Individualized PsA Treatment With an IL-23i or a JAKi
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Speakers:

1. **Saakshi Khattri, MD**
2. **Lindsay Tom, PA-C**

Topic	Transcript
Opening	**Saakshi Khattri, MD** Welcome to RheumNow. This podcast is sponsored and developed by AbbVie Medical Affairs and Health Impact. My name is Dr. Saakshi Khattri, and I'm a rheumatologist and dermatologist at the Icahn School of Medicine at Mount Sinai. I'm so glad to be back with a follow-up to our October 2026 episode. If you missed my discussion with Drs. Amin and Steinberg, be sure to check out the link on this podcast's RheumNow Therapeutic Updates page. Today, we will discuss how heterogeneous clinical manifestations in psoriatic arthritis can be used to inform treatment decisions. I am joined by Lindsay Tom, who is a physician assistant at the Northern Virginia Center for Arthritis. Lindsay, welcome to the podcast. **Lindsay Tom, PA-C** Hello, thanks for having me!
Starting on an advanced therapy in PsA: a multifactorial approach	**Saakshi Khattri, MD** When I'm choosing an advanced therapy for psoriatic arthritis, I'm not just asking, “How are the joints?” I'm asking, “Which psoriatic arthritis domains are active?” I want to know about the disease activity in the 6 domains outlined by GRAPPA: peripheral arthritis, axial disease, enthesitis, dactylitis, skin psoriasis, and nail disease.[1] Now, Lindsay, what other factors would you consider when making treatment decisions? **Lindsay Tom, PA-C** So, based on GRAPPA and EULAR guidelines, I also want to know about previous therapies, patient preferences, and extra-musculoskeletal manifestations, like uveitis and inflammatory bowel disease.[1,2] **Saakshi Khattri, MD** Totally agree. I think they are important considerations, and they tie in well with the patient case that I'd like to walk through today. So, I had a male patient in his mid-30s who had a diagnosis of psoriasis and psoriatic arthritis and was on a conventional synthetic DMARD when he came for a follow-up visit. He did say that he thought that he might have stubbed his second toe on his left foot because it was swollen and a little uncomfortable. Clinically, on exam, it was classic dactylitis. So, I did ask him about other, you know, extra-musculoskeletal manifestations. So, he did endorse that he had some nonspecific GI symptoms, but nothing that had, up till that point, warranted a visit to a gastroenterologist for any formal diagnosis.

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	Lindsay Tom, PA-C Did the patient express a preference for a particular therapy or personal goals that weighed into your treatment decision? **Saakshi Khattri, MD** So, his first and foremost thing was, “I need something that is not so frequent,” and he was super concerned about safety and immune suppression. With everything going on—his history, his nonspecific GI symptoms—ultimately, we decided on the IL-23 inhibitor risankizumab, or risa. IL-23 is a key contributor to the inflammation that's seen in multiple disease domains in psoriatic arthritis.[3] Let's review some of the clinical trial data that informed this treatment decision. But before we do, I'd like to remind listeners that risankizumab is indicated in patients 6 years of age and older for the treatment of moderate to severe plaque psoriasis in individuals who are candidates for systemic therapy or phototherapy and for the treatment of active psoriatic arthritis.[4] Risankizumab is also indicated in adults for the treatment of moderate to severely active Crohn's disease and ulcerative colitis.
Efficacy and safety of risankizumab in the KEEPsAKE trial program and a real-world treatment persistence study	**Saakshi Khattri, MD** The efficacy and safety of risa in PsA was assessed in the KEEPsAKE trial program, which includes 2 trials.[5,6] We are going to focus on KEEPsAKE 1, which included only bio-naive patients.[5] Lindsay, can you give us an overview of this trial? **Lindsay Tom, PA-C** Yeah, absolutely. So, this trial enrolled just over 960 adults with active psoriatic arthritis who were randomized 1-to-1 to receive either risa or a placebo.[5] The study met the primary endpoint, with more patients treated with risa achieving ACR20 at Week 24 compared to placebo. Dr. Khattri, what other clinical trial outcomes help inform your treatment strategy? **Saakshi Khattri, MD** The patient I mentioned previously had disease activity in the skin as well as the joints, so I'm interested in skin efficacy outcomes, like PASI scores. In KEEPsAKE 1, risa showed efficacy in the skin, with more patients treated with risa achieving a PASI90 response at Week 24 compared to placebo, which was a ranked secondary endpoint.[5] These efficacy results were not just seen during the randomized controlled trial period. Fifty-nine percent of patients continued on risa in the open-label extension, which demonstrated efficacy in the joints—ACR20—and skin—PASI90—out to 6 years.[7] It's important to note that open-label extension trials have a potential for enrichment of long-term data in the remaining patient population, since patients who are unable to tolerate or do not respond to the drug often drop out. **Lindsay Tom, PA-C** These benefits observed in the skin and joints are definitely significant for patients experiencing multidomain disease. I want to mention that risa has shown efficacy across other GRAPPA psoriatic arthritis domains, including nail psoriasis, axial disease, enthesitis, and dactylitis in the open-label extension.[7] So, Dr. Khattri, how do you see the data we've discussed impacting your clinical decision-making?

