Podcast Transcript

Treatment goals for RA: Is it time to transition MOAs?

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Speakers: **Dr. Christina Charles-Schoeman** and **Dr. Manish Jain**

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Introduction	**Dr. Charles-Schoeman:** Hi, everybody, welcome to RheumNow. This podcast is sponsored by AbbVie US Medical Affairs and Health Impact. My name is Christina Charles-Schoeman. I'm a professor in the Division of Rheumatology at UCLA Medical Center. I'm thrilled to be joined today by Dr. Jain, who I'll let introduce himself. **Dr. Jain:** Thanks so much. My name is Manish Jain. I am a private practice rheumatologist at my clinic, which I've named Ravenswood Rheumatology. I'm also a principal investigator and regional medical director for Flourish Research, so nice to be able to join you today. **Dr. Charles-Schoeman:** Thanks, Dr. Jain. I'm really looking forward to this discussion, which is going to center around achieving treatment goals in our patients with RA. I think, while we all agree that disease control is the goal for every patient, exactly what that means to each of us, as well as the patient, may be slightly different. We know that the guidelines, in particular the ACR guidelines, recommend to continuously assess disease control in our patients to think about a treatment change if they're not achieving that disease control.[1] And we'll talk today specifically about why that's important for each of our patients. And really, how we go about having those conversations and making those decisions.
Risk of uncontrolled disease	**Dr. Charles-Schoeman:** So, before we get into a discussion of treatment approach, I wanted to talk about why it's important to achieve disease control, even when many times I think our patients say they're good enough, they feel good enough, and they're hesitant about a treatment change because they're hesitant about, predominantly in my clinic, side effects of new therapies. So, if you have a patient with uncontrolled RA, what are some of the consequences of uncontrolled disease that you're thinking about and maybe talk to the patient about? **Dr. Jain:** Yeah, great question. It's hard for me to almost think of a consequence that isn't on the table for that patient with uncontrolled rheumatoid arthritis. I take care of a pretty varied practice population. Many of my patients they're quite stoic and they're tough cookies. And so, I really try to engage that patient in a discussion about, "Well, you know, here's the short game, getting you feeling better and improving your pain and your day-to-day." But also, engage them on that long game: long-term quality of life and other consequences to their health. And so, you know, helping my

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	patients understand a bit, that disease progression, it can really exist beyond those joints. And so, some consequences, you know, certainly within the joints, loss of physical function, that health-related quality of life, irreversible joint damage with that uncontrolled RA, missing work, healthcare utilization, being stuck at the doctor's office, patient-reported outcomes, thinking about the psychological burden of their disease, their functional status. But then, beyond that, helping them understand that as we play this long game, that tight disease control or at least not letting their RA run rampantly uncontrolled, can have benefits potentially to something like osteoporosis, cardiovascular risk. So, we're really big on CV risk mitigation in a private practice setting. So, helping that patient, understand, you know, heightened rates of heart attack and stroke with poorly controlled disease. A lot of my patients they're going to see a TV commercial and quote those risks of what they heard around the TV commercial. And I'm quick to remind them that uncontrolled RA doesn't itself have its own TV commercial. If uncontrolled RA had its own TV commercials about these are the consequences and side effects and risks, I think a lot more patients would be coming in expecting a different conversation. **Dr. Charles-Schoeman:** I was really surprised when the data has been building, we'll have some of it linked on the site to this podcast, but you know the fact that active disease is associated with a higher risk of serious infection,[2] right? Telling that to the patient, I think, kind of blows them away, that having a dysregulated immune system, is not good either, and that can actually associate with a higher risk of serious infection. I think many of us don't think about that. But there's actually some nice data suggesting that that's the case. As you go along in practice and see patients over years and years, I've seen these consequences.
Patient A	**Dr. Charles-Schoeman:** I saw a lady a couple weeks ago. She was about 60 years old. She's had longstanding RA and will not change therapy and tries not to come into the clinic. And, you know, she's got diabetes, and I think that onset of diabetes changed something for her in terms of thinking about her cardiovascular health. And, also, she started having trouble using that right hand to open, you know, the water bottles, and that interfered with her life, and that, I think, made a point where I was able to look at her hands and show her that swelling in the wrist and the elbow and the little digits. And so, that's why you can't do this, and that can become permanent right? And she thought about that ability not to use the right hand to open those water bottles, and that got to her. And so, for the first time, you know, she's working full time she's ignoring her pain, she went, "Wow! If this becomes permanent..."

