UCB Virtual Briefing: BE BOLD : Bimekizumab Efficacy & Safety Versus Risankizumab In Patients With Active Psoriatic Arthritis | 8th June, 2026

Yvonne Naughton:

'Hello everyone, and welcome to UCB's capital market to discuss the results of our Head-to-Head BE BOLD in psoriatic arthritis, which was presented on Saturday at the EULAR conference in London. My name is Yvonne Naughton and I lead the investor relations team here at UCB. This call is intended for capital market participants only. For any other participants, we ask that you please now disconnect. This event is being recorded and it's covered by the disclaimer and Safe harbor statement as stated on slide two of the presentation. Following this event, the presentation will be available for download, on the investor relations section of our website. Hosting our call today is UCB's executive vice president and head of patient evidence, Emmanuel Caeymaex. Joining Emmanuel to present that BE BOLD is Professor Iain McInnis, vice principal and head of the College of Medical, Veterinary and Life Sciences at the University of Glasgow. We are also joined by Professor Joe Merola, expert in psoriatic disease and dermatologist and rheumatologist.

In conversation with Emanuel, Joe will provide his perspective on prescribing practices, and how he expects these to be impacted by the BE BOLD data, after which Emmanuel will turn the call over to the operator for the Q&A. This call focuses on BE BOLD clinical data and perspectives on its impact on prescribing practices. We will not discuss any access, commercial, or financial updates for Bimzelx. We are happy to take these questions at another time. And with that, I'm happy to turn the call over now to Emmanuel.

Emmanuel Caeymaex:

Thank you, Yvonne, and welcome everyone. Delighted to have you. Thanks for your interest in UCB and Bimzelx, a key growth driver for UCB. So, I'm head of patient impact as Yvonne mentioned. Essentially in other companies, this would be called development and global product strategy. And I'm delighted to introduce this call and maybe remind everybody that Bimzelx is now a product that is available worldwide in five different indications. 125,000 patients are benefiting from the drug, and over the years we've accumulated about double that number in patient exposure. So it really is a product, a brand, that is making a big difference in rheumatology and dermatology practices. And it's approved in five indications. There's four in the make. So you're aware that we're testing Bimzelx in palmoplantar pustulosis, that is a phase three study, and also in three pediatric studies. So first of all, juvenile idiopathic arthritis, second pediatric psoriasis, and then last but not least, hidradenitis suppurativa in children and adolescents.

And so all of these programs are moving forward swiftly, and we look forward to providing you with further updates in the calls to come. So if we move to the next slide, you will see, of course, that in psoriatic disease we have been focused not only on demonstrating superiority versus what used to be the standards of care, adalimumab, ustekinumab and Cosentyx, but also are continuing to build on comparative evidence to inform clinical practice, designing studies with endpoints that essentially move the bar closer to what patients' expectations really are, but also closer to what physicians and payers look at in a contemporary setting. And the study BE BOLD was designed a few years ago acknowledging that the use of IL-23 inhibitors, and risankizumab in particular, was set to increase in the space of psoriatic arthritis.

And so in psoriatic arthritis, nobody's ever really shown superiority on a joint endpoint at approved doses. And we saw the opportunity for Bimzelx to essentially be the first here to demonstrate superiority versus one of the two brands that really is growing the IL-23 class usage in psoriatic arthritis. And it's an important question, because there isn't any comparative evidence. In fact, in psoriatic arthritis, there are very few, if any, trials at all that have shown superiority when it comes to the first symptom that people are looking at, which are joint symptoms. We've picked ACR50 because it's meaningful, so it's not just a measure of response, it's a measure of response that matters. And it was also the primary endpoint in our PSA program that we run in TNF in complete responders as well as in bio- naive patients. And so you will have seen from the abstracts that we've managed to show an 11 percentage points delta versus risankizumab in a manner that is highly statistically significant.

And 11 points, when compared with a response on that stringent endpoint of 38% or 40% up to 50%, is actually quite clinically meaningful, I would think, and look forward to our speaker's commentary on that today. So moving to the next slide. Thank you. So this is not just about how a patient does at three months, which really is when patients tend to be evaluated after initiation of a biologic. The point is that this is actually maintained over a year and then as we've recently published, over three years. And you will see that this ACR50 response in bio-naive patients and in TNF incomplete responders on a modified NRI, so stringent analysis, exceeded 50% at a year. So now we're going to look with the build at how that does over a three-year period. If we can just have the next click please. Yes, thank you. And so you will see that using this stringent measure of modified NRI, we still end up with more than 50% of patients achieving that stringent joint control goal in psoriatic arthritis at three years. And that really is testament to the stain power of Bimzelx, which is probably linked to the fact that it's a dual inhibitor of not just IL-17A but also IL-17F, which is the chronicity cytokine. And so it's great to know that the results that are obtained early for most patients stay over such a long period of time. Now, of course, the question was how does Bimzelx do compared to the other newest entrants in the class, meaning the IL23s and specifically risankizumab? Next one. And so to help answer that question, I have the pleasure to hand over to Professor McInnis, who probably is no stranger to many of you. Over to you, Iain.

Iain McInnes:

Thanks so much, Emmanuel. And if I could add my warm welcome, good morning, good afternoon, good evening, wherever you're listening. What a privilege it is to tell you a little bit about the BE BOLD study, and I do so on behalf of investigators and many learner friends and of course colleagues in UCB who were pivotal in bringing this trial into reality. The next slide will depict the various disclosures that I have. And if we move from that to the far more interesting conversation about what was the rationale, what was the background for comparing a P19 inhibitor with a dual 17AF inhibitor? Well, first of all, if you address your attention to the cartoon on the right-hand side of the slide, first of all, you'll see that there are numerous sources of IL-17A and IL-17F. These can come from the so called adaptive arm of the immune system, adaptive lymphocytes, if you like, but also from the innate arm of the immune system.

