Tucker

I'll take that, Martin.

I think first I'll just add to Martin's comment earlier. I think that—and it comes back to Ben's question as well. I think taking a different approach to dosing where it really is serial single dosing. This drug will not accumulate at the 240 mg. We have modeled that data, so that does give us relief on those other c-Kit expressing cells, which gives us the opportunity for the avoidance of some of the things which you would see if you saturate for 52 weeks. Certainly, if you saturate all the c-Kit for 52 weeks, you get the hair color change, you get the skin color change. That's been confirmed in the barzolvolimab studies. We believe we're different. That will play out in the studies.

With regards to what is an adverse event which is I think more saturated c-Kit, I think it's probably the hair and effects on the melanocyte, the constant blocking of the melanocyte with c-Kit. But then from a Cmax perspective, certainly the intravenous studies with barzolvolimab demonstrated nearly a 40% hypergeusia and taste change. So if you're giving a drug IV then it looks more Cmax. And certainly in our higher doses I think there is potentially a dose response. Again, to Martin's point, relatively small numbers right now, but certainly numerically we saw a couple of extra patients at the higher dose. That was very consistent with

actually what we saw in the healthy volunteer studies at the 280 mg dose as well. And again, these are mild taste aberrations. It's not Paxlovid.

And patients stay on drug. I think this is something we haven't discussed here today, patients are highly motivated to stay on this drug. They have a disease which impacts their quality of life very significantly, so we're not seeing patients coming off drug for what Martin said and I will repeat it actually, it's tolerability, not safety issues.

Then lastly, I think with regards to the neutrophils, I know that's been a big question around is there differentiation there. I think yes, I think there is. You'll see that we show the nadir and again it's consistent with the attributes of the drug and show a half-life. The neutrophils are coming back between doses, and again, when you saturate, as barzolvolimab does, then you see the neutrophils go down and they stay down.

We did not see any dose holidays or drug interruptions and I think in the barzolvolimab study they did.

Martin Metz

If I can just add one thing, because it's often not really considered. It's really the absence of symptoms in all or nearly all patients; this is what we as urticaria treating physicians are looking out for. And I can tell you, our patients, if we tell them, "Okay, I have a drug where I can guarantee you that you will be free of symptoms within a few weeks, but you will get white hair," so even if it's possibly ending up with 1 out of 10 who gets it, but if I tell the patient this will happen, almost all of my patients will go for it.

This is maybe not understood by everyone because you would think, "Oh, my hair," but the disease is that bad. I mean of course, we always have to have the leverage between adverse events and efficacy, but what we really want to go for—and again, it's not safety, right? It would be different if it's true safety aspects, but we're looking at something the patient can in the end decide is this something that is a problem for me or not. Here, I really want to go for what we saw with the 240.

Ed Tucker

Next question.

Lindsey?

Lindsey Wylie

Quite a basic quite question. You mentioned about skin biopsies that you had. What are you expecting, hoping to see in those?

Martin Metz

(Inaudible).

Ed Tucker

We have taken skin biopsies from some patients who consented in the trial. It wasn't a mandated requirement, as you know. That would preclude patients into the study. They would not simply sign up for that. So we approached this in that data and we're going to share that later in the year. That will be some of Martin's team as well in the Charité which will be helping us to analyze that data.

Martin Metz

But I understand your question because it doesn't really add to efficacy data or something, but what it does enable us is to better understand the disease. This is important for us also, so I'm thankful that you are doing this because we really want to know—this is stuff that I get asked, "Okay, what does it mean? Fifty precent reduction of tryptase, how does this translate into absolute mast cell numbers in the skin, or is it the mast cell numbers in the gut," and so on. Having good correlation—also super interesting to understand what rate of mast cell depletion do you actually require in the skin to see a reduction of symptoms? This is of course maybe a bit of a nerdy question, but still something that is very informative for us to better understand the role of mast cells in disease and also the disease as such.

Ronald Martell

Thank you.

