

**Collaborations in Rheumatology: A Conversation with Gastroenterology**

Speakers: **Dr. Kathryn Dao, Dr. Amar Naik**

| Section                                    | Transcript   |
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| Introduction                               | <p><b>Kathryn Dao:</b> Hi, this is Dr. Katherine Dao. Welcome to RheumNow.</p> <p>This podcast is sponsored by AbbVie US Medical Affairs.</p> <p>Today, I'm going to have a conversation with a gastroenterologist, Dr. Naik. Dr. Naik, would you mind telling us a little bit about yourself?</p> <p><b>Amar Naik:</b> Hi, for sure. Thanks, Dr Dao. My name is Amar Naik. I'm the founding partner at Midwest Digestive Health and Nutrition and director of the Inflammatory Bowel Disease program. Thanks for having me; nice to be here.</p> <p><b>Kathryn Dao:</b> Thank you for joining me. So, this is a very important conversation. And during this conversation that we're gonna have, we're gonna talk about different aspects of how GI and rheumatology intersects. So, from our diseases, I treat rheumatoid arthritis, psoriatic arthritis — to GI stuff where you're treating inflammatory bowel diseases, Crohn's, and ulcerative colitis.</p> <p>We're gonna be mentioning upadacitinib, and so, before we begin our discussion. I do want to review the indications and limitations for upadacitinib in RA, PsA, and IBD.</p> <p>Upadacitinib is indicated for adults with moderately to severely active rheumatoid arthritis and adults with active psoriatic arthritis who have had an inadequate response or intolerance to one or more tumor necrosis factor blockers.</p> <p>In addition, upadacitinib is indicated for adults with moderately to severely active ulcerative colitis and adults with moderately to severely active Crohn's disease who have had an inadequate response or intolerance to one or more TNF blockers. Limitations of use is that upadacitinib is not recommended for use in combination with other JAK inhibitors, biological therapies for the specified indications, or with potent immunosuppressants, such as azathioprine and cyclosporine.</p> |
| Similarities and differences in RA and IBD | <p><b>Kathryn Dao:</b> So, with that in mind, I wanted to start our discussion with some of the common themes with regard to our diseases that both you and I treat.</p> <p>For the most part, I treat a lot of rheumatoid arthritis patients and psoriatic arthritis patients, and I know that with you running the IBD clinic, you're seeing the Crohn's and ulcerative colitis. Could you tell us a little bit more about some of the similarities and differences that you might see in your patient group and my patient group?</p> <p><b>Amar Naik:</b> Oh, absolutely, Dr. Dao. Thank you. So, rheumatoid arthritis and inflammatory bowel diseases, or IBD, we'll call that. They are very, very similar kinds of phenomenon. They're basically driven by essentially what amounts to a dysregulated immune response to either potentially some potential bacterial antigens or some other kind of systemic stress that potentially is a big part of this. And so, what I've learned over the years is we have kind of taken lots of our disease management tips and skills from rheumatologists; the kind of extraintestinal manifestations are very common. You know, at least over 30% of our patients are suffering from joint pain, and</p>   |