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	Saakshi Khattri, MD When we have data looking at 6 years that's a good point to have when we are talking about advanced systemics for our patients that have a chronic inflammatory disease. Patients also want to know, “Will this drug continue to work for long periods of time?” After safety and efficacy, that's, like, the third most important question that patients ask for because they don't want to keep going back to the drawing board if a drug stops working for them over time. **Lindsay Tom, PA-C** And another thing that's really important to patients—and also to us—is safety. And the overall safety profile of risa in psoriatic arthritis was similar to what was previously reported in patients with plaque psoriasis.[4] The safety of risa has been evaluated out to 6 years in an integrated safety analysis across six Phase 2 or 3 clinical trials,[8] and no new safety signals were detected when we look back at the data from the KEEPsAKE trials.[4-6] **Saakshi Khattri, MD** In addition to safety, extra-musculoskeletal manifestations also impact my treatment decisions. Risa showed low rates of disease flares or new-onset IBD in a post hoc analysis of the KEEPsAKE trials.[9] Lindsay, you have a background in gastroenterology, right? What's your perspective on how GI symptoms may be important to consider in patients with PsA? **Lindsay Tom, PA-C** Yes. So, prior to rheumatology, I worked in gastroenterology, and so for me I definitely keep in mind how important it is to consider the gut when we're making these treatment decisions. Whether they're these obvious inflammatory bowel disease symptoms, or even the more mild, subtle symptoms, such as the patient that you had presented earlier, Dr. Khattri. For those patients, I like to typically refer them for GI evaluation, and ideally, I would try to coordinate with the gastroenterologist to identify a single medication that can effectively target both autoimmune conditions. **Saakshi Khattri, MD** I totally agree. When there are gut symptoms, we may also need to reach out to our colleagues in gastroenterology just to make sure that we're not missing IBD.
When a TNF inhibitor isn't enough: a JAK inhibitor for managing PsA	**Saakshi Khattri, MD** We've discussed a patient with PsA who just started advanced therapy. Now let's shift to a patient later in their treatment journey. Lindsay, can you tell us about a patient who may look like this? **Lindsay Tom, PA-C** Yeah. So, I recently saw a patient at my office with psoriatic arthritis. She is generally healthy, in her mid-50s. She had previously failed conventional synthetic DMARDs and more recently was started on a TNF inhibitor, and she came to me as a follow-up 3 months after starting that TNF inhibitor, but she was still symptomatic. She had tender, swollen joints, she had enthesitis now in both of her heels, and she still had some psoriasis present. Other medical history—she did not have any uveitis history, and, unlike your patient before, she actually did not have any GI symptoms. She did discuss that she has this strong family history of inflammatory bowel disease.