Sean Larkin

Hi, good evening. Thank you. I'm Sean with Regeneron. A question about the omalizumab experience. Would you consider these to be omalizumab experienced or inadequate responders, or nonresponders? How did you define that in the Phase 2 study, and how do you look at it going forward in the next stage trials? Also, if you have any input from payers, either in the U.S. or overseas.

Ed Tucker

The vast majority of patients who are motivated to come into our trial must have experienced omalizumab before coming. That was an entry criteria. What we see with the patients are really two types of oma refractory: those that simply don't get a response at all or it's very, very delayed. Then there's another set of patients who, let's say start with a UAS7 of 35, they go down to 25. Now, up until then those patients are quite happy because it's the first time they've actually had a clinical response, but Martin will probably say in a moment a UAS7 of 25 is still a lousy quality of life with that disease, and you've seen the results that we can drive. So, we have taken patients who have essentially had I would say minimal improvements in their UAS7 or no improvements.

In terms of intolerance, there is very little in terms of the intolerability of omalizumab, so it's more about the refractoriness of these patients.

Martin, do you have any other thoughts?

Martin Metz

No, exactly. It's really, as I said, oma is a good drug. It's a wonderful drug, I have to say, even though the U.S. derms don't agree, but the allergologists do.

No, so it's really these nonresponders and partial responders or not sufficient responder. I just want to add that it is a selection of very severe patients because we know that the oma-refractory patients are on average more severe, which the reason is that they are more likely to be type 2B patients which are more severe, more refractory in general.

But overall, there's no reason to believe that a Kit-targeted approach is different in oma—or in type 1 or type 2b patients because it's the effector cell that we're killing and then we don't have to care about how the mast cell gets activated.

Ronald Martell

Regarding your question for the regulatory authorities, we are in discussion with both EU and U.S. regulatory authorities, and we'll work with them in designing our registrational program, but I think tit's important to note that for the additional cohorts that we're adding here for BEACON, we're now enrolling oma-naïve patients as well.

Questions?

Alex Gray

We do have a couple of questions that came into the webcast. First one from Silvan Tuerkcan at Citizens JMP. Could you please give more color on where the data that—the movement in the data in the 180 mg dose? It seems like the tryptase levels improved and the CR rates improved. Provide a little color on that, please.

Ronald Martell

Ed.

Ed Tucker

Thank you, Silvan, for that question. Where we cut the data, the 31st of December 2024, one of the responder analyses included a last observation carry forward, so one of the patients we took their Week 11 data into Week 12, and at the time of Week 11 that patient was a well controlled patient, and then between Week 11 and Week 12 the patient had a CR. Now, that means that the 180 mg Q8 dose with regards to response rate moved from 29% to 43% because he was one patient. These are small numbers. So obviously it's moved in the right direction from my perspective; we're very happy about that. We're very happy for the patient as well. So that really addresses the question from Silvan there, I think.

Then with regards to the tryptases again, this is data which has been made available from the laboratories to update and have a more fulsome presentation of our data.

Alex Gray

Next one is from Greg Renza at RBC. What is your hypothesis as to why briquilimab might be potentially more potent than barzolvolimab in CSU?

Ronald Martell

Ed?

Ed Tucker

Thank you for that question as well.

Alex Gray

We won't ask Martin to do any more questions.

Ed Tucker

No, that's totally fine. I think the work which our lab have done actually really demonstrates that if you're blocking the natural ligament binding space with briquilimab, blocking stem cell factor, starving the receptor of its ligand, you've got a very potent effect on the receptor. Compare that with dimerization. If you're blocking dimerization in regions 4/5 on the receptor, there is the opportunity for signal leakage from the receptor to continue the intracellular phosphorylation cascade, and so we believe that may be some of the differentiation around whether or not there's potency differences. When you're (inaudible) Jasper have done some of this work and actually we've presented that data, both at this conference and earlier conferences, comparing what we call the tool compound conjugate SP04 which is a dimerization blocker, which shows the separation between our drug and a dimerization blocker, we also compared with imatinib, a small molecule c-Kit as well. So I would direct the audience potentially to that. It's great data.