And because immunologists are creative, imaginative beasts, we call them innate-like lymphocytes. So, two different sources of downstream effector cytokines. Now, existing therapeutics prior to the introduction of bimekizumab were exquisitely specific for IL-17A, leaving the IL-17F member of that cytokine suprafamily uninhibited, unimpeded, if you like. Now let's move to the left-hand side of the cartoon, and you'll see that upstream of the cells that are producing IL-17A and IL-17F, we have regulatory cytokines of which IL-23 is probably the most important across a whole range of immune-mediated inflammatory diseases, and certainly the psoriatic disease spectrum. But you'll notice that there is therefore a gap in the map here. There are cells that are capable of producing 17A and 17F, which are probably not driven by IL-23, hence the phrase that we've seen written in our literature, IL-23 independent 17AF production. Now, this is all very well when immunologists draw the cartoons, and we

draw them with confidence, but of course that needs to be tested in the human state and that's where BE BOLD comes to the fore.

Emmanuel mentioned there have been a number of head-to-head studies that the successful studies have been performed in cutaneous psoriasis. We've met with less success in the area of psoriatic arthritis. And when I think about it, really the most relevant study was EXCEED where we compared secukinumab and adalimumab against a musculoskeletal outcome, and we did not get superiority in that study. Some of you may also be referring back to SPIRIT head to head, which was a head-to-head trial. But remember in that trial, the outcome was a dual cutaneous and articular outcome. And here we have a study, which I shall demonstrate momentarily, sought to look at a specific joint focused endpoint. So let's look at the trial design in the next slide, which will tell us a little bit about the inclusion criteria adults, active PSA. And this is a clinical cohort that will be familiar to many clinicians in the field.

And these were patients who'd previously either been biologic DMARD-naive, treated with conventional synthetic DMARDs, of which methotrexate would be by far and away the most common in global practice, or they had been intolerant to a maximum of one prior TNF inhibitor. This was an active comparative study, one to one bimekizumab or risankizumab, risankizumab AP19 inhibitor. And what you should observe from the doses that are depicted here is that these are the licensed approved doses of these medicines. You may be asking if you are new to our field, "Well, why is there two doses for bimekizumab." Well, that is predicated and a higher dose requirement for those patients who have moderate to severe psoriasis. But you'll notice that in our cohorts that represented in the order of 30 patients in either arm who had that severity of skin disease. And that's because a majority of patients in psoriatic arthritis clinics actually have less frequent severe skin disease.

And this is something that Professor Merola and I can pick up in questions later on, just that juxtaposition of dealing with tissue domains. And then if you look at the bottom of the slide, you'll see that week 16 was our primary endpoint, and it was an arthritis specific endpoint, an ACR50. And of course, ACR50, there are three varieties of ACR. You can respond at the 20% level, 50% level or 70% level. And in years gone by when Joe was still at school and I was a young clinician, well, an ACR50 was an undreamt of primary outcome. We used ACR20, but now the confidence in the field has grown over the last decade, and really asking for primary outcomes that we believe will have clinical relevance, real resins in the community. And that's amongst other reasons why ACR50 was chosen. And then the study after week 24, it concluded the treatment period and there was, as would be required, a safety follow-up period.

Now I want to talk about the statistical analysis, which if you look at the next slide, is depicted, and you'll see this was the very common now in clinical trials, a hierarchical testing approach. And by this means we start with, "Well, what's the most important outcome?" And the first important outcome was, are these two drugs so similar to each other that they would be judged non-inferior? So that was the first outcome. And thereafter we asked the more provocative question, "Is one drug superior to the other when ACR50, a musculoskeletal outcome, is the sole chosen outcome?" Now thereafter in the hierarchy we moved on to the MDA, which is a composite measure capturing cutaneous, wellbeing and articular outcomes. And thereafter in the hierarchy, we moved to a combination of an ACR50 musculoskeletal outcome and PASI100, PASI is a measure of cutaneous psoriatic disease activity, the hundred depicts clearance.

And in the end, we would look off at ACR50 at week four. Now, the dark blue and light blue depict the fact that if you fail to move beyond a certain level of significance, everything else becomes nominal. That is when the statistical chain stops. So, let me tell you about the patients next, please, Deanna. The baseline characteristics are as depicted here. This is a pretty typical clinical trial cohort that Dr. Merola and I have looked at many times together, maybe highlighting around 20% of the cohort had previously

received a TNF inhibitor, and that as I've already indicated, only 10% of the cohorts had moderate to severe psoriasis. As for the rest of the characteristics, you can cast your eye down here, a pretty typical population of patients. And then the next slide we can have a look at what happened in the trial. So this is probably the most important slide of my presentation.

