Composite Measures to Inform Treatment Choices in Bio-naïve Patients with PsA

Podcast Transcript

Dr. Mease: Welcome to RheumNow, this podcast is sponsored by AbbVie, U.S. Medical Affairs. My name is Dr. Philip Mease. I'm the director of rheumatology research at Swedish Medical Center, Providence Saint Joseph Health in Seattle, Washington, and clinical professor at the University of Washington. I'm joined today by Dr. Saakshi Khattri. Dr. Khattri, could you introduce yourself?

Dr. Khattri: Hi. My name is Dr. Saakshi Khattri, and I'm a board-certified rheumatologist and dermatologist at the Icahn School of Medicine at Mount Sinai in New York City. Thank you so much for having me, Dr. Mease.

Dr. Mease: Wow, double-barreled rheumatology and dermatology. How long did that all take?

Dr. Khattri: You don't want to know, the whole thing with internal medicine and then taking a year to do, to be an attending in rheumatology and then two years to do research to get into derm was a total of 17 years.

Dr. Mease: So, we've got one well-trained commentator here today. Thanks, Dr. Khattri. We both know that PsA can be multidimensional and, therefore, challenging to manage because the disease manifests in such diverse ways. Patients with PsA that come into our practices often have heterogeneous manifestations.

I often liken it to an orchestra with my patient. So, at times each section of the orchestra is playing fortissimo, so joints and enthesis, spine, skin are all blaring away. But at other times, they're just maybe a single section that's playing like the flute section or the violin section. It may be that a single joint is acting up, or the person may have a particular aggravating aspect of psoriasis, such as scalp psoriasis or genital psoriasis.

So, it's our job to ferret out which of those domains is clinically active and how can we best treat each of the domains that are bothering the patient effectively. We have at our disposal numerous composite outcome measures that have been developed by GRAPPA, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis.

As PsA is a multi-domain disease, these measures may also be multi-dimensional, meaning they focus on several of these PsA clinical domains at the same time. Or they can be specific to a single domain. In this podcast, we will focus on a few: ACR response measures, minimal disease activity or MDA, the DAPSA score, and PASDAS.

With that in mind, let's consider these composite outcome measures in the context of risankizumab, or risa, from the KEEPsAKE 1 trial in patients with PsA who are bio-naïve, focusing on long-term data and discuss how these measures may also be utilized to inform clinical practice in patients with this complex, heterogeneous disease.

Before we jump into the discussion, I think we should remind our listeners that risankizumab is indicated in adults for the treatment of moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy and active psoriatic arthritis. Dr. Khattri, can you give our audience an introduction to the KEEPsAKE trial program?

Dr. Khattri: Absolutely. The KEEPsAKE program assessed the efficacy and the safety of risa, an IL-23 inhibiting antibody, in adult patients with active psoriatic arthritis. There are currently two KEEPsAKE trials, both phase three randomized controlled trials, double-blinded to 24 weeks with the primary

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endpoint of ACR20 at Week 24. The most important difference between KEEPsAKE 1 and 2 is the patient population. KEEPsAKE 1 had bio-naïve patients. KEEPsAKE 2 the patient population was mixed with about 53% were bio-naïve, and 47% had been exposed to a prior biologic DMARD with either an inadequate response or intolerance.

Both trials enrolled patients who had an inadequate response to conventional synthetic DMARDs though concomitant conventional synthetic DMARDs were allowed. Both trials met the primary endpoint of ACR20 at Week 24, 57% of patients in the risa arm achieved ACR20 compared to 34% in the placebo arm. These response rates were sustained through Week 100, with 64% of patients treated with risa achieving an ACR20 and 42% achieving an ACR50, and 27% achieving an ACR70. At Week 24 in KEEPsAKE 2, which was the mixed population, 51% of patients in the risa arm achieved ACR20 compared to 27% in the placebo arm.

So, Dr. Mease, we see ACR20 as the primary endpoint in uh many rheumatology clinical trials. How do you think the information conveyed in looking at ACR20, 50, 70 response rates helps inform decisions in the clinic for PsA patients that you see?

Dr. Mease: We don't typically use ACR response in our daily practice. It's a little bit complicated to obtain and calculate.

We tend to have it as a metric in our mind based on our listening to lectures about response or reading papers where the ACR20, 50, and 70 are highlighted as the key outcome measures for rheumatoid arthritis trials and for psoriatic arthritis trials. So, I would say that we use these numbers as benchmarks, and we can turn to the patient and say, well, this percentage of patients are achieving these kinds of thresholds, and these give us a clear sense compared to placebo that a drug is working.