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	Saakshi Khattri, MD So eventually, how did that biologic failure impact your approach to devising a treatment strategy, and what treatment did you and the patient decide on? **Lindsay Tom, PA-C** So given that she had minimal response to a TNF inhibitor, I did want to use a drug with a different mechanism of action. She also had this upcoming travel. That was so important to her. She wanted something that would have this faster onset and relief of symptoms. So that really led us to use the JAK inhibitor, upadacitinib, or UPA. And we do know many cytokines that drive inflammation in psoriatic arthritis signal via JAK pairs.[10-13] **Saakshi Khattri, MD** When I was a rheum fellow, we were sort of taught to stay within the same MOA. So, I'm so happy to hear you thought of completely changing to a different MOA. Now let's take a closer look at the efficacy and safety of UPA in psoriatic arthritis. I'd like to remind the listeners that upadacitinib is indicated in adults and pediatric patients 2 years of age and older with active psoriatic arthritis, and adults with moderately to severely active Crohn's disease and ulcerative colitis who have had an inadequate response or intolerance to 1 or more TNF blockers.[14] For patients with Crohn's disease and ulcerative colitis for whom TNF blockers are clinically inadvisable, patients should have received at least 1 approved systemic therapy prior to the use of upadacitinib. It is not recommended for use in combination with other JAK inhibitors, biological DMARDs, or with potent immunosuppressants, such as azathioprine and cyclosporine.
Efficacy and safety of upadacitinib in the SELECT-PsA trial program and a real-world study of MOA cycling vs switching	**Saakshi Khattri, MD** In the SELECT-PsA 2 trial, the efficacy and safety of UPA was evaluated in adults with active PsA who had an inadequate response to 1 or more biologic DMARDs.[15] A total of 642 participants were enrolled in the trial and randomized to receive either UPA 15 milligrams or a placebo. The trial permitted concomitant use of nonbiologic DMARDs. At Week 12, more patients treated with UPA achieved ACR20 compared with placebo, which was the primary endpoint. Lindsay, what other outcomes from this study are important to your clinical decision-making? **Lindsay Tom, PA-C** So, there are 2 things that struck me. First, differences in ACR20 between patients treated with UPA vs placebo were observed as early as Week 2 in SELECT-PsA 2.[15] That is important to so many of our patients, including the patient who I had discussed earlier. Second, joint efficacy with UPA was seen beyond the randomized controlled trial period. Among the 62% of patients continuing UPA and 50% of patients who switched from placebo to UPA in the open-label extension, joint efficacy was observed through approximately 3 years.[16] So, for the patient we discussed earlier, this could mean that they experience not only rapid joint relief but potentially durable joint efficacy with UPA. **Saakshi Khattri, MD**

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	I love that. We as clinicians should listen to our patients and sort of understand what are their goals. I do agree that UPA may be a good option for your patient, as it has shown benefits in skin, although UPA is not indicated for psoriasis. Specifically, at Week 16, more patients treated with UPA achieved PASI75 than those who received placebo, which was a secondary endpoint.[15] This skin efficacy was observed out to approximately 3 years, so UPA could provide the patient with both joint and skin relief.[16] **Lindsay Tom, PA-C** And it may also provide benefits for the enthesitis seen in my patient from earlier. As we know, enthesitis is so disruptive to patients' quality of life. Walking around on a vacation and traveling would have been very challenging if her enthesitis remained active. Now, with UPA, we saw that some patients showed no sign of disease activity in the entheses after 12 weeks of UPA treatment,[15] and long-term efficacy was also achieved in this domain.[16] And I also want to touch on both extra-musculoskeletal manifestations and safety when it comes to UPA. UPA showed low rates of disease flares or new onset for IBD and uveitis in a post hoc analysis of both the SELECT-PsA 1 and 2 trials.[17] Now, in terms of safety, the safety profile of UPA in SELECT-PsA 2 was consistent with results reported previously in rheumatoid arthritis trials.[14] Overall, rates of adverse events of special interest have remained consistent over time.[18,19] Important known risks for upadacitinib that were seen in clinical trials include nonmelanoma skin cancer and serious and opportunistic infections, including tuberculosis and herpes zoster.[14] **Saakshi Khattri, MD** It's important to know that UPA has a well-studied safety profile. Listeners, if you want to know more about the safety data from SELECT-PsA 2, there is more information on this podcast's RheumNow Therapeutic Updates page.
Closing	**Saakshi Khattri, MD** As we've discussed today, no 2 patients with PsA look exactly the same, and thus tailoring treatment based on disease domain involvement, related conditions, previous therapies, and patient preference is important for helping patients manage their PsA.[1] Lindsay, any final takeaways you want to share? **Lindsay Tom, PA-C** So, I'd say my final takeaway is really that when we have a patient who has treatment failure, I think that gives us the opportunity to reassess the therapeutic strategy. If it's an inadequate response to a TNF inhibitor, we don't necessarily need to stay within that same drug class. And the data we reviewed support the efficacy for upadacitinib after biologic failure of a TNF inhibitor. And in my patient, that oral route also aligned with her preference and with her lifestyle. So, as we continue to expand