On the left-hand side, you're looking at the primary outcome, and in the blue, 49% of patients achieving an ACR50 at week 16, and in the red pink, my daughter and I always disagree in color choices. I hope we can all agree that red pink is risankizumab, 38% of patients achieving the ACR50, and that's this 11% delta to which Emmanuel referred just a few minutes ago. And for what it's worth, this achieved statistical significance and we'll talk about its clinical significance in just a short number of minutes. Now on the right-hand side of this slide, you're seeing the time course of achievement of response, and what I would say the color code is the same all the way through for ease of viewing. You'll see that over time there is a numerical difference achieved for the Bimekizumab as opposed to Risankizumab treated patients. And you'll see that the lines would appear to separate as early as week four and in fact a nominal hierarchical testing that achieves statistical significance. So let's look at the next slide. Let's move through that hierarchy. And this is the minimal disease activity, which is a composite outcome, seven different criteria. And you'll see that this was not met. And that therefore means that our formal statistical testing stops at the primary where we have clearly demonstrated superiority for the musculoskeletal outcome. But the MDA is although numerically different, as an academic, a clinician, I have to say that the statistical test was not met and therefore we cannot confidently say they are different in the purity of trial design. There are some nominal P-values depicted in here about, particularly in the early time points. We can reflect on this later on, but one should remember that an MDA is seven different measures which all have to change and some of them actually. So if you have no enthesitis at the beginning, no dactylitis at the beginning, if your different domains of disease impact you differently as an individual, well, there are actually going to be really quite different potential outcomes for you in MDA. So this is not an entirely unexpected result. So if we could move on now to the next slide, which shows you what happens when we combine the articular ACR50 with the cutaneous PASI 100 over time. The NRI stands for non-responder imputation. Put simply, if you don't respond, if your numbers are lost, if you've fallen out the study or that the value is not recorded, we consider you a non-responder. So that's a conservative analysis.

And once again, you'll see that there is a numerical difference over time, particularly through week 16. And by the way, I should say that those responses appear sustained through week 24. Looking at the next slide, you'll see now we focus in on PASI 100. You'll notice we don't have ACR 100. Rheumatologists weep with envy when our dermatologists report PASI 100s. We don't have that facility yet in disease representing unmet need, but how valuable to our patient population to have at least one domain of their disease potentially cleared.

And once again, I would direct your attention particularly to the numerically higher responses and perhaps at those early stages, clear early separation in the achievement of clearance of cutaneous disease. And we'll talk about this, but that clearance has a huge impact. Those last few points and clearance, a huge impact in the dermatology quality of life that patients can achieve. And remember, the patient has the whole disease, not just the joints. So although BE BOLD is about superiority in the joints, these other outcomes capture the totality of the human being who comes into our clinic. And in the next slide, please; we're thinking a little bit about DAPSA, an articular measure and this is DAPSA LDA, low disease activity, REM remission, again, predicted and projected over time. The prediction being non-responder imputation.

And you'll see once again, clear numerical separation, which achieves nominal significance. But please, I do refer you back to hierarchical testing for absolute accuracy. And finally to safety, we report here safety for the BE BOLD study and you'll see that there was no significant new signal of concern in this

study, as expected and pretty much mechanism related. There is a higher frequency of candida associated infections in those patients receiving Bimekizumab. This is something we've seen throughout the Bimekizumab development program and is mechanism predictive. But I perhaps would urge you when thinking about the safety of different modes of action, particularly at this stage in their development cycle to refer also to large databases where we have extensive evidence of the tolerability, safety, and challenges that we must look out for either with P19 inhibition or dual 17A/F inhibition.

Next slide, please. So in conclusion, ladies and gentlemen, the BE BOLD study is the first head-to-head trial that has shown superiority on a pure musculoskeletal outcome between different modes of action in the treatment of people with psoriatic arthritis. That outcome was achieved at week 16. We are, of course, looking at an ongoing basis and we'll be discussing those data at a later time, but not today. We saw in the secondary outcomes because of the a priori statistical analysis program, only nominal values attributed to that, but there were a number of outcome measures which appear to support the superiority of Bimekizumab, at least at the clinical numerical level. The safety profiles are acceptable and commensurate with what we have seen before in other studies. And we find these really rather interesting because this will help us in due course to guide our treatment decisions. And those treatment decisions are partly, I think, what I'm looking forward to hearing about momentarily from my good friend and very learned colleague, Professor Merola.

So Emmanuel, let me hand back to you. And I thoroughly look forward to the conversation to come. Thank you very much for your attention.

Yvonne Naughton:

You're on mute, Emmanuel.

Emmanuel Caeymaex:

Okay. Thank you. Thank you very much, Ian. And Professor Merola, welcome.

Professor Joe Merola:

Thank you. Thank you.

Emmanuel Caeymaex:

Just got back from EULAR, I imagine, back in Texas.

Professor Joe Merola:

Yes. Ian and I were just commenting on our pure fatigue and exhaustion. So hopefully, he's coherent post EULAR, but some of us may be less so anyhow, so.

Emmanuel Caeymaex:

Great. So perhaps to start, could you describe the type of patients that you typically treat in your practice? And acknowledging that, obviously, you're one of the key researchers in the field of psoriasis and psoriatic arthritis.

Professor Joe Merola:

Yeah. No. And thank you for the invitation to be here. I'm quite pleased to be part of the program and chat a little bit with folks, hopefully give some insight. So I'll take a step back. So I am a little bit of a unique bird in having the dermatology and rheumatology perspective and I'm happy to try to walk that

line and share a little bit of where perspectives align and where they may align less so. I think for me in my practice, I see a very broad range of patients with psoriatic disease. I'm in an academic setting, but yeah, so we certainly see folks who have predominant skin disease all the way through to early musculoskeletal symptoms, to those who have multi-domain and difficult to treat disease that are being referred to me, to us for complex management. Maybe for level setting, if I may, Emmanuel, I'll just remind folks that when we think about psoriatic disease, psoriatic arthritis, we typically take this sort of domain-based approach.

So we're thinking about patients with peripheral arthritis, enthesitis, dactylitis, potentially spine involvement, axial disease, nail disease, plaque psoriasis, and even there we could sort of unpack subsets and subsets. So we're seeing all of those patients and they're across the heterogeneity of disease and their involvement and we see new starts to systemic therapy all the way through to, again, folks who have tried everything and they're sort of coming to us for what do we do now? To answer your question maybe again a little bit, how do we think about our treatments and approach to treatment in this, sort of a clinic setting?

