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Fireside Chats: Top Abstracts Related to Axial Manifestations in SpA

Chapter 1: Use of the BASDAI in Psoriatic Arthritis Patients With and Without Axial Disease

Announcer:
Welcome to ReachMD. This Medical Industry Feature titled, Fireside Chats: Top Abstracts Related to Axial Manifestations in SpA, is sponsored by Novartis Medical Affairs.

Dr. Laura Coates:
So, welcome to the ACR 2020 Fireside Chats. We're here for the next hour, for half an hour thinking about spondyloarthritis and then half an hour moving on to Still's Disease. So, my name is Laura Coates. I'm an associate professor at the University of Oxford, and I've been there for 3 years having moved down to Leeds. My particular interest is in psoriatic arthritis and I'm presenting today with Alexis.

Dr. Alexis Ogdie-Beatty: Hi, I'm Alexis Ogdie from University of Pennsylvania. I'm assistant professor of medicine and epidemiology there.

Dr. Laura Coates: So, this presentation is sponsored by Novartis. We really appreciate Novartis giving us the opportunity to share work from ACR. Novartis determined the topic areas, so thinking particularly around the axial side of spondyloarthritis, including axial PsA and then in Still's Disease, but within those topics, we've been given free reign to select what we felt were the most interesting abstracts from the meeting this year.

And so, between each pair in the different subject areas, and we've selected these top abstracts to talk you through and talk you through why we chose these to discuss today. So, it's a summary of the data that has been presented at ACR. I think one that's due to be presented tomorrow, but really represents our views on why these are important and what we've learnt. And we'll take back from the research that we've seen this year.

Dr. Laura Coates: So, these are our disclosures.

Dr. Alexis Ogdie-Beatty: All right, with that I'll get started in take away with the first abstract. So, the title of this abstract is "Use of the BASDAI in Psoriatic Arthritis Patients With and Without Axial Disease." This was presented on Friday as a poster. This is from our cohort in the United States. I can go ahead and advance to the next slide.

So, this is a longitudinal cohort study among patients with psoriatic arthritis. Patients are enrolled at any point in time so they can start therapy at a second visit or first visit. We chose to take a visit where patients were starting or changing therapy and then followed forward in time. This data counts from 2017 to January 2020.

We divided patients into 2 groups, patients who have axial disease and those who do not. And we defined axial disease in a variety of ways, but the way we're presenting here is axial disease is defined by either the clinician saying that the patient has axial PsA or that they have MRI, x-ray, or CT features of sacroiliitis or spine disease consistent with axial spondyloarthritis.

So, then what we did is we looked at differences in baseline scores among BASDAI items. So, here you can see just a few of these samples. We have the full BASDAI: the spine pain, stiffness, patient global, patient pain and RAPID3, just to get a sense of how other things were different. And we looked at the baseline score, mean baseline score by whether or not the patient had axial disease.

Now it was important to note that most of the axial patients also had peripheral disease. There's relatively few that had axial disease alone. So, these patients all generally also had peripheral disease. So, what we found is that the scores at baseline were not that

different between patients with/without axial PsA.

Then we looked at change over time in these individual items, as well as the BASDAI as a whole. And we looked at this among patients who were initiating therapy and it was specifically either a TNF inhibitor or an IL-17 inhibitor. And then followed up with their next visit somewhere around 16 to 24 weeks on average after that first visit and repeated the BASDAI, as well as these other scores. We then looked at the SRM or standardized response mean. So, that's the mean change divided by the standard deviation to give a same score across all different measures. And what you can see here, also, so much of the graph above, that there was really no significant difference in change in the BASDAI as a whole or individual items, including specifically the spine question BASDAI by whether or not the patient has axial disease.

So, maybe I'll let Laura throw out some points about why this is important or what we think is important about this.

Dr. Laura Coates: Yeah, so, I think axial psoriatic arthritis has become a really hot topic recently, and there's been a lot of interest around spinal disease in PsA, at least partly driven by the differential response that we see with some biologics that seem to work for the peripheral disease, but maybe not for the axial disease, or at least where there's some debate about that.