So that's how we mainly use it. And the measures are typically collected in all of these clinical trials that we were talking about. It's a key requirement for regulatory approval to show a difference between treatment and placebo for the ACR20 response.

So, the key elements that comprise the ACR responses are things like tender and swollen joint count, patient global, patient pain, health assessment questionnaire. There's a physician component. There's also a function aspect to it.

It's actually fairly comprehensive, albeit mainly focused on joint response. And there are other measures which we're going to get into in a moment which are a little bit more holistic.

And one of these is minimal disease activity or MDA. This particular measure at Week 24 was one of the ranked secondary endpoints in the KEEPsAKE 1 trial, and an MDA response was seen in 25% of patients treated with risa compared to 10% with placebo.

So, a clear separation. By Week 100, this response had climbed. Thirty-eight percent of patients achieved MDA during the open-label extension. Dr. Khattri, considering this long-term data for risa, how does this composite endpoint influence your treatment decisions?

Dr. Khattri: So, I love the MDA. Yes, I want to say it out loud. I love the MDA. I think, you know, as rheumatologist, that PsA is very heterogenous.

There are different domains of PsA, including skin. There's enthesitis. So, the MDA is a nice composite measures, looking at different domains of involvement. It is a multidimensional outcome measure that assesses skin, it assesses joints, functionality, patient's assessment of their disease, enthesitis, pain metric. So, it's a very nice blend of objective and subjective. And I really like the MDA. To meet MDA, you have to have five of seven criteria.

It's used in clinical trials. And while this whole thing might sound daunting, we as physicians are already collecting the MDA without calling it MDA.

We are doing a swollen joint count; we're doing a tender joint count that meets two components of MDA right there. We're asking a patient about pain. So that's the third one. We're asking a patient how they feel about their disease activity. That's the fourth metric. I'm sure we're looking at their skin as well. And then we're measuring for enthesitis and quality of life questionnaire. So, we are doing components of the MDA without really calling it an MDA in our practice. There's no lab parameters. I don't have to send a patient for a blood test to measure an MDA.

So I really like that, and patients like that as well. The MDA is something I use to monitor patient responses to treatment, and it helps me guide whether the patient is responding to the treatment that I've given them. And if they are not responding, I switch treatment. So, I definitely like the MDA and use it a lot in my practice.

Dr. Mease: That's great. And I would echo that MDA is my favorite measure as well. Most of it, virtually all of it, I can do right there at that moment with the patient. The only thing that requires a little bit of calculation is the HAQ score. And just like you were mentioning, you're just going to be asking a few questions about physical function.

And so, sometimes I cheat, and I'll use this Seattle HAQ, which is, “Did you go hiking last weekend?” And if they said yes, well, there you go. It's less than or equal to 0.5. So, there you have it. I don't know, what is a New York HAQ?

Dr. Khattri: I was going to say, I think the New York City HAQ might be if you can ride the Citi Bike to work.

Dr. Mease: The other thing that I'm aware of from research studies is that achievement of MDA, and sustainment of it, is associated with all kinds of good things, like lack of radiographic damage progression, overall improvement in work productivity, improved quality of life.

Let's move on to the other two composite endpoints we want to discuss today from KEEPsAKE 1, which are PASDAS and DAPSA. At Week 52, patients treated with risa had a 3.01-point improvement and PASDAS score from the baseline value of 6.4, and 32.78-point improvement in DAPSA score from the baseline value of 45.6. It's important to note that these endpoints were not controlled for multiple comparisons in the KEEPsAKE 1 trial.

Dr. Khattri: Dr. Mease, you mentioned that you use the MDA in your practice. How about the PASDAS, how does that come into play in your practice?

Dr. Mease: It doesn't. We do it in clinical trials. So, we collect all the items and then put them into the tablets, and that goes back to a central data collection place. And then there's, I mean, it's got things like square roots that you have to do and a calculations that frankly aren't going to be used in practice.

But, it's proving to be psychometrically probably the best instrument that we have. So, if you really want to see a change that's accurate and reliable, then we use the PASDAS score.

It includes assessment of tender and swollen joints, physician and patient global, pain and function. An enthesitis measure and a dactylitis measure, and an acute phase reactant. Notice that there's no skin assessment, but it turns out that then in the 400 or so patients that were in the dataset that went into the construct of the PASDAS measure, the skin score ended up being subsumed under the patient, largely under the patient global.

So, this is a cool part of the measure, is that it gives you thresholds and showing you that if you want to get into a state of remission or low disease activity, we've got quantitation of it. So, I think that it's a good measure but not practical for clinical practice. Now, Dr. Khattri, can you tell us what role a less complex measure like DAPSA plays in your management of patients with PsA?

