Podcast Transcript

A JAKi CHAT: Shared Decision-Making in RA
Sponsored by AbbVie Medical Affairs + Health Impact

Speakers: **Dr. Jeffery Curtis** and **Dr. Kevin Winthrop**

Scene		Speaker talking points
1	Opening (0:00–1:13)	**Dr. Curtis:** Welcome to RheumNow. This podcast is sponsored by AbbVie Medical Affairs and Health Impact. My name is Dr. Jeff Curtis. I'm a professor of medicine, epidemiology, and computer science at the University of Alabama at Birmingham. I'm joined today by my friend and colleague, Dr. Kevin Winthrop. Kevin, could you introduce yourself? **Dr. Winthrop:** Hi Jeff, thanks for having me on. I'm a professor of infectious diseases and epidemiology at Oregon Health & Science University, out here in Portland, Oregon. Good morning. **Dr. Curtis:** Well, thanks, Kevin. I'm looking forward to this discussion on best practices in shared decision-making and learning more about how you and how generally as a field, we might approach the critical conversations that we have with patients about the benefits and risks of medications and their other treatments. We know that guidelines from the American College of Rheumatology and EULAR encourage shared decision-making.[1,2] But, as rheumatologists, not everyone has had formal training or even much exposure to this concept of shared decision-making, and each of us might apply it a little bit differently in our own clinical practices.
2	**Importance of shared decision-making** in achieving disease control (1:13–5:42)	**Dr. Curtis:** So, to start off, I wanted to talk a little bit about why it's so important to engage in shared decision-making and to acknowledge that not necessarily all patients want to do this. We probably all have some patients who tell us, "Doc, you went to medical school, not me. I come here because I trust you. Give me your best recommendations." And I'm happy to do that. But it's important to clarify upfront with your patient sitting in front of you, how to best respect and value their own autonomy. So let's talk about shared decision-making. Kevin, how do you think about this general topic? **Dr. Winthrop:**

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		Yeah, it's a good question, Jeff. So, I'm a consultant, right? And I'm usually working with someone like you to help make decisions about a patient—a patient who has risk factors for a problem that might be associated with their underlying RA, or perhaps the therapies being considered to treat that RA. So, I'm having a, you know, a shared decision-making moment with the rheumatologist as well as the patient who's there in front of me, and I think it's all 3 of us trying to put our heads together to come up with something that'll maximize the benefit–risk equation for them. Certainly, there's the side effects or poor outcomes associated or inherent to your poorly controlled disease, right? Inflammatory disease run amok causes all sorts of problems, obviously, as you know, cardiovascular problems, infection problems, etc., increases risk of malignancy.[3-7] A lot of the things we worry about that are associated with some of the therapies we use are obviously part and parcel of the disease process of itself. So, it's very important that you achieve that low disease activity that you're seeking, not just for patient quality of life, but to lower the risk of those types of outcomes.[8-13] So I start my interaction with the patient talking about that, and then we get into talking about what therapies might be best for them. And as you know, I mean, a lot of the risk are inherent to the patient themselves—their age, their comorbidities, their other risk factors.[14-17] Some of these things are modifiable, and some of them aren't. So we really try to focus on what might be modifiable and what might not be. **Dr. Curtis:** Thank you. And that's a really helpful perspective. And I think that comanagement with specialty consultants like infectious disease or pulmonology can be really critical. It's also really critical to know what they're telling your patient, because you're going to be on the receiving end of what information that they receive and what they hear. So, it is good to be aware when you do work with external consultants that you have an understanding about how that may influence the patient's perspective. But some of what we are talking about today is impacted by timing. So in practice, I set the stage for shared decision-making and what the expected journey might look like early, at visit 1, at the time of RA diagnosis. I'll set that up by saying the goal of RA treatment is remission—hard stop—and I'll have a very deliberate and intentionally long pause, because that, in some sense, is one of the most important messages I can convey. Remission is basically no or minimal joint inflammation. Minimal or [no] joint inflammation generally means few or almost no flares, very low, or even no likelihood of progression of permanent joint damage and deformity and associated disability, losing function, a very low risk of some of the extra-articular complications of RA.[17-19] You mentioned cardiovascular disease that we know relates to higher disease activity that relates to flares.[3] So, I'll tie all of those things into "Why is it good to

