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PsA + COVID-19: Conference Highlights From ACR Convergence 2020

Announcer:
Welcome to CME on ReachMD. This activity titled “PsA + COVID-19: Conference Highlights from ACR Convergence 2020" is brought to you by Forefront Collaborative and supported by an educational grant from Lilly.

This replay of a live broadcast focuses on understanding some of the findings presented at ACR Convergence 2020 and providing insight into the evolving treatment landscape for psoriatic arthritis.

Dr. Feldman:
With new and recent evidence uncovering new treatment options for patients with psoriatic arthritis, the therapeutic landscape for the disease has changed dramatically in a relatively short period of time. But what does the latest research suggest, and how might this new information impact our treatment approach, especially in the time of the COVID pandemic? That’s what we’ll be exploring today.

Hi, I’m Dr. Madelaine Feldman, and welcome to this special CME live broadcast on ReachMD. Here with me is Dr. Phil Mease, who’s gonna share some of the highlights from this year’s American College of Rheumatology’s conference, ACR Convergence, 2020. Dr. Mease – Phil – welcome to the program.

Dr. Mease:
Thanks Madelaine. I’m very happy to be here.

Dr. Feldman:
A programming note to remind you, our audience, to submit questions via the chat feature on whatever platform you’re viewing this live broadcast. Dr. Mease will address a few questions immediately after our discussion. Well let’s get the ball rolling. To start off, Phil, what can you tell us about some of the new evidence on biologic disease-modifying antirheumatic drugs and the treatment of psoriatic arthritis?

Dr. Mease:
So there were a number of very interesting studies. The first one is a practical one for making decisions in our daily care of patients. So, this is data from the second part of the control trial. Well the point of it was to look at patients who were on methotrexate monotherapy for PsA. And let’s say they were having an inadequate response at 15 milligrams. So the question is, do you intensify treatment with methotrexate – going to 20 or 25 milligrams? Or do you add adalimumab at that point? So in the first 16 weeks of the trial, this was studied, and the endpoint was achievement of minimal disease activity criteria. MDA is a set of seven items, including tender and swollen joint count, enthesitis assessment, patient pain, and so on. And if you achieve at least five of these seven items, then you’re in a state of MDA, and it’s been shown to well-correlate with good quality function and good quality of life. So what was shown was that if you added adalimumab, nearly half of the patients achieved this state of MDA, but if you intensify methotrexate, only 13.6% did. So that was the key message from Part One. What happened in Part Two? So, the patient who achieved MDA, in either arm of the first study, generally maintained that. But what about the patients who did not achieve MDA in the adalimumab plus methotrexate arm? What happened there was if we went to weekly adalimumab, we could achieve MDA. And so it showed that increasing the dose frequency would help. In the group that was on methotrexate only, it was found that if you added adalimumab, as expected, they would then

achieve MDA. We also showed, in one of the arms, that if you were on adalimumab plus methotrexate, and dropped methotrexate, you could maintain the MDA state by just continuing adalimumab monotherapy. And as you know, lots of our patients prefer not to take methotrexate, for various reasons. So I think this gives us some practical advice about how to manage our patients. The next slide shows a study in which ixekizumab, an IL-17A inhibitor, was used in the SPIRIT-P2 trial, where patients were enrolled who were TMF inhibitor inadequate responders. And this is three-year data, which shows that patients were able to achieve these targets of therapy that we're aiming for, such as minimal disease activity, or something called the DAPSA – disease activity in psoriatic arthritis – low disease, or remission criteria. And again, nearly 50% of patients were achieving this. So, in either ixe dose arm, we found that these results were maintained and sustained. And so I think that this gives us confidence about the effectiveness long term, of use of an IL-17 inhibitor. And the next slide demonstrates the results of one-year data with a new agent for us called tildrakizumab. This drug is a P-19, IL-23 inhibitor, which has been approved in treatment of psoriasis, and here we're showing the results of a Phase 2 PsA study at a one year. And depending on the dose arm, you see, again very high levels of ACR-20 response that are shown here, and also achievement of this target of – of treatment that we're aiming for – the MDA in somewhere between a third and a half of the patients. o showing this new mechanism is also effective.