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|  | <p>that, well we call that enteropathic arthropathy. It can be quite debilitating and sometimes shed a light into clues as to what may be happening in their intestines.</p> <p>So, when you think of, potentially, the rheumatoid arthritis patients, they may be a little older. Our patients are young and with the same type of debilitating joint disease and inflammation both in their gut and in their joints. So, if you can imagine someone who has frequent, urgent stool eliminations or pain, malnutrition, and then having to quickly get to the bathroom with painful, inflamed joints, it's really, really a lot of suffering that patients undergo.</p> <p>So, we definitely have significant overlap, and we've got to learn a lot and collaborate a lot with our rheumatologists because of this.</p>  |
| <p>Background risks with systemic inflammation</p> | <p><b>Kathryn Dao:</b> Yeah. And whenever we see uncontrolled inflammation, I mean, I'm not just worried about the joints, right? Because there's systemic effects. We worry about an increase in cardiovascular disease, infections, malignancies.</p> <p>But I'm really worried about how the disease is gonna ravage a patient, and oftentimes, I'll tell the patient, "Look, your body is your house. When you have a fire, that's gonna burn down your house. And you can use a squirt gun. You can use a big, you know, garden hose, or let's bring out the fire hydrant. We got to control this inflammation because there's nothing left to come home to if you don't."</p> <p><b>Amar Naik:</b> Yeah, absolutely. And I think you bring up such an amazing point in the sense that, hey, we have to talk about the effects of the disease, the debilitating disease as side effects on the body, the impact of uncontrolled inflammation.</p> <p><b>Kathryn Dao:</b> Right. And so, we know that patients who have disease activity have a high risk for cardiovascular disease. So, do you discuss, with your patients, cardiovascular risk?</p> <p><b>Amar Naik:</b> Absolutely. I think it is important to discuss systemic inflammation. I sometimes, right or wrong, will even talk about some of the inflammatory serologic markers that not all of our patients, but many of our patients use, like, for example, C-reactive protein when we measure that. Even cardiologists per se have utilized that same marker to kind of risk-stratify sometimes patients with coronary disease. So, elevations in that inflammation marker could suggest, and kind of tie in together, some of the risk factors of inflammation throughout, and then what that kind of impacts from the cardiovascular standpoint.</p> <p>So, for example, inflammation in your blood vessels, inflammation in your, in your gut. There's, you know, almost like this whole other background of vasculitis that we see where there's inflammation everywhere, and then we have to potentially control this all throughout. And so, it's your gut and your joints, as like, where we see the target of things potentially deteriorating. But actually, what lies beneath is actually, you know, systemic and involving the whole body itself. And some of those things are your heart, and just like we talk about joints with the digestive tract, and there's skin, there's all other areas that all kind of manifest outwardly from the systemic inflammation.</p> |
| <p>Rheumatology and gastroenterology's</p>         | <p><b>Kathryn Dao:</b> So, one of the things that you know had caught me by surprise was that the European League Against Rheumatism, so EULAR. They had made a very bold</p>   |

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| <p>role in CVD monitoring and other primary care issues</p> | <p>statement. They said that the rheumatologist is responsible for cardiovascular disease monitoring.</p> <p>And I'm thinking to myself, <i>Whoa! What do you mean me?</i> I mean, usually, it should be like the primary care doctor and a patient's cardiologist, right? But actually, if you think about it, we, as rheumatologists, we see our patients pretty frequently and, just like you guys do, you guys see your patients pretty regularly, as well. So, are you monitoring these patients? How are you mitigating their risk?</p> <p><b>Amar Naik:</b> I love that question, and, being a huge football fan, we have become armchair quarterbacks for our patients, where they have this wonderful long-term relationship with us. We do disease monitoring serologically. We use, you guys have joint exam, we have endoscopic evaluation. But a member of our team sees them or has a touch point with them every 3 months, every few months, sometimes, for a variety of reasons, and making sure patients can stay on therapy, get on therapy, address their questions, etc.</p> <p>And so I think there's a little bit of onus in terms of us having to take some responsibility about their medical health. You and I are internists at the core, and then we come out into our own specific fields in rheumatology and gastroenterology. But we have to take ownership of talking about patients making sure they have cardiovascular health; making sure that patients can get, you know, for example, health maintenance. We play a huge role in helping our primary care docs with vaccinations, things like that, to ensure, you know, longer-term safety. So, I think we generally get that great doctor-patient relationship that you had envisioned, you know, when you're a young medical student, and you're really taking care of that whole person that has the condition rather than just treating that condition itself. And I think we have a lot of responsibility to communicate benefits, harms, risks, and how to live healthy, all throughout</p> |
| <p>Disease activity assessment in IBD</p>                   | <p><b>Kathryn Dao:</b> So, I think you have a much harder job than I do because, you know, the way you assess disease activity. Because if a patient eats something wrong, they might have abdominal pain and diarrhea; I mean, just out of curiosity, tell me about how you assess these patients with IBD.</p> <p><b>Amar Naik:</b> Oh, my gosh, it's so, it's very challenging. Because, if many of us have had, you know, like a bad food and had diarrhea and urgency. We can have that emphasis, and then, you know you have that for all the time, because if you didn't do anything wrong, and now you almost have this pseudo-PTSD, like I had diarrhea today, does that mean my ulcerative colitis is out of control? Things are going awry.</p> <p>I kinda look at it in terms of a 2x2. We have patients that are good and feel good. They are bad, and they feel bad, and we feel great about what to do there. And sometimes, patients are bad and feel good, and what that means is potentially you catch signs of the disease activity being active early when they're feeling great. You start seeing the inflammation markers rise; you start seeing things kind of drift off. So we have to kind of confirm with other objective data.</p> <p>And then you have patients that feel horrible. For a variety of reasons, perhaps scarring or damage. It's like, okay, we have to work on their diet a little better, work on cutting down or other things that can't be tolerated while we have actually also healed</p>   |