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		be in remission?" And we don't have to get into the nuances of how it's measured, but that concept, I think, resonates. But I'll set that up at visit 1. The flip side of that is that's my goal for patients. But what's also critical in that same conversation is to talk about the patient's goals. What's important to them? It usually is not going to be centered around remission. It's going to be related to function. It's going to be, what are the things you want to do, you know, being there for your family, for kids, for grandkids, for spouse, minimizing pain, being able to participate in important life events or family life events, and ideally returning to a quality of life that is close to their lived experience before they had rheumatoid arthritis. So, anytime that you can set up goals that are clinical goals like remission, or at least low disease activity, and then bridge that to, well, how will that impact or favorably have a bearing on what you, the patient, find important? I think you then establish a therapeutic alliance where your goals can then be effectively aligned with the patient's goals. That's on the efficacy or effectiveness side. Kevin, tell me how you think about best practices in approaching the safety–risk conversation, kind of the other side of that same coin.
3	Shared decision-making & CHAT: (5:43–10:44)	**Dr. Winthrop:** You know, some of the things you mentioned there I stress with the patient, too, obviously. I'm not the one making the ultimate decision on therapy, the patient is, really, and you're the disease matter expert. So, it's really the patient and you. But, I do hope that I can at least help the patient sort through some of their fears related to the medicine. As you know, there are differential risks between different classes of compounds.[17] So, does that translate to differences for individuals? It might. I really talk about the influence of age and how certain classes of medicines might be better or worse for them. People who have specific histories—they have histories of serious infections or opportunistic infections. They've had repeated shingles in the past and whatnot. I mean, certainly, it's going to steer you away from certain classes of medicine if they have certain backgrounds or comorbidities. So, you know, really getting into that with the patient and also exploring, like you said, their fears. I mean, they may have had shingles once, and they had a really bad experience, and they never want to have it again, for example. So maybe a JAK inhibitor is probably not the best choice for them. I see a lot of people with chronic, smoldering, underlying lung infections. I mean, in those people, if we're trying to preserve what they have, you know, probably a biologic or a target therapy isn't the best thing for them. But again, if they're not reaching low disease activity with you and really struggling from an RA standpoint, can we go to some other target therapies that might be safer? So, those are the conversations that we tend to have.

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		One of the things I think about with my patients is, how do I communicate succinctly some of these things? And I really like this paper that you and Liana Fraenkel put together, so maybe you can give a nice explanation of how to go about that. **Dr. Curtis:** Certainly. So the paper that we're talking about was published in the November 2023 issue of *Arthritis & Rheumatology*, and it draws on key behavioral and psychologic economic principles. But the idea is that humans rely on heuristics or mental shortcuts—that's what a heuristic is—and this applies quite nicely to medical decision-making.[20] And a lot of heuristics incorporate this idea of a bias. One of them that we're talking about, for example, is an availability bias or an availability heuristic, where the risk of a recent bad case may be overestimated. It looms large because it has such an emotional impact. Another issue that is a related concept is framing effects. You can describe framing in either positive framing or negative framing. So, for example, 4 out of 100 people per year may get herpes zoster. But you also want to frame it positively and negatively, as a best practice. So, correspondingly, 96 out of 100 people in the course of a year did not get herpes zoster. And although those are the exact same pieces of data, in fact, the emotional connotation for patients is often quite different. So framing things both in the positive and the negative can be very helpful because there is an emotional difference there. Finally, thinking about patient's context, you know, what's their baseline risk? And are there modifiable risk factors that will influence that? So, unwillingness to be vaccinated with, say, pneumococcal or flu or other vaccines; or not being willing to give up smoking; or being reticent to undergo recommended cancer screening—getting you off of steroids—things like that, things that you can do something about. So, all of those things can modify risk, and yet patients rarely think of that as explicit risks. Put that on the table, and those are their baseline risks due to treatment or vaccine prevention. Those are things that are helpful to focus the attention, not just on the drug that you want to talk about, but all the other things that are important for context. And then finally, thinking about how fear can delay decision-making or make people choose certain things. That's the idea of this affect heuristic—the emotional appeal for something really bad like cancer or a rare opportunistic infection. So those things are important to keep in mind, and the mnemonic that might help you approach those conversations is CHAT. The "C" is considering [your] patient's context and your and their preconceived biases. Highlight the risk of the treatment that you're talking about. That's the "H".