Dr. Khattri: Definitely easier to do. Certainly, something that I reserve for my patients that just have arthritic symptoms and they have no skin involvement. The DAPSA cut-offs for remission or LDA are also GRAPPA-endorsed. So that helps me as a target value. It is the sum of patient's global assessment, the assessment of pain, swollen joints, tender joints, and CRP, a score of less than equal to 4 indicates remission.

Where I use, as I said, is more for my PsA patients, as long as they don't have any skin involvement. Where I think I don't like it is the need for bloodwork

How about you, Dr. Mease? How do you use DAPSA?

Dr. Mease: We do use DAPSA. It's easier to collect. We recorded it in our registry data, and patients will like to track it just like they track the MDA. But like you, we tend to preferentially use the MDA because it's more multi-dimensional.

Dr. Khattri: We talked about all these, activity measures, Dr. Mease, the other important point that patients and certainly prescribers are concerned with is safety. So, what are your thoughts on safety?

Dr. Mease: I think it's just as important as getting across the efficacy data from trials when we're doing the shared decision-making process with patients.

So, I would say that it's just as important as discussing efficacy. Dr. Khattri, can you review some of the safety data that we've learned from the risa trials?

Dr. Khattri: Yes, absolutely. Safety is important for our patients and also for us as prescribers. If you look at the overall safety profile of risa, in PsA it was consistent with what was seen in the psoriasis space, increase ALT/AST-elevations were seen in the PsA space and not the psoriasis space.

However, no serious hepatic events were reported, and they did see some hypersensitivity reactions as well. In the PsA KEEPsAKE 1 trial through 24 weeks, they had the usual suspects: treatment-emergent AE such as nasopharyngitis, upper respiratory tract infection. As I mentioned, there was increased ALT/AST, there were headaches, and some hypersensitivity reactions. We all, as physicians, know that before we're starting a patient on a biologic, we are doing things to mitigate that risk, such as evaluating for tuberculosis.

Before initiating treatment, I ask my patients about a risk of hypersensitivity reaction, if they are on other, conventional synthetic DMARDs along with risa, I certainly monitor the labs a little bit more frequently, and then, vaccinations, no live vaccines while they're on risa, age-appropriate vaccines, ideally before they start. So that's what I'm doing in my practice.

Dr. Mease: And the fact that the drug is given very infrequently once it's in maintenance phase, just once every 3 months.

So, we've covered a bunch of territory today. We've talked about several measures. Dr. Khattri, could you briefly summarize, just to bring us to a close, what do you really like to use and why?

Dr. Khattri: We talked about ACR scores, we talked about MDA, DAPSA, PASDAS.

I love the MDA personally, and that's really the only measure that I use in my practice because it's multi-dimensional. It's looking at different components of psoriatic arthritis and involves skin as well. And I'm a little biased as a dermatologist because if there's no outcome measure that has skin, I stay away from it. So, I really love the MDA.

How about you, Dr. Mease?

Dr. Mease: I would agree. Patients really appreciate the fact that you're assessing each of these clinical domains. You're looking at the skin, you're feeling their joints.

And, I find the MDA to be the best overall outcome measure. But the DAPSA is a close second in terms of ease of use, very close to what the RAPID3 is.

And I think that the other kinds of assessments having to do with emotional health are things that I will do depending on my read of the patient at the time. I think getting at some of the emotional aspects of their disease and its impact on them I think are really important as well.

So, I think that you've been bringing up some great points today, Dr. Khattri and I really appreciate your taking the time to join me today.

Dr. Khattri: Dr. Mease, thank you so much for having me.

Dr. Mease: And thank you, listeners. If you would like to learn more about composite endpoints and the KEEPsAKE trial program, there's a downloadable summary of some of the topics we discussed today and links to other content on the *RheumNow Therapeutic Updates* page. Thank you for listening.

Voice Over: Risankizumab, a humanized monoclonal antibody to IL-23, is indicated for the treatment of active psoriatic arthritis and moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

Risankizumab is contraindicated in patients with a history of serious hypersensitivity reaction to risankizumab or any of the excipients. Serious hypersensitivity reactions, including anaphylaxis, may occur. If a serious hypersensitivity reaction occurs, discontinue risankizumab and initiate appropriate therapy immediately. Risankizumab may increase the risk of infections. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If such an infection develops, discontinue risankizumab until the infection resolves. Evaluate patients for tuberculosis infection prior to initiating treatment with risankizumab. Avoid use of live vaccines in patients treated with risankizumab. The most common adverse reactions (≥1%) are upper respiratory infections, headache, fatigue, injection site reactions, and tinea infections.

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