Dr. Feldman:
Well you know, as always, we have to sort of balance out efficacy with safety. So what about the safety of the agents that you just talked about, like ixekizumab, adalimumab, tildrakizumab? Are there any new findings or safety signals with these drugs?

Dr. Mease:
So let's take a look, at some of the data that's either from the abstracts that I just spoke about, or from additional abstracts. The first one is from the SPIRIT-P2, three-year data, which showed that about 6% of the patients overall in the study, discontinued due to AE's, which were typically either infection or injection site reactions. I consider this a relatively low rate over the course of three years. And the data otherwise showed relatively low rates of infect – serious infection. We didn't see opportunistic infections, we didn't see a malignancy signal, we don't see a BTE signal so – there were – there have been a couple of cases of IBD in the IL-17 treated patients. In the control study that I just referred to serious adverse events across all the groups were less than 5%. And the safety profile was more or less what we expect from adalimumab. There is a, as you know, a SPIRIT head-to-head trial, comparing ixekizumab versus adalimumab, and looking at 52-week data from that particular trial, we did see an interesting difference between ixekizumab and adalimumab. There were more serious adverse events with adalimumab – about 12% of the patient population, versus 4% in the ixekizumab. Some of this was infection, some of it was – I have to say, was not actually related to the medicine. It would be like a road vehicle accident or bike accident, or something like that. But nonetheless, there was a little bit more in the way of infection on the ada side, but on the ixe side, there were more injection site reactions and a couple of cases of IBD. With tildrakizumab, it's turning out the IL-23 inhibitors really are very good, from a side effect point of view. Low rates of serious infection, no IBD, no major adverse cardiovascular events, no malignancy signal – so I think with this new group, we're going and we'll see a little bit more with guselkumab shortly pretty good safety record.

Dr. Feldman:
Well, that's sounds good. We've talked about tildrakizumab, which is IL-23, and then you just mentioned another IL-23 inhibitor, called guselkumab. I understand you did participate in a number of trials addressing its safety and efficacy. What can you tell us about guselkumab?

Dr. Mease:
So, guselkumab is also a P-19, IL-23 inhibitor. And its Phase Three trials were DISCOVER-1 and -2. -1 was a mixed population, with 30% TNF-inhibitor inadequate responders. And DISCOVER-2 was a purely CSD-marred population, a little bit bigger trial. And what has been shown with all of these with these two trials and the patients in them – is extended data out to one year, which shows really good benefits in things like work productivity, sustained resolution of enthesitis, as well as dactylitis. We saw ongoing high thresholds of achievement of remission and low disease activity. And interesting as sub-study which was reflected in an abstract, and which we looked at the BASDAI and other measures of spine symptom improvement, was a sub-study in which 30% of the patients in both trials were shown to have sacroiliac joint x-ray abnormalities, consistent with sacroiliitis. And in those patients that had elevated BASDAI scores – elevated spine pain scores, we saw that there was a significant improvement of symptoms with guselkumab treatment versus placebo. Why is this interesting? It's because we've seen a previous trial with another P-19, IL-23 inhibitor, risankizumab, where they did an exploratory trial in ankylosing spondylitis and failed to show difference from placebo. So there had been sort of an idea, maybe the IL-23's don't work as well in the spine. So this opens up the question again. And it's, it gives us at least the need and desire to have better understanding about IL-23 inhibition role in the spine disease of psoriatic arthritis. There is also an interesting aspect and that is, it's the first set of trials where the FDA has recognized fatigue to be on the label. And we know that fatigue is a big deal to our patients some that is related to inflammation, some related to other factors. But this clearly showed improvement of fatigue, and the overall

safety was similar to what I just mentioned with tildrakizumab – very little in the way of serious infections, no IBD, no malignancy signal, and so forth. So, I think this is going – the IL trinities are gonna be a solid addition to our armamentarium.