And I think it's very much about which of those domains of disease are involved, because again, every patient may have variable involvement, although many patients have more than one area of involvement. We try to align the treatment with comorbidities, whether it's to try to treat or at least align with comorbidities that they may have as part of psoriatic disease, of course, safety tolerability. I think you saw the reassuring data from my colleague a moment ago from at least the BE BOLD study, but we can talk about that a little bit more in a global sense. And then patient preference and then in the US, and I'm sure in lots of other areas we have to align with access. But for all of these reasons, I think there's some complexity here, but we appreciate therapies where we know that we're sort of treating and firing on all cylinders, where we can treat across the full breadth of domains of disease, where we have good safety tolerability, we meet patient needs and align with their preferences very well.

Emmanuel Caeymaex:

Thank you. And obviously, these comparative studies don't happen every year in psoriatic arthritis. So I was wondering how the BE BOLD study might influence your prescribing practice in your setting.

Professor Joe Merola:

Yeah. I'm happy to take that too. And I'm glad Iain already commented on this. So put my dermatology hat on for a moment, that all of my rheumatology colleagues are so jealous of the plentiful head-to-head studies we have in psoriasis and we have these beautiful network meta-analyses based on oodles of data. And here in PSA, we have had to date almost nothing really, very, very little, and Ian sort of outlined that. So I think it's incredibly important and we're very grateful to UCB for having done... I'll be, pun intended, right, being bold to put this study together, but it really is important for us for many reasons, which hopefully I'll cover. I think if I'm honest, it does reinforce what I knew clinically. I mean, I don't think there was a deep surprise in the outcome of overarching efficacy here. And I'll tell you a little bit what I mean, but I think I had the data points in the past based on other items of differentiation, axial disease, inhibition of radiographic progression. Right.

There were other things that were not looked at in this study that have informed my opinion historically about the class and particularly in this population with psoriatic arthritis. I think for me, in addition to reinforcing what I believed clinically, which is important, we really need these kinds of high quality data to inform our field and these are the kinds of data that we look for when we're talking about treatment guidelines, developing treatment guidelines in the US, internationally. When we put NMAs together,

these data weigh heavily because they're very high quality data in a very well controlled setting. And so, for me, it really jogs not only what I do, reinforces what I believe I knew to be the case, but I think it will really help the field move forward and have conversations with my colleagues in a data-driven sort of manner.

Emmanuel Caeymaex:

Indeed. And yeah, we're glad to contribute to this comparative body of evidence in psoriatic arthritis and psoriatic disease in general. Now one of the questions is how clinically relevant is this 11 percentage points difference on the primary endpoint?

Professor Joe Merola:

Yeah. Similarly, Iain touched on this a bit too. We have a hard time, by the way, moving the bar in psoriatic arthritis. So we will take every edge and lead that we can get for our patients with psoriatic arthritis. Again, a little bit distinguishing maybe from the skin arena where we've been able to really push the bar and we're talking about PASI 100. Iain alluded to that. I think it's an important time to take a step back and to ask a little bit also about how does time matter. I would say not only is it the delta that we saw, but it's the fact that it separates early and that that's sustained out to week 24. For many years, I think anyone in the field has heard, quoted a very famous study that with a delay in diagnosis and delay in treatment of as little as six months, we saw very significant differences in patients with regard to damage, bone erosion, function, loss of function, quality of life impact.

And that's been the case for decades. We've been talking about that and there was even a, sounds like a bit of marketing, but yeah, I think we had heard over and over again that time is bone, that time matters. And I think really this idea that patients want to be better sooner, that we make decisions as clinicians increasingly earlier time points I think makes all of this data very relevant. So yeah, patient symptoms are going to be impacted by this in a relatively short amount of time. And I think the one thing we haven't had a chance to see, I know Iain and I will both be excited to continue to unpack this data, but is additional PRO data over time to help us unpack as well what this means for patients.

Emmanuel Caeymaex:

And obviously there's details about the study which not everybody may be aware about. So let me just say something around dosing, right? So in psoriatic arthritis, Bimzelx is dosed 160 milligrams every four weeks, right, from the very beginning of treatment onwards.

Professor Joe Merola:

Yes.

Emmanuel Caeymaex:

Whereas in psoriasis, for the first 16 weeks, it's doubled that dose. Now as Professor McKinney's mentioned, about 85% of patients were treated at the psoriatic arthritis dose, so the lower dose. So given that that is the fact, to what extent were you surprised to see the level of skin clearance at that dose versus perhaps the dose that is usually used in psoriasis patients?

Professor Joe Merola:

Right. Well, I think that the focus of this study, if I'm honest was, it's meant to be a PSA study, PSA endpoints. We also know... I prefer to get my skin data from psoriasis studies. I can put my dermatology

hat on for a moment because we know it's a different population. These patients have lower in the PSA study and no different in the BE BOLD study, they have low BSAs. The vast majority of these patients, I don't want to misquote, but I think only about 10, 11% or so of the patients in this study actually had moderate to severe psoriasis, which is why such a small percentage received the dose you mentioned a moment ago Emmanuel. I'll comment on the data here, but I think it's also, I've derived my impression of it being a highly effective skin drug, arguably one of the highest efficacy skin drugs we have based on the psoriasis data to date. I think the fact that it is behaving as well as the psoriasis dosing of one of our other most highly effective skin drugs I think is very much reassuring. I reach for the full dose whenever possible in our patients with psoriasis. I think we always want to be best foot forward and with such a good therapeutic window here where we get such good safety efficacy, I always lean into the higher dose where appropriate and in a patient base where they tend to be higher weight, et cetera. I think the full dose really has provided some of the best data in the field. As an aside, I enjoy teaching. I have a lot of residents and fellows around me. One of the things I've told them is I like to quiz them on what the PASI 75 is in the psoriasis data for BIMZELX and it's approaching 100%. It means that I can almost guarantee almost any patient that I see that they will improve. And here we are looking at PASI 90 and even PASI 100 data.