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		Anchor the baseline, that's the "A." There's some baseline risks, you know, as well as other clinical risk factors, some of them modifiable like you mentioned. And then finally tune in to [your] patient's motivations. What's important to them and their emotions. How are they reacting to what you're talking about? So that's the "T" part of the CHAT. And anytime that you can tie that back to [your] patient's goals and motivations is very helpful and will hopefully be useful as a mnemonic to remember the individual components for those discussions. **Dr. Winthrop:** I totally agree. I just try to focus on what's preventable, right, or what's modifiable. I mean, you can't make someone younger. But all those things you just mentioned, you know, you can often work on. I was just going to add, too, I mean, I really try to get people off Prednisone. A lot of these people are on steroids, and that is a huge, modifiable risk factor for a lot of the outcomes you were just mentioning. And that's really key for those that can get off or at least get down to the lowest dose possible to help prevent some of these things. So I mean, that's really where you can focus. And you know, how can we change that risk? Can we get them to stop smoking, etc.? So I think those things are really important.
4	Digital Data Guide & UPA Safety (10:45–15:19)	**Dr. Curtis:** Well thanks Kevin. To support shared decision-making, it's essential to have the right knowledge and the tools and approaches to help make sense of data in a clear way. One new tool that we've been discussing to help contextualize benefits and risks of upadacitinib in a quantifiable, but hopefully simple and visual way, is the new interactive digital data guide created in partnership with AbbVie. So before we dive into actually how you might use that tool in a practical clinical setting, let's hear about the indications and the limitations of use of upadacitinib in rheumatoid arthritis. **Voice-over:** Upadacitinib is a Janus kinase, JAK, inhibitor indicated for the treatment of: Adults with moderately to severely active rheumatoid arthritis, RA, who have had an inadequate response or intolerance to one or more tumor necrosis factor, TNF, blockers. Limitations of Use for RA: Upadacitinib is not recommended for use in combination with other JAK inhibitors, biologic disease-modifying antirheumatic drugs, bDMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine. **Dr. Curtis:** What we're talking about is this new interactive digital data guide that was created in partnership with AbbVie.

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		For those who might be accessing this in an audio-only format, go to RheumNow.com to access the therapeutic update page with a link to the web app. So the idea is, hey, here's, you know, an icon array of that represents 100 people. And if we're talking about a risk of serious infections with upadacitinib where maybe 3 or 4 out of 100 per year develop a serious infection, you can actually see the 3 or 4 highlighted, and the 96 or 97 who didn't have the infection highlighted in a very quantitative, visual way. That's the idea. And a related concept is [that] it allows some customization of risk—not fully to the extent like some of the cardiovascular risk scores—but it at least allows a discussion around, well, "What is risk based on age?" And, "What is risk based on cardiovascular risk factors?" It allows you to model that in a visual way. This is not some complicated calculator you have to type 10 things into that probably would take too much time, but it does enable you to understand, you know, on upadacitinib, for example, "What is the risk for this kind of a patient?" And to have a fair and balanced discussion. So, have you used that kind of approach in other quantifiable ways in your patients, Kevin? **Dr. Winthrop:** I saw yesterday actually in clinic working with Dr. Atul Deodhar here at OHSU, you know, one of his patients with RA, longstanding, that's been difficult to control on Prednisone, has kind of blown out of TNF drugs, been in the hospital twice in the last couple of years with pneumonia, has underlying lung disease related to the RA, and some bronchiectasis. I mean, these are the kinds of patients I see, and you know, using a tool like this would be very useful, because I can [see], "Hey, look, here's kind of the baseline risk of a serious infection in someone starting UPA and it's around 3 to 4 per 100 patient years." I mean, that's what we know from clinical trial data. And this person happened to be elderly. This tool, I'll just mention, goes beyond infection, of course. It looks at all adverse events of special interests, you know, when it comes to JAKs, you know, things we think about is venous thromboembolism, MACE. So I mean, certainly talking about cardiovascular events, specifically, cardiac arrest or MI, and things like that, pulmonary embolism. You know, a lot of the patients I see are like this patient. They've had problems with TNF drugs, particularly because that's where they started in terms of trying to control their RA. Obviously, those drugs are incredibly efficacious, but they have their own safety risks.[17] But suffice it to say, to answer your question, this tool is useful. It looks at all of the outcomes of special interests, both infection and cardiovascular and malignancy. **Dr. Curtis:** Yeah, I mean, the cancer risk is a big deal that ties into one of the other heuristics that's described in that paper, the affect heuristic, because obviously, there's a lot