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	So, she got the cost. She got on another advanced therapy. We're finally making progress, you know. So again, I think it's not just us. It's always, you know, the patient as well, and I get down that I'm not going to change, but then I have a moment like that, and I go, "Okay, keep going. Keep going." **Dr. Jain:** Yeah, it's almost like it's that sentinel event. Control your disease. Really, the better you're going to do. Because, in my anecdotal experience, it just clearly points to the right answer what we need to be doing for our patients. **Dr. Charles-Schoeman:** Yeah. And there's a study that we talked about in a session I did at this recent ACR, you know, I didn't know this study that the longer the disease duration, the less likely patients are to actually ever get to that remission,[3] right? And that's really, that's telling data.
Disease monitoring	**Dr. Charles-Schoeman:** So, I think, we'll move on to discuss the tools that we have to make sure that our patients achieve disease control in the clinic. We know that TNF inhibitors, most common first choice that many of us in the US use for our patients after synthetic DMARDs. We also know that a lot of patients don't get disease control with that first-line TNF inhibitor, and we'll need to transition to second-line therapies. So, the ACR guidelines are saying, "In the absence of disease activity improvement, therapy should be reevaluated within 3 months."[1] I think what we know, looking at the data that's coming out, is that doctors are busy. There's a nice paper that'll be cited on this podcast link from the American Rheumatology Network. Over 15,000 patients, and only about half initiating the first-line TNFi, did have that baseline disease assessment, either a CDAI or a RAPID3.[4] Because doctors are busy. It's hard to do all this in a busy clinic seeing 20/25 patients in a day. There was some additional data from that that we looked at over 1,600 patients, moderate to severe RA. And then about half of them were remaining on that first-line TNFi after initiation at a year, despite the lack of achieving disease control.[4] And specifically, that's looking at remission or low disease activity. **Dr. Jain:** Which is the goal that, I mean, that is— **Charles-Schoeman, Christina M.:** Yeah, yeah. **Dr. Jain:** That is evidence-based goal that we are there to strive for. **Dr. Charles-Schoeman:** Yeah, and I think that really put it in my face. You know, we all know this, but it's you're busy, you're in clinic, you're room to room, and sometimes it just doesn't get done. I'd love to hear how you do it. For us, you know, several years ago we just, you know, we got that

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	homunculus brought into the electronic medical record the calculation for the CDAI, the smart phrase, and I think it's just changed practice of being able to bring it in with a couple of clicks. Show the patient: here's your score. Some of mine still just want a sed rate, right? Right, that CDAI is beyond what they can capture. But I think that's really made it easy for me just to plug that in every visit and to go over it with the patient. **Dr. Jain:** I think it's really smart. So, in my practice, you know, I've got three wonderful APPs also. And so, one of the challenges I face is really standardizing our practice. Our practice shouldn't really differ, based on whether seeing me or one of my wonderful PAs. And so, the protocol we use in our practices is RAPID for all. But really, I want my APPs to get comfortable with CDAI, and I want to utilize CDAI early and often. It's like riding a bike, you know. You just keep getting better and better. **Dr. Charles-Schoeman:** Yeah. Yeah. Totally. **Dr. Jain:** I have CDAI in my head now, and I love that you mentioned engaging patients in on that number, right? You would never manage diabetes, for example, without engaging that patient on their A1C. Patients are going to come in knowing, “Yeah, like, Doc, I went down 7.5 to 5.9," and right, they share in that success over that number. That’s why I love that you're showing that raw CDAI number to patients and helping them engage and share in that success. I think it's great. **Dr. Charles-Schoeman:** Yeah. And I think for years, you know, several years ago it was always hard for me to get that, you know, patient global 0 to 10, because they're going to tell you about their back pain, they're going to tell you about their shoulder that they threw off, you know, in the yard and stuff like that. And focusing them, "No, this is your global for the for the rheumatoid arthritis." But I think, in doing it over time, they get it, right? They know that what you're going to ask, you're going to ask for a number, and they know why. And I think it just becomes habit forming for you and for the patient. Certainly, I know I've progressed over the years, and how I get that done, and I do think it's useful.
TNFi cycling vs MOA switch	**Dr. Charles-Schoeman:** Alright. Next, we're going to talk about whether we're going to cycle a TNF inhibitor or we switch that MOA after a primary TNF failure. I think the data is really building in terms of if you are a primary TNF failure, meaning you do not obtain low disease activity or remission within 3 to 6 months with your first TNF inhibitor, there certainly is data to think about switch of MOA. And we know that a lot of patients are not achieving that disease control with their first TNFi. I think, looking at the guidelines, ACR guidelines clearly say