So I think to answer your question again, I think the half dose is impressive in what it can pull off. And for our patients with skin predominant disease, the full dose is really some of the most robust that we have in the field. So I would contextualize it around this being a PSA study.

Emmanuel Caeymaex:

Yes. Thank you exactly, which it is. And you were presenting in front of a full room at EULAR on the last day and apparently there was a waiting line which some of my colleagues described to be like a waiting line outside of a London club on a Saturday morning. So it certainly attracted a lot of attention. So across efficacy or safety, was there anything else that you heard from colleagues or that you picked up in the convention center before or after the presentation of those results?

Professor Joe Merola:

Yeah. Well, first off, I will acknowledge and own the pressure cooker there. It was packed indeed. It was a huge swath of people, as you mentioned, outside all listening with earbuds. And so it definitely raises one's blood pressure and heart rate, to say the least, at the podium. But no, I think there was a lot of enthusiasm. I think it underscored, to me, I have my bias, but I think it was one of the most important data drops at the meeting and people really were eager to see it. They stood around to the very end of the meeting in many cases to hear the data. So I think that speaks to the unmet need for these data and how people hopefully will be viewing them and will take this back to their clinical practices ultimately.

Emmanuel Caeymaex:

Thank you. Thank you very much. So we'll stop the fireside chat here and give everybody on the line an opportunity to ask questions. And so I'm sure we have a system to identify who raised their hand first. And so let's see.

Moderator:

Ladies and gentlemen, we will now begin our Q&A session. If you have a question, we ask that you please use the raised hand function at the bottom of your Zoom screen. Once your name has been announced, you may ask your question. If you want to withdraw your question, please lower your hand using the raised hand function at the bottom of the Zoom app. Thank you.

Our first question comes from Stacy Ku at TD Cowen. Stacy, you may now unmute your line and ask your question. Thank you.

Stacy Ku:

Can you all hear me okay? Yes, I see it. Okay. Well, good morning, good afternoon and thanks so much for taking your questions, a wonderful presentation and fireside chat. So we have a few follow-up questions for Dr. Merola and Dr. McInnes first before a question to Emmanuel. First, Dr. Merola, following up on Emmanuel's question on EULAR and the community response, as we think about the US, just maybe help us understand what percentage of rheumatologists view the IL-23 class as differentiated to IL-17s in joints and how would you expect the study could change prescribing? So this is the first question.

And then the second for both doctors, Merola and McInnes, as we think about the rheumatology angle, how do you expect other clinicians will balance the decision making of BIMZELX versus other 17s, obviously excluding access? So that's our second question.

Our third is to Emmanuel. To the extent that you can comment, just help us understand as it relates to the US, what kind of potential payer dynamics we might see when it comes to the BE BOLD advantages. Is it more on the rebating side or more on the access side? Do you expect this is going to have ramifications as it relates to the rheumatologist's view on IL-17AF? Just help us understand as both of these classes of physicians are treating the psoriatic arthritis patients. Thanks so much.

Professor Joe Merola:

All right. I believe I'm kicking off and I'll try to repeat the question since we had a roll of questions. As I understood the question, it's about my US colleagues. I think this is a globally relevant answer, but how my US rheumatology colleagues view these two classes with regard to PSA. So look, I'll start first with our little microcosm because I can't speak to every community rheumatologist's view, but I think among the PSA expert community, I think we think of the IL-17 class in general and in particular and above IL-17AF opportunity as really the go-to and I would even argue best balance of efficacy, safety tolerability for psoriatic arthritis. I truly believe that because we have the experience to date both in the clinic but also the data, everything from what Iain shared earlier in SPIRIT head-to-head where we learned that IL-17 inhibition was as good as our gold standard TNF in joints, but far superior in skin, nails, et cetera, has borne out.

I think that some of the gaps in data historically around radiographic progression, around axial disease, et cetera, I think has elevated the class around psoriatic disease, psoriatic arthritis. I will say on balance that I think in recent time, not so much risankizumab, but guselkumab has shored up the value of IL-23 and psoriatic arthritis through a number of studies, but I think that underscores why these data are so important that we have a look at head-to-head data as it relates directly to our patients with peripheral joint disease and using a joint focused clinically meaningful outcome like ACR50. So for me, this is very timely data to really solidify our impressions of IL-17, IL-17AF adjacent to IL-23 inhibitors in PSA.

Iain McInnes:

Yeah, I'll maybe just add to that. I think there were three questions. I'll come in on that middle one, which is Emmanuel will be the master of where the marketplace lies in all of this, but it's a very interesting question as to whether clinicians in the field perseverate all day and night about how cytokines work. And sadly for me as a clinician scientist, I suspect it's rather little. So let's think about what does guide clinical decision making and I'm just going to build a little on what Joe has said. Well, the first thing is recommendations and guidelines at the international and the national level. So we have

guidance from ACR, we have guidance from EULAR and we have guidance from GRAPPA and it's always worth. Remember there's the third group out there in terms of advising on therapeutic decision-making in psoriatic disease. And then I also want to pay due respect to other societies in the global stage, particularly in Asia, who by large line up close to where EULAR and sometimes ACR lands.