Dr. Feldman:
Ah, that's interesting the – about the fatigue that they've added, I like that. That's good. Well let's switch back over to the IL-17 inhibitors for a minute. Which studies can you highlight for us in addition to those that you mentioned with ixekizumab?

Dr. Mease:
So, there were several IL-17s to mention. One is secukinumab, which is an IL-17A inhibitor. But also there's bimekizumab not yet available to us, which is an IL-17A and IL-17F inhibitor, so covering a little bit more of the IL-17 landscape. With secukinumab, we saw a number of studies that were either addressing the long-term extensions of previous studies and PsA's, such as FUTURE 5 where we saw extended data with high rates of achievement of remission or low disease activity, as measured by various outcome measures and showing sustainment over time. There was some data that showed that when it was used as a first-line biologic agent, it'd had really excellent results. And also, there was an interesting sub-study that showed that it improved dactylitis, which we know is a biomarker of more severe disease. There was further data on the secukinumab versus adalimumab head-to-head trial in which they had similar robust achievement of minimal disease activity and remission. And then with bimekizumab, we saw sustained results in both the articular domains as well as skin domains, improvement in patient-reported outcomes, such as quality of life and function and a similar safety profile overall, as we've seen with other IL-17s. So that will be a very interesting drug that has a slightly broader dimension of effect.

Dr. Feldman:
For those of you just joining us, you're listening to a special CME live broadcast on ReachMD. I'm Dr. Madelaine Feldman, and with me to talk about psoriatic arthritis and key highlights from ACR Convergence 2020 is Dr. Phil Mease. Quick reminder for you, our audience, to submit your questions via your viewing platform, so Dr. Mease may address them during our post-discussion Q & A session.

Okay, so Dr. Mease. Continuing with our discussion, what can you tell us about the clinical trials presented at this conference regarded targeted synthetic DMARDs, such as the JAK inhibitors in the treatment of psoriatic arthritis?

Dr. Mease:
So, Madelaine, the main news at this meeting as well as the just previous ULAR meeting was data on upadacitinib. Many of you know upadacitinib because it's been introduced for the treatment of rheumatoid arthritis – already approved. To relatively specific JAK-1 inhibitor in the dose that we're using it. 15 milligrams is the dose that's approved for RA. And here we're seeing data, from the SELECT-PsA-1 and PsA-2 trials – the Phase 3 trials where both the 15 and 30 milligram doses were looked at. In the PsA-1 trial, there was also an adalimumab reference arm, and interestingly the 30 milligrams did slightly better than the ada, and the 15 milligrams was very similar to it. Here we're showing again, I sound like a broken record but this targeted treatment that we're aiming for, which is either remission or inactive disease it's called in some of the measures, or a low disease activity which is the MD – or minimal disease activity. And you can see there that these are achievable endpoints. The patients are highly satisfied. Except for the PASI's, these were measurable and practiced. And so, I think that it's another solid entry into our armamentarium, once it's approved. And so, I think that that's very exciting information about upadacitinib.