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|   | <p>the mucosa, so we have to then work at making them feel better. So, you're right. It's very challenging.</p> <p>Knowing your patient is the best kind of solution to trying to figure out if this is gonna be okay or not and addressing the pattern. It's very challenging, as you can imagine, like something so subtle.</p>  |
| <p>Extra-articular manifestations in IBD and partnership across specialties</p> | <p><b>Kathryn Dao:</b> The other thing that I was wondering also is that, a lot of times, I look for extra-articular manifestations. And so, patients with psoriatic arthritis, they may have, I mean, not just skin disease, but they can have uveitis, they can have colitis, and different kinds of colitis. In terms of your practice, do you just only worry about the gut? Or do you also assess other aspects?</p> <p><b>Amar Naik:</b> Well, that's what makes this so beautiful in terms of utilizing precision medicine and utilizing the patient that's there. There's something about the IBD patient that also has pretty significant joint inflammation because not everybody does, right? But there's many that do. And we have a lot to learn from that. There are people that have more dermatologic phenomenon, the patients that have had more, I mean, immunologic kind of like forming antibodies, etc., right?</p> <p>So, you know what my favorite clinic was right when I started, and it was when I had a dermatologist and a rheumatologist and a GI. Us being there together in an era where things were still developing. That was my favorite clinic. That's where I think the future is of cross-collaboration is. So, it definitely makes a huge difference.</p>  |
| <p>Treatment options after TNFi failure</p>                                     | <p><b>Kathryn Dao:</b> So, you know, the ACR, American College of Rheumatology, we have guidelines with what they would recommend us using to treat as first-line therapy, second-line therapy. I'm sure the AGA has something similar. So, what do you do for patients who've already tried and failed TNF inhibitors?</p> <p><b>Amar Naik:</b> You know, it's TNF failure is a very real thing, unfortunately. And oh, I wish it weren't. There are patients that I like sorting them out by patients who TNFs never really quite worked for them to the degree that they should have. And there are some patients who, they worked for a while, and then you lost response, right? Even though you've been monitoring and doing well with them. And it's just the nature of their systemic inflammatory condition and how their immune system is working.</p> <p>And so, I think, when TNFs fail, historically in inflammatory bowel disease trials, those patients don't do as well on subsequent therapies sometimes, and I don't really know why. I don't know if it's because of suppressing the TNF, this has occurred. Or it's a disease severity issue in inflammatory bowel disease. So, disease severity, saying, there's features of that IBD that the patient has very severe phenotype; so we have to be very aggressive versus disease activity at any one snapshot point time. Maybe how that scope looks, how that, you know, hemoglobin is low, how that the degree of leukocytosis, etc. And so, I like to think about, you know, if TNFs have failed, and the disease is active, and we're having problems, I like to think about other modalities.</p> |
| <p>ORAL Surveillance</p>  | <p><b>Kathryn Dao:</b> Yeah, you know. So, when the ORAL Surveillance trial came out, it was a study looking at tofacitinib versus a TNF inhibitor in patients with rheumatoid arthritis who have high risk for cardiovascular events, and they were looking at cardiovascular events. They were looking at malignancy, and during the study trial, I mean their</p>   |