So the first thing is that those recommendations and guidelines will be impacting and practice and we will expect a little time for BE BOLD to get into those recommendations. We have to accept that. The flip side is that there were lots of people wanted to hear Dr. Merola talking Saturday at the EULAR congress and that's partly because he's a charismatic, brilliant speaker and a really smart guy, but they were also there in addition to that because they wanted to know the answer. So just to reemphasize, the question I think touched on the, do clinicians see this as one general bundle? Well, I think in the past they possibly did. When I went out and talked to clinicians, they'll tell them about TNF inhibitors. They'll talk about oral inhibitors. I think Janus kinases, to some extent, maybe PD-4 apremilast.

And I think they were taught to think We used to hear a lot about the IL-23, IL-17 axis, that's what was talked about. And the cutaneous psoriatic studies that Emmanuel alluded to earlier on have clearly shown that that is not a fair bland landscape, that actually you can differentiate in head-to-head trials in the skin when you're comparing bimekizumab with a pure 17A inhibitor or for that matter with the TNF inhibitor or with ustekinumab P14 inhibitor. BE BOLD tells us that if you then do a head-to-head for musculoskeletal, ACR50 being the primary as we've now well described today, that actually now differentiates in the musculoskeletal compartment. And I think that will be quite impactful.

But can I say something and with due respect to our host, UCB, we're not saying that risankizumab or the p19 inhibitors are not good drugs. So for Joe and I, as clinicians who are balanced clinicians in the field, they're excellent drugs. That's probably why the MDA didn't differentiate in BE BOLD because actually risankizumab is a good anti-cutaneous psoriasis drug and it also has proven efficacy and is in the marketplace because it's effective in people with psoriatic arthritis with musculoskeletal domain disease.

The point here is that bimekizumab may offer a bit more and that was the clinical value that Joe and Emmanuel talked about just a few moments ago. And I think BE BOLD will add to a literature. It will build that momentum for thinking about distinct modes of action at distinct stages of clinical decision making. I think the early impact will be the publicity and impact of BE BOLD, both at EULAR and the subsequent publications. And then in due course, it will be felt as recommendations come through.

Emmanuel Caeymaex:

Thank you.

Moderator:

Thank you.

Emmanuel Caeymaex:

Very good questions as usual. So in terms of payer dynamics, I would say that it depends a little bit on the payers, but as you know, they have clinical evaluation groups who put a lot of emphasis on the type of evidence we have just been producing. So randomized controlled studies, superiorities, so you don't need to go through a common placebo response to derive the relative efficacy between different drugs. So it will really help those colleagues within the payer groups to defend a position that ultimately should support giving patients early choice and giving physicians choice across these various therapies.

Today in the US, there's actually more use in new and switch patients of IL-23 inhibitors than of IL-17A inhibitors in psoriatic arthritis. So you can see that the community is heavily influenced by DTC, by access, by of course, the quality of the data. And so it's important for us to be able to illustrate that there actually is a difference when it comes to joints and we've demonstrated that in a prospective manner and the 17A and F class, which Bimzelx is the one and only that's approved, can thus benefit from this and really set itself apart from a class and in particular the drug we compared against here that has been gaining substantial share over the last couple of years.

Now outside of the US, it will help us divorce Bimzelx from other molecules. And as you know, there's these practices to look across different classes of interleukins as price adjustments get made very much in a top-down fashion with limited space for negotiation for pharma companies. But this type of evidence really gives us a tool to ensure that the price revisions are limited and that we can argue based on clinical effectiveness since that is what is being valued and looked at.

In the US, in terms of pricing, it's hard to kind of unravel what is pricing and what is positioned in a formulary, but clearly those landmark studies like the one comparing Bimzelx with Cosentyx in psoriasis are the most important ones to either open up access or maintain access at a decent net price.

Stacy Ku:

Thank you so much. Really appreciate it.

Moderator:

Thank you. I request to keep questions to one to two to give everybody the opportunity to ask their question today.

Our next question comes from Xian Deng at UBS. You may now unmute your line and ask your question. Thank you.

Xian Deng:

Hi, thank you for taking my question, so just one please. I mean, we heard this number many times, like roughly 1/3 of psoriasis patients actually have PSA, but just wondering how about the other way around? So how many actually PSA patients actually have skin problems? Do all of them have some degree of skin problems? And what I'm trying to understand is that to both professors, so just wondering what do you think is the best way to utilize the BE BOLD data here? Do you think this is better utilized to just make bime the go-to in PSA or do you think you should also go to the dermatologist colleague and have some sort of way of identifying psoriasis patients who are very likely to develop joint symptoms and then utilize the data push there? So yeah, thank you very much.

Professor Joe Merola:

Sure. Well, thank you for the question. I'm happy to start and Iain can correct me and/or keep me honest, but I will say that the vast majority of our patients with psoriatic arthritis have some form of skin disease, whether it be plaque disease, whether it be nail disease. That said, certainly most do not have moderate to severe plaque psoriasis, but instead, as you see from the trials and real world registries and datasets, that it may be mild psoriasis in the context of psoriatic arthritis as previously defined. That's an evolving landscape as well, how we define mild psoriasis in terms of impact on disease and such. I'll spare you the long-winded point about that. But I think to your point about maybe the dermatologists and then maybe Iain or others want to comment more about the rheumatology view on this. I think many of my dermatology colleagues, to be honest, would say, first of all, they want to know that they are treating the joints when they're treating the skin. They like the reassurance that they're checking a

box to that end. So they know that they're using a drug that is approved for psoriatic arthritis. Many of them do prefer to see that the reassurance that there is inhibition of radiographic progression so that they feel as though they're not missing a gap in some way. I've heard that from many of my colleagues. I think that that's real. On the flip side, many of my, again, derm colleagues would argue that the patients that they are seeing in their clinics are not necessarily, to be fair, the BE BOLD or even most of the pivotal PsA trial patients in that they aren't necessarily running to the dermatologist if they have 10 to 20 tender swollen joints, for example. They would say, instead, I'm seeing the patient with enthesitis or maybe a few joints or the achy patient who I'm concerned has PsA but I'm not sure, or they seem to have early PsA. So I do want to be balanced on that front because I think that this is practice informing for those seeing PsA. It should inform my derm colleagues who believe a patient in front of them might have PsA, especially that fits this profile. But I do think there are different subpopulations of patients that you're alluding to. Those with skin predominant disease, those with severe PsA, those with maybe more mild PsA, but severe skin disease. And I think we may think about them a little bit differently as well. But Iain, maybe you want to say something more intelligent or at least, you know.

