Podcast Transcript

PsA GRAPPA domains: Outcomes with a JAKi

Sponsored by AbbVie Medical Affairs + Health Impact

Speakers: **Dr. Sergio Schwartzman** and **Dr. Eric Ruderman**

Topic	Transcript
Opening	**Dr. Schwartzman:** Hello, and welcome to this RheumNow podcast. This podcast is sponsored by AbbVie US Medical Affairs and Health Impact. My name is Dr. Sergio Schwartzman. I'm a rheumatologist in New York, affiliated with the Hospital for Special Surgery and Cornell Weill Medical School [Weill Cornell Medicine]. With me today is Eric Ruderman from Northwestern. Eric, would you like to say a few words about yourself? **Dr. Ruderman:** Sure, Eric Ruderman, I'm in Chicago. I am a rheumatologist at Northwestern University Feinberg School of Medicine and Northwestern Medicine. **Dr. Schwartzman:** So today, in this podcast, we hope to focus on the different domains that GRAPPA has identified as a source of decision-making for choosing therapies. We know that PsA is a very complicated disease with a lot of co-manifestations and comorbidities.[1] I hope to show you a high-level overview of psoriatic disease and then review 2 studies that were done with upadacitinib in patients with 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 PsA who have had an inadequate response or intolerance to one or more TNF blockers. It is not recommended for the use in combination with other JAK inhibitors, biological DMARDs, or with potent immunosuppressants, such as azathioprine and cyclosporine.[2]
Considerations for treatment selection	**Dr. Schwartzman:** So with that then, Eric, would you be so kind as to review the different domains and how these have been defined by GRAPPA?[1] **Dr. Ruderman:** Sure, thanks, Sergio. And a bit of history—I've been working in psoriatic arthritis for many, many years, and I think all of us who do so have recognized that this is really an all-encompassing disease, and in the past we've thought about both skin disease and joint disease. The GRAPPA organization, which is both rheumatologists and dermatologists, a number of years ago began to think about treatment guidelines, and in doing so they actually expanded that list and thought about 6 different domains that are involved in PsA. And as they looked at treatment options, they looked at the options that were available for addressing each of the aspects of disease, of psoriatic disease in general, that an individual patient can have.[1] And the 6 domains specifically are: peripheral arthritis, which is really the inflammatory arthritis that we think of with psoriatic arthritis; axial arthritis, which is inflammatory back pain. It turns out probably about 40% of patients have a certain amount of inflammatory back pain,[3,4] particularly inflammatory back pain that's

JAKa-US-00112-MC Approval date: March 2026 v1.0
Please see Important Safety Considerations on page 7

Topic	Transcript
	problematic for them; the third domain is enthesitis, or inflammation at the points at which tendons attach to bone, which in psoriatic disease is often the main point at which patients have inflammation; dactylitis, or what we sometimes refer to as sausage digits, which are diffuse swelling of the fingers and toes; then there is a skin psoriasis, the psoriasis that really is sort of the hallmark of psoriatic arthritis; and then finally nail disease.[5] And in using these different domains, you can look at the disease activity in any individual domain and then think about the treatments and the drug options that we have that address those specific aspects of disease.[1] I should note that in addition to those 6 domains there are a couple of really important comorbid conditions, which include inflammatory bowel disease and uveitis, and those elements of disease may play a role either in choosing a certain treatment or potentially avoiding treatments, such as avoiding interleukin-17 inhibitors, for example, in a patient who has active inflammatory bowel disease.[1]
Outcomes with upadacitinib 15 mg across domains	**Dr. Ruderman:** So, a drug like upadacitinib, which may come up if we're thinking about a patient who has perhaps started on a TNF inhibitor and has either ongoing arthritis, or perhaps ongoing back pain, and you want a drug that has been shown to work across all of the different domains of disease, and particularly those domains that you're thinking about. Upadacitinib, you know, in the clinical trials, in SELECT-PsA 2, for example, the primary endpoint was joint disease—it was an ACR20 at Week 12—and it met that primary endpoint,[6] so we know this is a drug that works for joint disease. It achieved exploratory endpoints in enthesitis, in dactylitis, in axial disease, and I can come back to that in a little bit.[6-8] It also treated skin disease reasonably well, that, a significant percentage of the patients in the trial achieved a PASI75,[6] and although the drug upadacitinib is not indicated specifically for psoriasis,[2] it's really nice to have a drug that we know is going to treat skin disease. **Dr. Schwartzman:** So, I'll make a few points. I think Eric did a very good job of covering SELECT-PsA 2, which was the pivotal study in patients who had been intolerant or failed a biological agent and were then treated with upadacitinib.[6] There's a second study called the UPJOINT study.[9,10] The UPJOINT study was a separate real-world study of upadacitinib outcomes in patients with PsA who were refractory to classic synthetic DMARDs and/or biological DMARDs. This study's primary endpoint was the achievement of MDA at Week 24.[9,10] That probably is worth mentioning as well, because in that study they looked at nail disease, and with upadacitinib there was benefit in that study as well.[9,10] And for some of our patients with nail disease, we know that stigmatizes them. So, in the real world, these patients, when they go to shake hands, for example, are embarrassed that whoever they're shaking hands with thinks that they have fungal disease.[11,12]