And there's been a lot of work looking at secondary outcomes, including BASDAI scores in psoriatic arthritis disease studies, and kind of using this to argue that there is a response to a drug based on BASDAI in patients who have predominantly peripheral disease. And I think this study, along with some previous studies, but this is probably one of the larger ones now really shows that, that we shouldn't be doing that, that BASDAI is a really helpful patient-reported outcome measure. It's something that we rely on a lot in clinical practice for axial disease, but it's really heavily influenced by peripheral joint disease. So, it's basically behaving just like a global VAS score. It's not specific to the spinal disease. As Alexis has talked you through here, even if we look at specific questions, so the question specifically about pain in your neck, back and hips, still doesn't differentiate between the peripheral and the axial patients. So, I think it's a real caution around using outcome measures. And this idea that it's very hard to separate out the different domains of PsA. It's really important to do so when we're thinking about choosing therapies and looking up which therapies work for which elements of the disease, but it's really hard, especially from the patient perspective, for them to accurately separate out the different aspects of their disease.

Chapter 2: The Relative Diagnostic Utility of Inflammatory Back Pain Criteria in an Inception Cohort of Patients with Psoriasis, Iritis, and Colitis Presenting with Undiagnosed Back Pain

Dr. Alexis Ogdie-Beatty:
Yes. Great. We can move to the next one.

Dr. Laura Coates:
Okay. So, the next one, definitely following on the theme, looked at the relative diagnostic utility, utility of IBP criteria, inflammatory back pain criteria, in an inception cohort of patients who presented with a risk factor for spondyloarthritis, so psoriasis, iritis, and colitis, but then presented with undiagnosed back pain.

So, if we look at the data, you can see this is from a large European study looking at patients who were under 45, had at least 3 months of back pain and some sort of risk factor or extra-articular feature of axial spondyloarthritis. So, they're clearly a high-risk group, as opposed to the general population where an awful lot of back pain is going to be normal mechanical back pain rather than inflammatory back pain. And they use different IBP criteria. So, you can see here, the ASAS, the Berlin, the Calin criteria to look at whether the IBP criteria could actually predict or decide who was going to end up with a diagnosis of axial spondyloarthritis.

And that was done according to the physician. So, this is using the physician as a gold standard. They were asked after clinical examination and history, “Do you think this is axial SpA?” Then the patients got labs and radiography and they were asked again, “Now, do you think it's axial SpA?” and then potentially an MRI as well. So, it was at different stages in that diagnosis process.

And this slide shows you the rheumatologists diagnosis as the external reference. And you can see that the sensitivity is pretty good. So, an awful lot of people with sacroiliitis, with active axial disease will have positive IBP criteria, but the specificity is really poor. So, actually having inflammatory back pain as defined by these criteria, isn't particularly good at defining who's going to end up with a diagnosis of spondyloarthritis.

And then on the next slide, you can see the same data, but this time looking at MRIs. So, if you look on the graphs on the right-hand side, this is using MRI as the gold standard rather than the physician, but basically shows the same thing. So, reasonable sensitivity, obviously a little bit lower because not all of those patients will have the positive MRI, but again, the specificity, which is the one underneath is really quite low, you know, less than 40%. So, not particularly helpful in picking up whether this is axial spondyloarthritis.

And if you look on the left-hand side, you can see the different criteria. So, whether it's ASAS, Berlin, Calin, or the global score, and whether it's the different risk factors, so the psoriasis or the uveitis or the IBD, really doesn't make much difference. So, again, more

caution about using clinical measures in axial spondyloarthritis. Alexis?

Dr. Alexis Ogdie-Beatty:
Yeah, I think this is, like you said, very similar to the last one and that's kind of a cautionary tale about using different definitions of back pain. So, a couple of things here that first of all, if you have uveitis, psoriasis or IBD and you have back pain and you're of the right age, and we're already talking about a high pretest probability of you having axSpA. Now, if we think about every single thing we do in medicine is a test. So, if we're asking a question, you can consider that as a test or physical examination, that's a test. So, they looked at applying IBP criteria as a test, and it calculated likelihood ratios for that as well in this study, and found that the likelihood, positive likelihood ratio, if you have a, like psoriasis, let's say, and back pain and your aged less than 45 and you ask those IBP criteria, the likelihood ratio is around 1. And so we think about a good test. A good test has a likelihood ratio around 10 and somewhere around the 4 range you might start getting into a reasonable test, but we're talking about it not even reasonable test for having axSpA among patient with already those criteria.

So, I think this also shows that there's still a lot of work to do in defining who these patients are. But I think, you know, the bottom line is that these patients are already at very high risk for having axSpA if you've got one of these three things, you have back pain and you're under age 45. So, somebody to kind of, will look out for more criteria to help differentiate those people who might need imaging, for example.