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	that switching to a different treatment class is conditionally recommended over switching to the same class for patients who are not at target.[1] And again, I think going back to the data is where I live, and we'll put some studies on the post to look at that. There was a recent meta-analysis of RCTs, observational studies, that looked at various outcomes, ACR responses, DAS28, need to withdraw therapy, and I think it was clear in the message that if you are that primary TNF failure, the outcomes are better if you switch to a different MOA.[5] And, I think, if you get that disease control, and there's again back to the data if you switch that MOA after a primary TNF failure, they're more likely to stay on the same therapy.[6] And patients like that, right? Docs like that in terms of not having to change the therapy. **Dr. Jain:** Insurance likes that. **Dr. Charles-Schoeman:** That's well, yeah. I mean, our staff likes that. So, I think it's really in everybody's interest to get them under disease control. So, I'd love to hear your thoughts on that, Dr. Jain. **Dr. Jain:** Yeah, in general, I like facts and not feelings to support what I'm doing in practice, but I kind of feel like I've got a little bit of both when I think about switching MOAs. Thinking about the facts, right? We've got RCTs that carry a lot of weight, and I think there'll be some more RCTs as the space evolves. So right, that data is pretty clear that those patients who are switching MOA do better across a variety of metrics, be them objective or maybe even patient-reported outcomes. So that data is clear. Then I think about my feelings as well, and I just go through my mental Rolodex. I'm 12/13 years in practice now; holy cow, every year a few more gray hairs coming online. But you know, I just think through my mental Rolodex of patients when I put them on that second TNF inhibitor, for example. And okay, did I recapture the magic, you know? Do we get the honeymoon back? Maybe we did, but how durable was that? And just as I go through that mental Rolodex, that's kind of growing in every year of practice that I'm on I don't know that I have a lot of, you know, major wins on that Rolodex. And so that, to me, kind of using both that anecdotal experience that I've now accumulated really, I think, substantiates what the data is showing us in our day-to-day. What about you, doctor? What's your mental Rolodex look like? **Dr. Charles-Schoeman:** Yeah, I mean, you say that mental Rolodex. I don't know. My mental Rolodex changes from day-to-day, hour to hour, but what I was thinking as you were going through that is, I was thinking about the

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	patient, and I think there are some patients that you can tell them the data. You can tell them the risk. You can tell them the cardiovascular risk, and they're just not going to change. I think back to a 70-year-old lady I saw many years ago, who just was so hesitant to change therapy. Maybe would change something for a couple of months but was on a biologic therapy for years and years and really had development of heart failure that was diastolic with preserved ejection fraction over a series of years with uncontrolled disease that she couldn't get past the fear. And you see those consequences of the disease, and she eventually died from uncontrolled heart failure and renal failure from that. **Dr. Jain:** "Clock is ticking," that's a phrase I use a lot with my patients. "Guys. Clock is ticking. Clock is ticking," and just almost trying to, you know, without freaking them out, like drive that concept of urgency. We are under the gun to get this under control. **Dr. Charles-Schoeman:** Yeah.
Upcoming studies and closing	**Dr. Charles-Schoeman:** But I think we're going to get some more help with data to help us and to help our patients in the clinic. There are several upcoming clinical trials that may give us some more insights. There's the SUNSTAR, abatacept versus tocilizumab in our TNF-IR patients.[7] There's going to be the ADDORA-switch, that's going to be looking at TNFi versus non-TNFi after adalimumab failure based on the adalimumab serum concentration.[8] And then we're going to have the SELECT-SWITCH study, this is upadacitinib versus adalimumab, in the TNFi failure population,[9] helping us to know, where do we go next with this? So, any thoughts additionally from you, Dr. Jain? **Dr. Jain:** Yeah, I want to also echo that excitement about RCTs. I like RCTs that directly help me in clinic that I can point to with my patients. Yeah, I like RCTs that make me a better clinician. A lot to be excited about moving forward. **Dr. Charles-Schoeman:** Yeah, yeah, I mean, just being able to tell them, what's the likelihood that you'll have a response and then the patient decides with you, "Okay, well, that's fine, but I want to stick here. Or I want to do this." It's just so useful having those conversations. Okay, so we're at the end of our time. What we've talked about is needing to really work towards that disease control for every patient. How we do it. We've looked at the risks of uncontrolled disease, and how we go about checking the disease control at every visit, putting that into our practice. There's a ton more we could discuss on this topic. But I think this is what we have for today. So, Dr. Jain, you're awesome. Thank you so much for joining me.

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	And everybody who's listened, if you'd like to learn more about that data that I mentioned, definitely visit the RheumNow page. There's a nice infographic and some links there that I think will be really helpful. So, thanks so much for everybody's attention and [for] listening to our podcast. Take care. **Dr. Jain:** Thank you.

Abbreviations:

ACR, American College of Rheumatology; APP, advanced practice provider; CDAI, Clinical Disease Activity Index; CV, cardiovascular; DAS, disease activity score; DMARD, disease-modifying antirheumatic drug; IR, inadequate response; MOA, mechanism of action; PA, physician assistant; RA, rheumatoid arthritis; RAPID(3), Routine Assessment of Patient Index Data (3); RCT, randomized controlled trial; sed, erythrocyte sedimentation rate; TNF, tumor necrosis factor; TNFi, tumor necrosis factor inhibitor.

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