In the next slide we are seeing data with filgotinib, another relatively selective JAK-1 inhibitor and in this particular sub-analysis we're looking at the clinical domain of enthesitis. And it was shown that there was a high degree of achievement of resolution of enthesitis at the 16-week mark, the primary endpoint. And then as you tracked it out to 52 weeks, an increasing number of patients achieved this response. And I think of enthesitis as being a tougher treatment domain to treat. It's not well-vascularized there's a lot of mechanical pressure on it, especially at the Achilles tendon or plantar fascia. And so I think it's not surprising that we need to have a little longer to see the full benefit, but up to three-quarters of patients are achieving that level of benefit. And then, we saw, as a late breaker the introduction of deucravacitinib. To say that several times in a row to get it – deucravacitinib. It's apparently deucrava for short. And so this was a Phase 2 trial and we've already seen one Phase 2 trial with psoriasis. And in that trial, we saw PASI 75 rates of 69% higher than what we've seen with some of the standard JAK agents. And this is because TYK2 appears to have among other things an ability to inhibit the cytokine IL-23, but also IL-22. It has to do with the configuration of the JAK and TYK molecules at the cell surface rece cell surface. So we anticipate that there are gonna be very high skin responses, and, and effective in the dermatology world for psoriasis potentially as well as in the rheumatology world. And in the PsA trial, we saw good solid rates of improvement of ACR responses, enthesitis as well as function, quality of life – the kind of thing we expect from a solid, JAK inhibitor. So this is going forward and the other thing that will be interesting as we get more data will be, how does it do safety wise, compared to the other JAKs? In these trials, we didn't see really anything in the way of serious infection or BTE. We anticipate that the drug may help inflammatory bowel disease. So, it's going to be interesting to see whether there is some differentiation from a safety perspective as well, with this new entrant.

Dr. Feldman:
Deucrava, okay. Well, let's shift gears a little bit. You know, there's no denying that COVID-19 has added challenges to the already complex management of rheumatic diseases. What do you think are some of the practical implications of the studies presented at ACR Convergence, that might help us treat psoriatic arthritis in this whole COVID-19 pandemic?

Dr. Mease:
There were a number. And and it was exciting to see and as you see on this slide – I'm not gonna go through all the details of these various studies – but, I would say the majority of them came down on the side of saying that the advisement that we've received from the ACR and EULAR organizations – that if we dial back to April when we were struggling with answering all patient calls about, "Do I have greater risk for developing COVID if I'm exposed, given my underlying autoimmune disease?" And, "Do I have a greater risk for having a severe course of it, including hospitalization, and heaven forbid, intubation because of the treatments that I'm on?" So our patients were desperate to know whether or not they should be stopping their medicines to decrease risk and decrease severity. So these are these abstracts on the left-hand side reflect various registries – either country-specific registries, or as you know, there is a global rheumatology/COVID registry, where rheumatologists from around the world are entering patients who've developed COVID. And there are several take-home messages from these. One is that as far as they can tell – although, keep in mind these are not carefully controlled studies there doesn't seem to be a higher rate of either infection because you have a disease like rheumatoid arthritis or lupus, or necessarily a more severe course, including hospitalization if you're on one of our treatments. And so, the general advisement seems to be sound, that if your patient says, "Should I stop medicines?", you should say, "No." However, if they develop COVID, that's another story, but if they haven't then I would say no, it's better to keep your disease under control rather than to have it flare, because there's some suggestion that uncontrolled autoimmune disease may be more of a garden for COVID to land in. And the other is that if you flare and have to use prednisone in doses greater than ten milligrams to control it, then that's a baddie and that increases your risk. Now on the other hand, there were a handful of studies, again, that were either center-specific or country-specific, that suggested the converse – that there was a little bit more risk by having a background autoimmune disease, and that there could be a slightly more severe outcome by being on the drugs that we use. So I think the full answer isn't in, but I would say that the preponderance would be to practice safe just do the safe things that you know to do. Try to shelter in place as much as you can, wear a mask, and wash your hands. And there was even an abstract that suggested that maybe one of the reasons why some of the better outcomes were observed had to do with the fact that autoimmune disease patients are more likely to protect themselves they're more likely, perhaps, to stay at home, to follow the rules, to wear a mask, to have their spouse go out and do the grocery shopping and maybe get their boss to let them work from home more readily and that this could also contribute to some of the better outcomes that have been seen.

Dr. Feldman:
Well, lastly, Dr. Mease, are there – are there any key take-home messages you'd like to share with our audience today? Sort of a short summary.