Ronald Martell

There's also something materially different about the antibodies if you look at the Tmax and Cmax. Our clearance from the subcutaneous tissue to the other five compartments and then ultimately engaging with a mast cell certainly looks different. We don't know what to attribute that to, but it is materially different.

Alex Gray

Next question is from Justin Zelin at BTIG. What is your latest thinking regarding dose selection moving forward in development? And how do you view your data in light of the competitive landscape?

Ronald Martell

Why don't you take the first one and I'll …

Ed Tucker

I think we covered a little bit of dose selection with Ben's question earlier. I think it's always we're going to see the totality of information that's available to us. BEACON is going to be extremely informing for us, especially with the extra data that we're generating from the latter cohorts, which fill in the exposure response and the PK analysis which were ongoing and we'll have again more fulsome data from these higher dose cohorts.

We've also got the data coming in from SPOTLIGHT study as well and also from the open-label extension, so that's going to give us a lot of data to analyze and then make good decisions for the Phase 2b.

Shall I hand over to you, Ron, for the second part?

Ronald Martell

Sure.

Look, our perspective is that—and it's what I started off the conversation with, that we have an opportunity to have not only a differentiated approach but we have a differentiated molecule, and the data are now starting to show themselves. Whether you look at basic preclinical data, looking at the PK, or you're looking at the tryptase reductions and how that might translate into results, you're looking at the onset of the responses, the depth of the UAS7 reductions, and yes, it's small numbers but looking at the patient experience from the adverse event profile, it's meaningfully different. We really look forward to the mid-year data when we have enough of a cohort—look, on one hand, it's great. We only had an incident of 15 total incidences of CK-related adverse events, but that's also not—doesn't enable us to really extrapolate that

into much more or a trend or a projection. So, we need to wait for the mid-year data but we think briquilimab is doing what we asked of it.

Alex, I think we have time for one more. Is there one more in the room or online?

Alex Gray

I have one more from Pete Stavropoulos at Cantor Fitzgerald. What was the rationale for adding omalizumab-naïve patients to the additional cohorts in BEACON? Can we assume that that change will go forward to future studies?

Ronald Martell

It absolutely will go forward into future studies. Ed or Dr. Metz, want to talk about…

Martin Metz

Yes, it needs to. Because if you go into studies leading to Phase 3 studies and if you then only go for oma non-responders, well, this is your population that you're dealing with, and then you can only get it approved for patients that are oma non-responders. This is not what we want to have. So, you need to be able to show that you have efficacy over all of these patients and then you have a drug for all of these patients. That would certainly be my advice that you should not—I mean it makes sense at this point to look at these oma non-responders because it's the most severe patient population and you get them also faster recruited into these trials, but at some point you have to show that it works in CSU in all of these patients.

Ed Tucker

I would just add two comments there as well to Pete's question. Thanks, Pete, for asking. The first is I think it's scientifically the right thing to do to study both populations, both the oma naïve and also the oma treated. The data we've shown here today is in the oma experienced that have been refractory. This is the toughest population, so we anticipate good responses in the oma-naïve. Barzolvolimab didn't see a difference and I think to Martin's earlier comment we don't anticipate because if we're defeating the mast cell, it doesn't really matter what the history of the omalizumab therapy was.

Then the second is, which is more from an operational perspective, finding oma-naïve patients is much easier than finding oma refractory patients. There's more of them, so we can anticipate that our recruitment enrollment into the study can go a little faster. So, we're quite upbeat about achieving the enrollment goals that we've set ourselves in these cohorts.

Ronald Martell

Thank you. So, thank you all for coming tonight. We really appreciate you being on the journey here with us. Really want to thank Dr. Metz for his presentation tonight, but more importantly than just tonight, for being the primary PI for both the BEACON and the SPOTLIGHT study, and for all the work that he does for CSU patients and picking up the mantle for his dear colleague Marcus. So, thank you.

Really look forward to the rest of this year. We love our data and we're gratified when AAAAI accepted it for the Late-Breaker this year, validating the scientific relevance of this data, and really look forward to the read-out in the middle of the year. That really enables us then to move this as per our plans into registrational studies in the second half of this year.

Thank you all for coming.