JAKa-US-00112-MC Approval date: March 2026 v1.0
Please see Important Safety Considerations on page 7

Topic	Transcript
	And I think, as we mentioned in terms of the UPJOINT study, there are some limitations with that data, because it's data that was obtained observationally outside of the controlled clinical trials and is descriptive only. But the presence of nail psoriasis was an additional endpoint that was not ranked or adjusted for multiplicity.[9,10] So, no clinical or statistical conclusions can be drawn. For both SELECT PsA[6-8] and the UPJOINT study,[9,10] there's more information to be found on the RheumNow Treatment Updates article page for this podcast.
Hypothetical patient cases	**Dr. Schwartzman:** As maybe we move forward, maybe, Eric, you can give us an example of a patient where you think that these guidelines[1] would be potentially operative. **Dr. Ruderman:** So let's say we have a patient who comes in, who has been on a TNF inhibitor for a year or two. They have some skin disease, but particularly they complain of ongoing joint disease. They have pain and swelling in their fingers or perhaps a wrist. And they come in and say, “well, what can I do next”? And we look at the landscape of treatments, and when you break it down into domains, you look at treatments and say, “well, if you've been on a TNF inhibitor, what next might work for that patient”? You want a drug that's going to treat all of that, and what the patient wants. Would they prefer to think about an oral agent? Would they prefer to think about another injectable drug? And that opinion matters a lot. I'll circle back to one other thing that I did start with and mention was spine disease and inflammatory spine disease. And that, I think, is an important thing to think about, because we have a lot of patients who come in and that's a big part of their issue. It's not necessarily the primary issue, but it, you know, if you talk to them and say, “if I make you better, what needs to be better”? And a lot of times, the spine disease and the axial pain is a piece of that, and you want to make sure you have a drug that is going to address that. Now, the challenge is, we don't have great data for axial involvement in PsA.[13] And in my mind, I think the drugs that also work for axial spondyloarthritis, either non-radiographic or radiographic axial spondyloarthritis, make a lot of sense in that situation, because you know they work for inflammatory back disease. And so a drug that is also approved for ankylosing spondylitis or non-radiographic axial spondyloarthritis[2] may be helpful, and you want to think about that when you're making decisions.[13] **Dr. Schwartzman:** A point that we should highlight, having spoken about axial disease, is that upadacitinib is indeed indicated for the treatment of adults with active ankylosing spondylitis and adults with active non-radiographic axial spondylitis with objective signs of inflammation who have had an inadequate response to one or more TNF blockers.[2]

JAKa-US-00112-MC Approval date: March 2026 v1.0
Please see Important Safety Considerations on page 7