Chapter 3: Effects of Filgotinib on Spinal Lesions in Patients with Ankylosing Spondylitis: Magnetic Resonance Imaging Data from the Placebo-Controlled, Double-Blind, Randomized TORTUGA Trial

Dr. Alexis Ogdie-Beatty:
All right. So, we'll move from here into some imaging of axSpA. So, this was the Filgotinib's trial that it was presented before, but this is now the subset of people who had MRI imaging. And they're going to show us a little bit about how things change with Filgotinib. So, next slide.

So, this is going to be presented tomorrow, but kind of having looked at things already. So, what they did in this study is among patients who received Filgotinib or placebo, basically anyone in the trial, there were 116 people enrolled, but about 88 or so actually had imaging of their full spine. So, in this case, they did it, not the typical SI joint scoring, but they use a different score called the CANDEN score. And this score takes into account the posterior elements, kind of more of the spine elements themselves in the spinal column. And it looks at inflammation and then there's some subscores for erosions, for example, an ankylosis, as well as bone marrow edema. And what they found and you can kind of see in these 2, these 3 different graphs here is that the curves do separate. So, you can tell who was receiving therapy with Filgotinib compared to placebo.

And then, if we go to the next score, so recall, this is like a 12-week phase 2 trial. So, how much is really going to change over 12 weeks? Well, you can see actually there's a decent amount of change in the inflammation score in that least mean, at least for mean, a negative 4.4 compared to placebo is 0.09. So, basically no change in the placebo group. A little less change in the fat score, which actually goes up. So, I'm not sure if you have any insight into that, Laura. It's supposed to go up, but kind of interesting there, but then no change in erosions or ankylosis, but we really wouldn't expect to see that really at 12 weeks.

So, this is kind of in line with expectations. So, first study showing a JAK inhibitor and the impact on this particular score within MRI spine and axSpA.

Dr. Laura Coates:
Yeah. So I think we picked this for a number of reasons really. So, obviously JAK inhibitors and axial disease are an exciting new development in an area of spondyloarthritis where we are much more limited in our treatment options. We are quite lucky in PsA at the moment in terms of having a number of drugs that work. But some of those drugs have not translated well into the axial element of the disease. So, it's really good to have another option to have an oral option that works, which is exciting.

And then I guess the discussion around the scoring systems. So, as you've seen in the previous two abstracts, do not do particularly well just on history and patient-reported outcomes, be it for diagnosis or for disease activity. So, having the MRIs is really important to give you some sort of surety and reassurance that this is definitely having an effect on a very objective outcome measure. And for that you need these really well-developed scoring systems.

And then I think, again, looking into the axial PsA side of things, this is an AS trial, but this new scoring method may be really beneficial in the axial PsA studies. So, it's covering more different elements of the spine as Alexis outlined, and that may be even more important than the axial PsA patients compared to the AS patients. And if we're not looking, for example, in the facet joints for disease activity, then we're potentially missing disease in our patients. So, I think this is really useful to show a new, very well-developed score from experts in the field from, from Canada and Denmark, hence the CANDEN score, and confirming that very good differentiation between

drug and placebo. So we know this has the sensitivity to change, at least in the inflammatory components rather than the structural damage components.

Dr. Alexis Ogdie-Beatty:
And also, just throw out there, one of the other new abstracts was a late breaking abstract with the tofacitinib axSpA data. So, I think we're learning in general more about these drugs and axSpA, as you said.

Dr. Laura Coates:
Yeah, I think it's going to be a great opportunity to have new drugs and to have orally effective agents for spinal disease, which has, has just not been an option. So, it'll be nice to have a different MOA coming, coming to the table next year.

Chapter 4: Cluster-randomized Pragmatic Clinical Trial Evaluating the Potential Benefit of a Tight-Control and Treat-to-Target Strategy in Axial Spondyloarthritis: The Results of the TICOSPA Trial

Dr. Laura Coates:
So, this is a cluster-randomized, pragmatic clinical trial evaluating the potential benefit of a type control and treat-to-target strategy and axial spondyloarthritis. So, this is the TICOSPA trial following on from TICORA and TICOPA, in the other elements of inflammatory arthritis.