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|         | <p>primary endpoint is to show non-inferiority of tofacitinib compared to a TNF inhibitor. Well, they failed to meet their primary endpoint.</p> <p>So, when those warning labels came out, I mean, we got so many phone calls from our patients. There were so many people who were trying to get an expert opinion, they called me, and they're like, "Well, what do you think? Should we take them off the drug, should we not?" And all this.</p> <p>And I was like, "Well, first of all, you know, is the patient okay? Are they doing well on their drug? And if their disease is under control, then I would recommend that they stay on the drug." Alternatively, if the patient has a lot of concerns, just had a heart attack or something, then yes, maybe you should switch it, you know, but each case should be individualized.</p> <p>And so, I just didn't know how GI approached this. I know you guys have younger patients than we do. And to me, it would be better if you can control, you know, all their comorbidities. Tell them to stop smoking, get their blood sugar under control. Tell them to exercise 150 min a week. Watch your diet, have a healthier lifestyle. I think that has impact in reducing cardiovascular risk, in addition to controlling their disease activity.</p> <p><b>Amar Naik:</b> You said that perfectly. If you found something that works for patients who haven't had a lot of things work well at all for them over their time, and they've struggled, struggled, struggled. People can struggle for 10 years and be 30 years old. Right? And that's, that's sad. That's so defeating, and you finally get your life back. And you're 32, and you missed your twenties. And you're right. That's a different population from the standpoint of looking at the risk factors, right? Like, oh, obesity, hyperlipidemia, blood pressure, prediabetes, etc., controlling those things, they're eating better. They're off their corticosteroids, which can increase the risk for all of those things to potentially negatively affect them. And so that's been a big deal.</p> <p><b>Kathryn Dao:</b> Yeah, this isn't like a very simple discussion because everybody is a little bit different in terms of how they manage these patients. And how patients actually respond.</p> |
| Closing | <p><b>Kathryn Dao:</b> So, any last words because this has been a great conversation, and I wish I could continue it for the next 2 hours, but I don't know if we're gonna lose any audience members.</p> <p><b>Amar Naik:</b> Yeah, we could talk seemingly forever. No, I really appreciate this. Look forward to talking, hopefully sometime soon and again. And then, I think we, collaborating together, the conversation just can be opening the lines of communication could solve so many problems. And better our patients. And so, this is really great. And I wish we could, we could do this more often, and even on a more tangible clinical kind of standpoint. So, this is fantastic. Thank you.</p> <p><b>Kathryn Dao:</b> Thank you so much for joining me. And audience, thank you so much for listening. If you'd like to learn more about upadacitinib clinical data in patients with RA, in patients with ulcerative colitis, or Crohn's disease there's a downloadable summary on the RheumNow therapeutic updates page. Thank you so much again for joining me. This is Dr. Katherine Dao.</p>   |

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| Important safety information | <p><b>VO artist:</b> It is important to note that upadacitinib has a boxed warning for: serious infections that may lead to hospitalization or death, mortality, malignancies, including lymphomas and lung cancers, major adverse cardiovascular events, and thrombosis, including deep vein thrombosis, pulmonary embolism, and arterial thrombosis. Avoid upadacitinib in patients at risk of thrombosis.</p> <p>Consider the individual patient's risks and benefits prior to initiating or continuing therapy.</p> <p>See full Prescribing Information for additional information about hypersensitivity reactions, non-melanoma skin cancers, other serious adverse reactions, avoiding live vaccines and the importance of immunizations, medication residue in stool, and the most common adverse reactions.</p> <p>Review upadacitinib full Prescribing Information for additional information at <a href="http://www.rxabbvie.com/pdf/rinvoq_pi.pdf">www.rxabbvie.com/pdf/rinvoq_pi.pdf</a></p> |
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