Iain McInnes:

That's a highly unlikely eventuality, Joe. Let me just be quite succinct and add a couple of things to Joe's excellence answer. Number one, there is a syndrome of psoriatic arthritis sine psoriasis. The history books tell us it's about 5% of patients. That number varies depending on where you are and what you're not. And that was a group of people whose joints looked like PsA, but there was never any obvious or good evidence of a skin lesion. Now, whether that's because the skin lesion was missed or never disclosed or transient, we don't know. And Joe's telling me that I don't even, I wouldn't recognize a psoriatic plaque if it was 10 centimeters in front of my nose as I think what Dr. Joe is saying there.

Professor Joe Merola:

Not at all. Although I will go on record, Iain, I think a lot of those are missed to your point.

Iain McInnes:

I agree.

Professor Joe Merola:

One has to go looking, searching, but carry on. Yeah.

Iain McInnes:

No, no, I agree completely. The second part of your question was about prevention that implicit in your question and the answer is that that is work in progress. And I do not think we yet have an evidence base that can support a strong argument for disease progression and trajectory interruption for any mode of action. And that is not what BE BOLD was about, nor what the discussion today is about. Very good question, but that's not an evidence base that we can offer you at this time. And thirdly, just developing very quickly, Joe's comment. We now advise that clinicians treat the domains of psoriatic disease and you'll hear, I'm using that word quite, psoriatic disease. It's a clinical collection of tissues that are involved. And I think what you heard from Joe was that we also advise clinicians to use the best evidence base for each domain of disease, which is why when we tend to go to the pure cutaneous psoriasis head-to-head trials to guide, well, what's the best MOA for a skin dominant patient?

And that's why BE BOLD is quite interesting because now we have a head-to-head where we can say, "If I have a choice of MOAs and somebody with mainly musculoskeletal or musculoskeletal troubles, some

problematic disease, I can now say, "Well, here's evidence that this MOA may be better than that." And I'll pause there, but that domain-driven therapeutics and that is going to drive the treatment disease in the next five years and having this quality of evidence to guide one MOA versus another is really hugely helpful to us.

Moderator:

Thank you. Our next question comes from Peter Verdult at BNP Paribas. Peter, you may now unmute your line and ask your question. Thank you.

Peter Verdult:

Hello.

Moderator:

Hi, Peter.

Peter Verdult:

Can you hear me? Sorry. Apologies. I'm in New Orleans at ADA, so apologies for any of the background. Thanks to all the speakers for your time, people of BNP. Just two, the minor one of the clarification is a backward looking commercial question Emmanuel, not forward-looking, but just I think Rheum is around 20% of BIMZELX sales in '25. Could you just pass out of that, what is psoriatic arthritis in 2025? And then my main question is for the doctors, both the doctors really. Can I just put you on the spot? I'm still not sure how you're using Bimzelx today. Ballpark, what percentage of your psoriatic arthritis patients you're using Bimzelx in today and how that might change if I could push you on the back of the BE BOLD data, what sort of ballpark changes might we see if I take you to as an example? Thank you very much.

Professor Joe Merola:

Emmanuel, maybe please.

Emmanuel Caeymaex:

I'll just start with a question on within the rheumatology indication, psoriatic arthritis is by far the largest one. It's a bit different in the US and in Europe where it's a bit more balanced, but I would say globally it's probably 3 to 1.

Iain McInnes:

Joe, do you want to...

Professor Joe Merola:

I'm happy to start. I mean, it'll seem biased to the call, but I will say honestly that I have every reason to use Bimzelx as a first-line agent in my PsA patients and we certainly try to get it for our PsA patients whenever possible. I'm talking about new starts or folks who are not doing well on other agents in particular, those who may be on TNF-23 or even other IL-17A drugs who are not fully controlled. That said, I will say that payers don't always agree with me. I mean, I sit in Dallas, Texas. I can't speak to every region of the country, but by medical decision-making, I consider this a go to drug.

I know that I'm going to win the confidence of my patients early with these drugs. It gets them clear quickly. It makes them feel better quickly. That drives adherence. It makes us feel good doing what we do every day and so I have no reason not to have it as a first line drug. That said, I will say that we will often get some pushback and have to back into other MOAs because of payer requests, not for clinical want. That's just the reality in my microcosm locally.

Iain McInnes:

In the interest of time, I shall simply say that very similar arguments pertain in other country and PR regions. This is a compelling mode of action. The head-to-head data are helpful to clinicians in making decisions, but one has to remember that this is a multifactorial conversation and it is very difficult to predict what one trial will do. Having said that, over time, as that percolates through into guidelines and recommendations and when payers take that on board, that's when we would hope to see the impact more, obviously.

Moderator:

Thank you. Our next question comes from Charles Pitman-King at Barclays. Charles, you may now unmute your line and ask your question. Thank you.