So, this was a cluster-randomized, controlled trial. So, it differs really in terms of design from TICORA and TICOPA in two main ways, I think. The first is that this was cluster-randomized. So, rather than each patient being randomized to treat-to-target or type or standard care, each hospital that was involved was randomized either to standard care or to a treat-to-target regime. And obviously that's beneficial because it potentially reduces the noise, or the contamination between doctors, if you train half of your doctors to do treat-to-target, then the other half are probably going to find out about it and maybe are going to do it in the standard care group without really meaning to, but it does also potentially mean that your groups are a bit more different because you're using, you know, 10 hospitals in one group and 10 hospitals in another. So, the patients may be different. The doctors may be different. All sorts of other factors may be different. But the, the tick type control approach was very similar to the previous studies. It used ASDAS as the type control criteria, aiming for ASDAS less than 2.1, but with visits every 4 weeks as we did in TICORA and TICOPA, and then rheumatologists, in the usual care groups or patients every 12 weeks, which is probably more like routine practice although I have to say, particularly with COVID as well, I suspect a lot of centers may struggle even to get 12-week appointments routinely for their patients.

And then the other key differences is the cluster-randomization was the primary outcome measure chosen for this trial, and that was the improvement in the ASAS health index after a year of the study being running. So, you can see here, the first bars on the left is that changing ASAS health index.

It's a 30% improvement in the ASAS-HI and that's not a disease activity measure. It's a quality of life measure, essentially. So, disease impact or quality of life measure. And what you can see is this study did not meet its primary outcome. So it did not show that tight control in an axial spondyloarthritis improves over usual care.

Now, in some of the secondary outcomes, they did show a numerical difference. They also potentially showed a benefit in terms of the health economics when taking into account the population costs in people being out of work or work unstable. But it certainly didn't meet all of its secondary outcomes and most crucially didn't meet the primary outcome in this study.

Dr. Alexis Ogdie-Beatty:
I think one of the things that we've talked about the most is the mismatch of the outcome and the target. And I think that makes some sense and I understand why they chose something different in that it's something that really matters to patients is that their quality of life improves. That brings up a few questions though, is if you're targeting the disease activity, and so you're targeting either CRP and a few items of their BASDAI. And then you're measuring the outcome as being something totally different, which isn't necessarily always improved, you know, in fatigue, and some of these other things don't always improve with therapy because they're so multifactorial, you can see how you could miss that target.

And so it was in some ways, a little bit of a risky target, maybe. Also, they use the threshold of 30% improvement, which I guess they had some data for it, but I don't know why, what made that 30% improvement, for example. So, is that important to patients? Does that meet a significant threshold?

So, you know, I think it raises more questions than maybe it produces, that it answered, but I mean, that's good. So, I think that. You know, what should we be targeting and treat the target? Is, is it really right? Just to target the CRP when we know that half of our patients in practice don't have an elevated CRP? Is it right you know, just these few items of the BASDAI and this score as opposed to referring for sleep management, referring for chief fatigue, especially if your outcome is going to be quality of life? So, I think there's a lot

to learn about what is the target and how do we treat-to-target in axSpA? I know we've also talked about kind of the interesting thing about the economic analysis, because you can show an economic improvement in terms of population metrics, in terms of work productivity and stuff, but then those patients received a lot more biologic therapy, they had a lot more visits, which in different health systems have different costs. So, it kind of interesting to know if that really evened out.

Dr. Laura Coates:
Yeah. I mean, the use of biologics was well over double in the tight control versus the standard care group. So, in terms of direct health costs, this was relatively expensive to do. Although obviously if it is keeping people in work, then that may well be worth doing. But I think the other issue that we have in axial spondyloarthritis, which kind of comes back to the previous abstracts, we haven't got many treatment options. I think when we designed the approach for TICOPA, we did as much as we could with limited evidence, but it was very much a step up approach.

So, we tried conventional DMARDs. Because we're in the UK, we had to try these 2 of those before patients are eligible for biologics, then we went on to biologics. So, there's, there's very much a kind of clear escalation and step up approach, which you can apply in RA and Ps, in PSA, but in axSpA you're really going straight from anti-inflammatories to biologics.

And you've only got 2 biologics or 2 classes. So, how much do you keep switching? You know, if somebody does reasonably well, but their ASAS is still not 2.1, do you switch to a second or a third biologic when you're worried that you're running out of options? So, I wonder if part of it reflects the actual availability of treatment options and the kind of approaches that you can bring into that treat-to-target approach.

Dr. Alexis Ogdie-Beatty:
Yeah, I fully agree. I would, I keep, I mean, I'm a more reticent to switch sometimes for my axSpA patient that's, you know, mostly doing okay but it has a couple of things going on. I would, I would be a little more reticent, reticent to switch in that axSpA patient compared to the PsA patient where we have more options, we do more combination therapy and so on.

So, yeah, I think there's a lot to learn here. The other thing that they mentioned was, you know, maybe 52 weeks is too short of a time to expect much of a change in quality of life. I hope that's not the case, but...