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		of emotional connotation with the big cancer word.[20] That risk in multiple analyses, even in oral surveillance, has been shown to probably not start immediately, but only develop after people have been on therapy for a year and a half or more.[21,22] And again, trying to tie that into risks and benefits, I'll say, "Look, you know, after 1.5–2 years or more, we'll have known if you're going into remission. And so let's talk about that. But you know, probably on day 1, or even within the first 6 months, let's figure out how you do clinically." Any treatment that we use, you have to always balance the safety and the long-term safety against the long-term benefit. And sometimes people forget about that—that undertreated RA has its own risks—and if I can get you to remission, that may offset even some drug-related risks like for malignancy, which definitely need to be talked about and not minimized.
5	Close (15:20–18:56)	**Dr. Curtis:** We're getting close to time, but just to recap. So where we've been—so ACR and EULAR encourage shared decision-making. It's an important step to getting patients under good control, quantifying risk, visualizing ideally with this new tool we've talked about. There's a lot more we could talk about. Kevin, thanks for joining me today. Any last thoughts? **Dr. Winthrop:** No, I think we covered it. I like this concept. I mean, this quote, unquote, shared decision-making has kind of been the buzzword. We all kind of laugh about it, but it is what we do. I mean, it's what we're supposed to be doing. And it's really exploring what the patient knows and what they want to do, you know, after you give a nice explanation, hopefully a thorough explanation, of the risks and benefits of certain approaches. And people are going to be different, based on their age and their cultural, their heritage, I mean their backgrounds. People have different fears. So you really got to explore those things, listen to the patient, and then help guide them in making the right decision. **Dr. Curtis:** Agreed. Listeners, the upadacitinib digital data guide that Kevin and I referenced a couple times and we discussed is available online for you to check out today. You'll find that link in the latest therapeutic update on RheumNow.com. It allows you to estimate and customize for multiple outcomes, most of which we mentioned, and do some personalization based upon patient's age and other unique risk factors. The goal is for it to be a useful tool for future shared decision-making conversations. **Voice-over:** It is important to note that upadacitinib has a boxed warning for serious infections, mortality, malignancies, major adverse cardiovascular events, and thrombosis.

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		Patients treated with upadacitinib are at increased risk for developing serious infections that may lead to hospitalization or death. Malignancies have been observed in upadacitinib-treated patients. In RA patients treated with another JAK inhibitor, a higher rate of lymphomas and lung cancers was observed when compared with TNF blockers. Non-melanoma skin cancers have also been reported. Periodic skin examinations are recommended in patients at increased risk, and patients should wear protective clothing and use sunscreen. Additionally, a higher rate of all-cause mortality, including sudden cardiovascular death, as well as major adverse cardiovascular events, pulmonary embolism, and venous and arterial thrombosis were observed with another JAK inhibitor compared with TNF blockers in RA patients 50 years of age and older with at least one cardiovascular risk factor. Thromboses have also been observed in upadacitinib-treated patients. Avoid upadacitinib in patients at risk of thrombosis. Consider the individual patient's risks and benefits prior to initiating or continuing therapy. The most common adverse reactions in RA, greater than or equal to 1%, were upper respiratory tract infections, herpes zoster, herpes simplex, bronchitis, nausea, cough, pyrexia, acne, and headache. Please also read the additional safety information within the RX UPDATES on RheumNow.com titled "A JAK Inhibitor CHAT, Shared Decision-Making in RA" regarding hypersensitivity reactions, other serious adverse reactions, avoiding live vaccines and the importance of immunizations, and medication residue in stool. Review upadacitinib full Prescribing Information for additional information at www.rxabbvie.com/pdf/rinvoq_pi.pdf **Dr. Curtis:** Thanks so much for listening. **Dr. Winthrop:** Thanks, guys. Cheers.

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INDICATION

Upadacitinib is a Janus kinase (JAK) inhibitor indicated for the treatment of:

Adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more tumor necrosis factor (TNF) blockers.

> **Limitations of use for RA:** Upadacitinib is not recommended for use in combination with other JAK inhibitors, biologic disease-modifying antirheumatic drugs (bDMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine.