Charles Pitman-King:

Hi, guys. Charles Pitman-King from Barclays. Thanks very much for taking my questions two from me. Just briefly a clarification on the treatment guidelines expectation. I'm just wondering when you would expect these treatment guidelines to account for the BE BOLD data and then how quickly you would expect that to be reflected in prescription uptake. Noting, obviously, you already previously perceived Bimzelx as a preferred first-line treatment. I'm just wondering when you would expect any change from that. And then just secondly, my question relates to the longer term durability of the delta. Obviously, slide 13 showed a sustained delta to Risankizumab on ACR50, but then we saw some catch up on PASI 100, noting obviously the speed of onset advantage versus the candidiasis safety disadvantage. What are your thoughts on the potential for Skyrizi to catch up on the ACR50 endpoint on a longer duration for these chronic patients who need long-term treatment? Thank you.

Professor Joe Merola:

Yeah. I may leave the second part from my colleague who presented the data, if that makes sense. To your first point, I'll just say, I think it's okay to share that both the GRAPA guidelines are in progress for a refresh presently. And I believe these data likely would inform those, though I can't say for certain. The ACR guidelines are also due for a refresh this year and would not likely be out this year but subsequently. So I'm hopeful that these data would inform those committees and there is a current refresh. I think that's the best I could certainly say on that front. I can't speak to EULAR, Iain may know, but this is the kind of data certainly that makes it to the SLRs and if not, hopefully would be reviewed by committees because of the high quality head-to-head nature of the data.

Iain McInnes:

Yeah, I wouldn't wish to speak for EULAR. They'll make their own decisions public in due course. I wouldn't like to overemphasize though the BE BOLD disclosure will influence practice from the word go. It will be in the mind of clinicians next week when they're facing that decision, which MOA do I go for within PR recommendations in a local area. The wider impact consolidating that in practice does tend to go with recommendations and that influences the medium term of how different MOAs will play out.

Your second question, if I can very briefly deal with it. I showed you today that there continues to be by and large numerical separation. We will be disclosing in due course later in the year how the longer term follow-up for the study plays out with one MOA against another, and that's because it takes time. And Paracelsus in the 1400 said, "The physician's very friend in time is time."

And so too, this is our time. We just have to see how it plays out. But we did disclose data today up through week 24 and you see that by and large, the lines are still numerically separate. That's a different conversation for a different day. Your remark around trade-off though for efficacy against safety, by and large, candidiasis is a very well managed and by and large tolerated adverse event, which very rarely in clinical practice leads to cessation of therapy. And my judgment would be that it is unlikely that there will be a realistic trade-off for candidiasis against the use of this mode of action.

Moderator:

Thank you. Our next question comes from Kerry Holford at Berenberg. Kerry, you may now unmute your line and ask your question.

Kerry Holford:

Thank you very much. Two for me, please. We noted that the ACR50 results for patients on both arms of the BE BOLD study looked better than we had seen in the original pivotal trials for both of the drugs. Just curious to hear your views here from the physician perspective, any proposals as to why, whether the way in which outcomes have been measured, assessed, has differed over time. And then my second question is on the topic of the secondary endpoint, MDA. Professor McInnes, you touched on this briefly, but intrigued to hear your view as to why statistical significance wasn't achieved on that measure. And I guess given the complexity of using a composite score, which I think you said consists of seven individual measures, was it the best secondary endpoint to use and how influential is that composite score when it comes to the regulator and physician prescribing?

Professor Joe Merola:

Iain, do you want me to...

Iain McInnes:

You take the first piece. I'll deal with the second, Joe. How does that sound?

Professor Joe Merola:

Sure, sure, sure. So I will say in any of these studies where we don't have a placebo anchor and we have two open treatment arms, we certainly see some upward drift and this is across many studies and we can imagine the psychology of both the patient and assessor in these dynamics and in these studies. So indeed, I do think it's some of the best data including for Risankizumab that we've seen to that end. But we certainly do see this. We see this in these functionally open labeled studies where everyone knows they are on active drug and such. So a little bit, it is what it is and I think it's hard to unpack that any further, but it certainly is a known epidemiologic trend. And then Iain can comment on MDA. I think it's really an endpoint that's meant and has been used in placebo controlled studies to be able to show a difference, but I'll leave that one to him.

Iain McInnes:

Yeah, there was a poster in the poster tour at EULAR Congress in London last week from OMARAC demonstrating that MDA does perform well when compared to placebo. It didn't consider the situation with active. It's a very astute question, if I may say, but if you could remember that this trial was powered to show a difference for a musculoskeletal outpoint. It was not part to show a difference in a cutaneous outpoint. So we wouldn't have necessarily predicted superiority to come through if some of the outcomes which are contained in the MDA are cutaneous as they are. So in fact, the MDA is a state to which we aspire to get the patient.

I think it was a perfectly reasonable choice of endpoint in the statistical testing. One seeks, first of all, your primary subject of interest, in this case, musculoskeletal disease, and then one seeks a state. Actually, I guess UCB could have moved some of the outcomes around potentially to their own advantage, but they chose not to do that. The way the trial was designed was to say, what is the difference in musculoskeletal outcome and does that then land in state? So I think actually the choice of hierarchical testing is pretty defendable and just again, allows me to reemphasize the head-to-head comparison here. The unique element in BE BOLD is demonstrating the superiority in the musculoskeletal compartment. MDA is really asking and addressing a different question. So although the question is astute and well-taken, it's not really what the trial was all about.

Moderator:

This concludes today's Q&A session. I will now hand back to UCB for any closing remarks. Thank you.

Yvonne Naughton:

So I'd just like to thank everybody for coming on the call today and if anybody has any other questions, we can take them after the call. Thank you very much.