Dr. Laura Coates:
Yeah, that was, I think that was a big leap. So, obviously, TICORA and TICOPA use disease activity measures as the primary outcome, we used ACR20 in TICOPA, but we still showed improvement in quality of life.

So, it's not that we didn't need to quality of life outcome. It just wasn't a primary outcome. So, I think there is more of a difference here compared to the previous studies that have come before.

Dr. Alexis Ogdie-Beatty:
And the other thing they mentioned is they didn't include imaging, which, you know, ideally in best case scenario they would.

But obviously it's hard to see much. I mean, again, we saw the MRI, you can see changes, but it adds a lot to the cost of the study as well. So, but I think in an ideal world that would have been nice to see.

Dr. Laura Coates:
Okay. And then we've got one last abstract.

Chapter 5: Efficacy and Safety of Secukinumab in Patients with Spondyloarthritis and Enthesitis at the Achilles Tendon: 52-Weeks Results from a Randomized, Placebo-Controlled Phase 3b Trial

Dr. Alexis Ogdie-Beatty:
All right. So, this is another of what a poster presented Saturdays by Frank Behrens.

This is looking at is a new clinical trial first results from this 52-week trial presented, and this is efficacy and safety of secukinumab for spondyloarthritis enthesitis, specifically at the Achilles tendon. So, we can go to the next slide.

So, in this study, patients with psoriatic arthritis or axSpA were enrolled that had heel enthesitis.

This is kind of cool that it's both SpA populations, PsA, and axSpA, and they examined patients who had MRI-positive heel enthesitis. So, there was a separate abstract by Xenofon showing, you know, what proportion of patients actually had a positive MRI that were screened for this study.

So, that was kind of interesting in and of itself to look at baseline characteristics, but then they follow patients over the course of 24 weeks was the primary outcome for a heel enthesitis resolution. And there's a variety of other outcome measures, too. This study did not

meet its primary end point.

So, there was not, even though there's a numerical difference in the proportion of patients achieving heel tendon enthesitis at 24 weeks, it was not statistically significant. There were some significant differences in other outcome measures, as you might expect for PsA or axSpA population being treated with secukinumab that they had improvement in their global disease activity, for example. There was also an improvement in their global and their heel pain, the score that they tested as well. So, from this one really interesting novel study design in that it was the first attest, a randomized first randomized trial to focus on one single enthesis, but some caveats to think about too, which I'll let Laura kind of talk about.

Dr. Laura Coates:
Yeah. So, as Alexis mentioned, not all of the patients actually had MRI positivity at baseline. And what will be interesting to know is whether that MRI positivity links in with the clinical response. We don't have that data yet, but we know that quite a few of the patients were thought to have a positive MRI, but actually on the central read, they did not.

So, it raises the issues around diagnosis and enthesitis. Imaging's not necessarily the gold standard. It's not always positive in every patient. But we know that a lot of patients have pain near to an enthesis, and that may not necessarily reflect emphasizes and therefore would not necessarily respond to a drug like secukinumab. So, I think it's really positive that we're seeing trials in these other elements of disease, like enthesitis and axial PsA, but it's these caveats of how we measure things. And this is really one of the first studies that looked at one site. Most of our clinical outcome measures, look at the patient.

So, we add up a number of tender joints or a number of swollen joints. And there's been much less work done on individual joints or in this case, individual tendons. So, we don't know as much about the outcome measures in that situation and about how well people respond. It makes it a lot harder to plan the trial along with that imaging issue.

Dr. Alexis Ogdie-Beatty:
Yeah. I think the imaging part is really striking to me to that these patients had to have an MRI positive heel enthesitis read locally in order to be enrolled. And then when they read them centrally, there's a lot of, you know, misdiagnosis there. So, and we see that all the time in clinical practice that it will come back saying either yes, enthesitis or no enthesitis or tendonitis.

So, there's so many different words and every radiologist has kind of trained differently how to read these. And so there's not really standardized ways of reading an MRI for enthesitis. Related to axSpA, for example, that adds a lot of mechanical enthesitis or tendonitis in here as well. And you might not, you wouldn't expect mechanical tendonitis to necessarily get better with secukinumab or any IL-17 or TNF inhibitor, for example.

Dr. Laura Coates:
Yeah, absolutely. So, I think you can see quite a strong flavor running through these 5 abstracts that there, the links between them in terms of the imaging and the clinical measures that we're thinking about in spondyloarthritis.

So, I was going to say where we're at time for our section. So, it's my pleasure to handover for the second half of this meeting to talk about Still's Disease.

Announcer:
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