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	our treatment options in psoriatic arthritis, upadacitinib really has become a valuable therapeutic option for many of our patients. So, Dr. Khattri, what are your key takeaways from today's discussion? **Saakshi Khattri, MD** My patient reported that he had some nonspecific GI symptoms. I really think that we should take a comprehensive history and think of other extra-articular manifestations that can certainly impact our treatment decision. We can't have a one-size-fits-all approach or a cookie-cutter approach to our patients that have psoriatic diseases. Thank you so much for your time today, Lindsay. Listeners, if you'd like to see specific efficacy and safety results from the studies we've discussed today, check out the RheumNow Therapeutic Updates page for this podcast. The Therapeutic Updates page also includes a link to an interactive visual tool that you can use to learn more about the benefits and risks of UPA in PsA. Finally, please listen to the important safety considerations next, including the box warning for upadacitinib. Thank you for listening today.
Risankizumab safety considerations	**Risankizumab important safety considerations** Risankizumab is contraindicated in patients with a history of **serious hypersensitivity reactions** 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. There is a potential for drug-induced **liver injury/hepatotoxicity** during induction treatment of UC and CD. Monitor liver enzymes. Monitor liver enzymes and bilirubin at baseline and during induction (12 weeks). Monitor thereafter according to routine patient management. Consider other treatment options in patients with evidence of liver cirrhosis. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded. Avoid use of **live vaccines** in patients treated with risankizumab. The **most common adverse reactions, greater than or equal to 1%, reported during treatment of plaque psoriasis and psoriatic arthritis** are upper respiratory infections, headache, fatigue, injection site reactions, and tinea infections. The **most common adverse reactions, greater than or equal to 3%, reported during treatment of UC** are arthralgia during induction dosing and arthralgia, pyrexia, injection site reactions, and rash during maintenance dosing. The **most common adverse reactions, greater than or equal to 3%, reported during treatment for CD** are upper respiratory infections, headache, and arthralgia during induction dosing and arthralgia, abdominal pain, injection site reactions, anemia, pyrexia, back pain, arthropathy, and urinary tract infection during maintenance dosing. **Review accompanying risankizumab full Prescribing Information for additional information by visiting www.rxabbvie.com/pdf/skyrizi_pi.pdf or contact AbbVie Medical Information at 1-800-633-9110.**

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Upadactinib safety considerations and boxed warning	**Upadacitinib important safety considerations and boxed warning** It is important to note that upadacitinib has a boxed warning for serious infections, mortality, malignancies, major adverse cardiovascular events, and thrombosis. **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. Please also read the additional upadacitinib safety information within the RX Update corresponding to this podcast on RheumNow.com regarding hypersensitivity reactions, other serious adverse reactions, avoiding live vaccines and the importance of immunizations, and medication residue in stool. The **most common adverse reactions in PsA, greater than or equal to 1%,** were: Upper respiratory tract infections, herpes zoster, herpes simplex, bronchitis, nausea, cough, pyrexia, acne, and headache. The **most common adverse reactions in UC, greater than or equal to 5%,** reported are upper respiratory tract infections, increased blood creatine phosphokinase, acne, neutropenia, elevated liver enzymes, pyrexia, and rash. The **most common adverse reactions in CD, greater than or equal to 5%,** reported are upper respiratory tract infections, anemia, pyrexia, acne, herpes zoster, and headache. **Review upadacitinib full Prescribing Information for additional information at www.rxabbvie.com/pdf/rinvoq_pi.pdf or contact AbbVie Medical Information at 1-800-633-9110.**

Abbreviations:

ACR20, improvement of at least 20% in the American College of Rheumatology core criteria; **DMARD**, disease-modifying antirheumatic drug; **EULAR**, European Alliance of Associations for Rheumatology; **GI**, gastrointestinal; **GRAPPA**, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; **IBD**, inflammatory bowel disease; **i,** inhibitor; **IL**, interleukin; **JAK**, Janus kinase; **MOA**, mechanism of action;

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PASI, Psoriasis Area Severity Index; **PASI75/90**, improvement of ≥75/90% in Psoriasis Area Severity Index; **PsA**, psoriatic arthritis; **risa**, risankizumab; **TNF**, tumor necrosis factor; **UPA**, upadacitinib.

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