Topic	Transcript
	Dr. Ruderman: Upadacitinib is not recommended for use in combination with other JAK inhibitors, with biologic disease-modifying anti-rheumatic drugs, or with potent immunosuppressives, such as azathioprine and cyclosporine.[2] **Dr. Schwartzman:** I'd like to come back a little bit to one of the points that Eric made about upadacitinib that I think is helpful for us managing patients with psoriatic disease. As we look at the manifestations of psoriatic disease, both the classic for the disease itself—that's the skin, nail, and joint disease—and we look at the extra-dermal and extra-articular manifestations of the disease, this is a drug that has a lot of potential for those patients. So as we look through our therapeutic armamentarium and we look at the complexity of psoriatic disease, both IBD and autoimmune eye disease fall into treatment choices that we have to make. **Dr. Ruderman:** So it's not uncommon that we'll see somebody who has Crohn's also has psoriatic arthritis and is perhaps failing a TNF inhibitor because their Crohn's is not well controlled, and the gastroenterologist is looking at what to do next. And that's where I think mechanism becomes really important, because I think that's where a JAK inhibitor or an alternate TNF inhibitor might make sense for those patients. **Dr. Schwartzman:** In a post hoc analysis of SELECT-PsA studies, IBD and uveitis occurred less frequently in patients treated with upadacitinib 15 milligrams vs patients receiving placebo.[14] Additional studies are needed to validate these observations.
Safety	**Dr. Schwartzman:** All right, so, the safety profile of upadacitinib in SELECT-PsA 2 was generally consistent with results reported previously in rheumatoid arthritis.[6,14,15] **Dr. Ruderman:** Yeah, I think that, you know, all of us in rheumatology have been used to using this drug in RA for a number of years. We're used to the class, and I think we know some of the safety concerns and the issues to watch out for, so I think that's really helpful to know. Anybody who's listening to this who wants to know more about the safety data from trials like SELECT-PsA 2,[6,7] there is more information on the updates article page in RheumNow for this podcast, or you can just take a look at the Prescribing Information, including the BOXED WARNING, relative to upadacitinib.
Closing	**Dr. Ruderman:** In sum, I think we've talked about where the GRAPPA approach to disease domains in psoriatic disease can be helpful, and the value of a drug like upadacitinib in managing this disease and managing the various domains of disease. It's really important to recognize that this psoriatic disease is really a disease, it's not psoriatic arthritis alone, and it can span multiple clinical domains.[1] And then choosing treatment really requires us to think about the active domains in any individual patient

JAKa-US-00112-MC Approval date: March 2026 v1.0
Please see Important Safety Considerations on page 7

Topic	Transcript
	and pick treatments that address all of those domains. And that's where a drug like upadacitinib, which covers all 6 domains, becomes an important option in managing this disease in patients who fail the TNF inhibitor and need another choice.[1,6,7] **Dr. Schwartzman:** Both Eric and I, you know, have practices that are dominated by patients with psoriatic arthritis. That's just the nature of our practices, and I would argue that there are no 2 patients with psoriatic disease that are exactly the same. And that is both in terms of their different domains, but also in terms of their comorbidities, their co-manifestations, and things like their family history. So, in looking at our therapeutic choices, for the management of individual patients we would like to use a medication that covers the most domains possible. **Dr. Ruderman:** Thanks Sergio, this has been a great conversation. For those who are listening, there is additional information and specific results from the SELECT-PsA trial that you can find on the RheumNow Updates article page for this podcast. If you want to talk more to patients about other benefits and the risks of upadacitinib and long-term safety across rheumatologic indications, there are also links to previous RheumNow Pages that you can look at, so please continue listening for the important safety considerations that include the box warning. Thank you for joining us.
Indication	The current approved indications and important safety information for upadacitinib are as follows: **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. **Adults and pediatric patients 2 years of age and older with active psoriatic arthritis (PsA)** who have had an inadequate response or intolerance to one or more TNF blockers. **Adults with active ankylosing spondylitis (AS)** who have had an inadequate response or intolerance to one or more TNF blockers. **Adults with active non-radiographic axial spondyloarthritis (nr-axSpA)** with objective signs of inflammation who have had an inadequate response or intolerance to TNF blocker therapy. **Limitations of Use for RA, PsA, AS, and nr-axSpA:** 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.

JAKa-US-00112-MC Approval date: March 2026 v1.0
Please see Important Safety Considerations on page 7

Topic	Transcript
Important Safety Information	**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, including deep vein thrombosis, pulmonary embolism, and arterial thrombosis, have also been observed in upadacitinib-treated patients. Avoid upadacitinib in patients at risk of thrombosis.** Consider the benefits and risks for the individual patient prior to initiating or continuing therapy. **Common Adverse Reactions in RA, PsA, AS, and nr-axSpA**: The most common adverse reactions (≥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 Update on RheumNow.com titled “PsA GRAPPA domains: Outcomes with a JAKi” 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 http://www.rxabbvie.com/pdf/rinvoq_pi.pdf or contact AbbVie Medical Information at 1-800-633-9110.

INDICATIONS

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.

JAKa-US-00112-MC Approval date: March 2026 v1.0
Please see Important Safety Considerations on page 7

Adults and pediatric patients 2 years of age and older with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to one or more TNF blockers.

Adults with active ankylosing spondylitis (AS) who have had an inadequate response or intolerance to one or more TNF blockers.

Adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation who have had an inadequate response or intolerance to TNF blocker therapy.

> **Limitations of Use for RA, PsA, AS, and nr-axSpA**: 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

JAKa-US-00112-MC Approval date: March 2026 v1.0
Please see Important Safety Considerations on page 7

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 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, PsA, AS, and nr-axSpA: 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.