IMPORTANT SAFETY CONSIDERATIONS AND BOXED WARNING

Serious Infections: Patients treated with upadacitinib are at increased risk for developing serious infections that may lead to hospitalization or death. These infections include tuberculosis (TB), invasive fungal, bacterial, viral, and other infections due to opportunistic pathogens. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids. Test for latent TB before and during therapy; treat latent TB prior to use. Consider the risks and benefits prior to initiating therapy in patients with chronic or recurrent infection. If a serious infection develops, interrupt upadacitinib until the infection is controlled.

Mortality: In a postmarketing safety study in RA patients ≥ 50 years of age with at least one cardiovascular (CV) risk factor comparing another JAK inhibitor to TNF blockers, a higher rate of all-cause mortality, including sudden CV death, was observed with the JAK inhibitor.

Malignancies: Malignancies have been observed in upadacitinib treated patients. In RA patients treated with another JAK inhibitor, a higher rate of lymphomas and lung cancers was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with upadacitinib, particularly in patients with a known malignancy (other than a successfully treated non-melanoma skin cancer [NMSC]), patients who develop a malignancy when on treatment, and patients who are current or past smokers. NMSCs have been reported in patients treated with upadacitinib. Periodic skin examination is recommended for patients who are at increased risk for skin cancer. Advise patients to limit sunlight exposure by wearing protective clothing and using sunscreen.

Major Adverse Cardiovascular Events (MACE): In RA patients who were ≥ 50 years of age with at least one CV risk factor treated with another JAK inhibitor, a higher rate of MACE (CV death, myocardial infarction, and stroke) was observed compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with upadacitinib. Patients should be informed about the symptoms of serious CV events and the steps to take if they occur. **Discontinue upadacitinib in patients that have experienced a myocardial infarction or stroke.**

Thrombosis: Thromboses, including deep vein thrombosis, pulmonary embolism, and arterial thrombosis, have occurred in patients treated with JAK inhibitors, including upadacitinib. Many of these adverse events were serious and some resulted in death. In RA patients who were ≥ 50 years of age with at least one CV risk factor treated with another JAK inhibitor, a higher rate of

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thrombosis was observed when compared with TNF blockers. Avoid upadacitinib in patients at risk. Patients with symptoms of thrombosis should discontinue upadacitinib and be promptly evaluated.

Hypersensitivity Reactions: Upadacitinib is contraindicated in patients with known hypersensitivity to upadacitinib or any of its excipients. Serious hypersensitivity reactions such as anaphylaxis and angioedema were reported in patients receiving upadacitinib in clinical trials. If a clinically significant hypersensitivity reaction occurs, discontinue upadacitinib and institute appropriate therapy.

Other Serious Adverse Reactions: Patients treated with upadacitinib also may be at risk for other serious adverse reactions, including gastrointestinal perforations, neutropenia, lymphopenia, anemia, lipid elevations, liver enzyme elevations, and embryo-fetal toxicity. If upadacitinib exposure occurs during pregnancy, please report the pregnancy to the surveillance program by calling 1-800-633-9110.

Vaccinations: Avoid use of live vaccines during, or immediately prior to, upadacitinib therapy. Prior to initiating upadacitinib, it is recommended that patients be brought up to date with all immunizations, including prophylactic varicella zoster or herpes zoster vaccinations, in agreement with current immunization guidelines.

Medication Residue in Stool: Reports of medication residue in stool or ostomy output have occurred in patients taking upadacitinib extended-release tablet. Most reports described patients with shortened gastrointestinal transit times. Instruct patients to contact their healthcare provider if medication residue is observed repeatedly.

Common Adverse Reactions in RA: The most common adverse reactions (≥1%) were upper respiratory tract infections, herpes zoster, herpes simplex, bronchitis, nausea, cough, pyrexia, acne, and headache.

Review accompanying upadacitinib full Prescribing Information for additional information, visit www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110.

Abbreviations:

ACR, American College of Rheumatology; bDMARD, biologic disease-modifying antirheumatic drug; EULAR, European Alliance of Associations for Rheumatology; JAK, Janus kinase; MACE, major adverse cardiovascular event; MI, myocardial infarction; OHSU, Oregon Health & Science University; RA; rheumatoid arthritis; TNF, tumor necrosis factor; UPA, upadacitinib.

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