Dr. Mease:
Yeah. So I think that we've seen quite a bit from this ACR meeting. First of all, I think it was done pretty well. Not that many glitches that I saw from a technology point of view, and I really appreciated jumping from one presentation to another, one poster to another. I was busy – I had 46 abstracts in this meeting, so I was just busily responding to chat, and getting to interact that way with colleagues, and so that was not bad. In terms of PsA, I thought as we've seen in recent meetings, PsA is coming into its own. Lots of interest in pathophysiology, lots of interest in new mechanisms of treatment, lots of interest in how to measure and get to a state of remission or low disease activity. So this is a good time for a person involved in PsA research, and interested in learning about how to manage PsA. I think that we're seeing some maturation of the field, in that we're seeing a few head-to-head trials, and I think that will encourage people to do more in the future, which I think helps clinicians make decisions. I think there were some intriguing combined primary efficacy endpoints, like the SPIRIT head-to-head, where they combined a skin result along with a joint or arthritis result, and so simultaneous achievement which was I think a more holistic approach. We might see more combination trials in the future, try to achieve even better outcomes. And we saw a lot more in the way of interest in how our treatments might impact extra-articular manifestations of the disease. We've seen a lot of interest in axial PsA. Is axial PsA the same as or different than axial SpA, or ankylosing spondylitis? And there is some suggestion that maybe so. We certainly have seen radiographic differences some clinical differences, maybe some genotypic differences, and maybe some treatment outcome differences. And I think we're gonna see more coming in about the impact of COVID and that we'll learn more about that. And hopefully, at some time, we're gonna get – start seeing some data on what happens with vaccination.

Dr. Feldman:
Well, it was quite a broad landscape you went over for us, but thanks for sharing those key takeaways. But before we wrap up this live broadcast, we're actually gonna be answering a few questions from our audience. So let's get started. So the first one I have here is,

“Was there any new evidence presented about gender differences in responses to therapies for psoriatic arthritis?”

Dr. Mease:
Very interesting question. So a little background is that in some of the clinical registries, like – I’m involved with the U.S. corona registry – we have seen in registries, for their all-comers without restrictions of people not having background fibromyalgia, etc. that there is some suggestion that women may not have more severe disease, as measured by composite measures that include patient-reported measures, like tender joint count or pain. And then also, we’ve seen some data that suggested they may not respond as well to certain treatments, or may not achieve minimal disease activity as readily. So there was an analysis of the EXCEED head-to-head trial, between adalimumab and secukinumab, where that was seen. At baseline, women had a little bit more in the way of severe composite measures, and a little bit harder time achieving some of the high-threshold measures like MDA. So, is this immunobiology differences? Is it a bit more fibro in the female population? There could be a number of factors, but I think they all probably contribute. And so I think this will be looked at more carefully in upcoming trials and we might look at this in practice.

Dr. Feldman:
Yeah, those gender differences – those were quite interesting. We have one more question. You talked a little bit about this already. Can you highlight what is new about axial psoriatic arthritis? And when they do PsA studies – this is my question – do they ever differentiate those that are axial versus peripheral, or is it just all lumped together?

Dr. Mease:
So, historically not. It’s all lumped together, and we have depended upon ankylosing spondylitis trials to teach us about medicines and their effect. But I think that we’re now recognizing that there are differences. And for example, the patient may not have sacroiliac changes but may have prominent cervical spine changes. They’re more women. They are less likely to be HLA-B27 positive. They have more peripheral disease. They have asymmetric sacroiliitis when it’s present. And now there’s a suggestion there might be some differences in response to treatment to our various medicines. So I think this will be an area of future investigation in much more depth.

Dr. Feldman:
Absolutely. I wish we had more time, but that’s about all the time we have for today. But before we go, I really want to thank you, Dr. Mease, for helping us better understand some of the findings from ACR Conversions on psoriatic arthritis, and providing insight into the evolving treatment landscape for psoriatic arthritis. It was great speaking with you tonight, and thank you once again.

Dr. Mease:
Thank you, Madelaine.

Announcer:
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