JAKa-US-00112-MC Approval date: March 2026 v1.0
Please see Important Safety Considerations on page 7

Abbreviations:

ACR20, American College of Rheumatology 20% improvement score; **AS**, ankylosing spondylitis; **bDMARD**, biologic disease-modifying antirheumatic drug; **DMARD**, disease-modifying antirheumatic drug; **GRAPPA**, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; **IBD**, inflammatory bowel disease; **JAK**, Janus kinase; **JAKi**, Janus kinase inhibitor; **MDA**, minimal disease activity; **nr-axSpA**, non-radiographic axial spondyloarthritis; **PASI75**, 75% reduction in Psoriasis Area Severity Index score from baseline; **PASI90**, 90% reduction in Psoriasis Area Severity Index score from baseline; **PsA**, psoriatic arthritis; **RA**, rheumatoid arthritis; **TNF**, tumor necrosis factor.

References:

1. Coates LC, Soriano ER, Corp N, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. *Nat Rev Rheumatol*. 2022;18(8):465-479. doi:10.1038/s41584-022-00798-0
2. RINVOQ (upadacitinib) [package insert]. North Chicago, IL: AbbVie Inc.
3. Ritchlin C. Axial Psoriatic Arthritis. Medscape Rheumatology Decision Point. Accessed February 12, 2026. https://decisionpoint.medscape.com/rheumatology/viewarticle/1002305
4. Mortezavi M, Thiele R, Ritchlin C. The joint in psoriatic arthritis. *Clin Exp Rheumatol.* 2015;33(5 suppl 93):S20-S25.
5. Bagel J, Schwartzman S. Enthesitis and dactylitis in psoriatic disease: a guide for dermatologists. *Am J Clin Dermatol*. 2018;19(6):839-852. doi:10.1007/s40257-018-0377-2
6. Mease PJ, Lertratanakul A, Anderson JK, et al. Upadacitinib for psoriatic arthritis refractory to biologics: SELECT-PsA 2. *Ann Rheum Dis*. 2021;80(3):312-320. doi:10.1136/annrheumdis-2020-218870
7. Mease PJ, Lertratanakul A, Anderson JK, et al. Supplement to: Upadacitinib for psoriatic arthritis refractory to biologics: SELECT-PsA 2. *Ann Rheum Dis*. 2021;80(3):312-320. doi:10.1136/annrheumdis-2020-218870
8. Baraliakos X, Ranza R, Östör A, et al. Efficacy and safety of upadacitinib in patients with active psoriatic arthritis and axial involvement: results from two phase 3 studies. *Arthritis Res Ther*. 2023;25(1):56. doi:10.1186/s13075-023-03027-5
9. Werner SG, Schwarze I, Baraliakos X, et al. Effectiveness and safety of upadacitinib in treating oligoarticular and polyarticular psoriatic arthritis: primary analysis from the UPJOINT-study. *Rheumatol Ther*. 2026;13(1):45-64. doi:10.1007/s40744-025-00802-5
10. Werner SG, Baraliakos X, Reckert S, et al. Treatment with upadacitinib in active psoriatic arthritis: efficacy and safety data of the first 192 patients from the UPJOINT study, a multicentre, observational study in clinical practice. *Rheumatol Ther*. 2023;10(6):1503-1518. doi:10.1007/s40744-023-00589-3
11. Kyriakou A, Zagalioti SC, Trakatelli MG, et al. Fungal infections and nail psoriasis: an update. *J Fungi (Basel).* 2022;8(2):154. doi:10.3390/jof8020154
12. Sobolewski P, Walecka I, Dopytalska K. Nail involvement in psoriatic arthritis. *Reumatologia.* 2017;55(3):131-135. doi:10.5114/reum.2017.68912

JAKa-US-00112-MC Approval date: March 2026 v1.0
Please see Important Safety Considerations on page 7

13. Poddubnyy D. Managing psoriatic arthritis patients presenting with axial symptoms. *Drugs*. 2023;83(6):497-505. doi:10.1007/s40265-023-01857-w

14. Burmester GR, Winthrop K, Blanco R, et al. Safety profile of upadacitinib up to 3 years in psoriatic arthritis: an integrated analysis of two pivotal phase 3 trials. *Rheumatol Ther.* 2022;9(2):521-539. doi:10.1007/s40744-021-00410-z

15. Burmester GR, Cohen SB, Winthrop KL, et al. Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis. *RMD Open*. 2023;9(1):e002735. doi:10.1136/rmdopen-2022-002735

Please see Important Safety Considerations on page 7