Podcast Transcript

SELECT-GCA 2-Year Outcomes
Sponsored by AbbVie Medical Affairs + Health Impact

Speakers: **Dr. Anisha Dua** and **Dr. Ben Boone**

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Introduction	**Dr. Dua** Welcome to RheumNow. This podcast is sponsored and developed by AbbVie U.S. Medical Affairs. My name is Anisha Dua. I'm a professor of medicine at Northwestern University and run the Vasculitis Center there. And I am joined today by Dr. Boone. Welcome to the podcast. Can you introduce yourself for us? **Dr. Boone** Hello, my name is Ben Boone, and I'm a private practice rheumatologist based in Louisville, Kentucky. **Dr. Dua** Thanks, Dr. Boone. I'm looking forward to our discussion on the 2-year outcomes from the Phase 3 SELECT-GCA trial. This trial compared the efficacy and safety of upadacitinib, an oral selective JAK inhibitor, with a 26-week steroid taper to placebo with a 52-week steroid taper for the treatment of patients with active giant cell arteritis.[1] So, the data we're discussing today was recently presented at ACR Convergence in 2025, but before we get into the details, let's hear about the indications and limitations of use for upadacitinib in GCA. **Voiceover:** Upadacitinib is a Janus kinase (JAK) inhibitor indicated for the treatment of adults with giant cell arteritis. Limitations of Use for GCA: Upadacitinib is not recommended for use in combination with other JAK inhibitors, biologic DMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine.
SELECT-GCA clinical relevance	**Dr. Dua** All right, with that, let's get into some of the new and exciting data. We know that there are so many difficulties in treating these complex patients with GCA. So, I'm excited to talk about what we can do next. So, you know, we know that this disease has historically been very difficult to treat, and that glucocorticoids have really been the first-line treatment for GCA, but there's so many significant adverse effects, and there's a lack of steroid-sparing treatment options.[1] We know that relapses have been a major problem with this disease, and they tend to occur during the first 2 years,[2] but there's still a lot of uncertainty around long-term disease management in GCA. And since glucocorticoids are used to treat flares, relapsing disease can lead to more glucocorticoid-related side effects. There's the short-term side effects of trouble sleeping, weight gain, mood changes, just feeling really jittery and uncomfortable, to the longer-term things like high blood pressure, osteoporotic hip fractures, new onset diabetes, glaucoma.[3,4] It's such a long

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	list, and every patient comes in with one of these other things. So, I think it's an important area of study, and so really clinically impactful. What are some of the issues that you encounter, Dr. Boone, when you're treating patients with GCA? **Dr. Boone** Yeah, I mean, of course, GCA is one of those diseases where a relatively high amount of steroids is a necessary evil.[3] I tell my patients they're a blessing, but they're also a curse. And I, just like you said, I've experienced my own fair share of patients for whom steroids have had tremendously harmful impacts, having fractures, or inability to sleep, gaining lots of weight, having to start insulin for the first time.[3,4] Steroid-sparing or targeted therapy can certainly help us get off steroids more quickly and stay off steroids more reliably long-term.[5,6] I think most rheumatologists have an inclination that 1 year of targeted therapy in GCA just isn't enough time, with most people likely using it a minimum of 2 or 3 years. Some may even treat people indefinitely, as long as they can tolerate the treatment, especially for those who had some of those severe manifestations. I think we'll see today how the SELECT-GCA 2-year data really validates this inclination we have to use targeted therapy for longer periods of time. But before we get there, let's remind ourselves of how things went with Year 1, or what we've called Period 1, of the study. As we know, upadacitinib was recently approved for the treatment of GCA.[7] Period 1 of SELECT-GCA, which was reviewed in a previous Rx update, was a 52-week randomized, double-blinded study. UPA15 plus a 26-week glucocorticoid taper met the primary endpoint, demonstrating superior efficacy compared to placebo plus a 52-week glucocorticoid taper in attaining sustained remission at Week 52. This was achieved at 46% in the UPA group vs 29% in the placebo group. Sustained remission here was defined as the absence of signs or symptoms of GCA from Week 12 through Week 52 while adhering to the protocolized glucocorticoid taper.[1] The question that Period 2 of SELECT-GCA answers is: Does continuing UPA compared to withdrawing it after a year result in better efficacy outcomes for maintaining remission while also demonstrating a consistent safety profile? So let's take a look now at how patients made their way from Period 1 into Period 2.
SELECT-GCA study design	**Dr. Boone** Period 2 of SELECT-GCA was a blinded 52-week extension period coming out of Period 1. Patients who attained remission in Period 1 for at least 24 consecutive weeks before that 52-week visit were re-randomized to either get on UPA 15 mg or switch to placebo in a 2 to 1 ratio. In this group, there were 68 patients in the UPA 15-mg arm, which we'll call the "continued UPA" group, and 35 patients switched to placebo, which we'll call the "withdrawn UPA" group. These two groups were assessed for efficacy, comparing continuing UPA15 vs withdrawing UPA from Week 52 through Week 104.[8] So, Dr. Dua, do you mind telling us a bit about the study population and efficacy results in Period 2 of SELECT-GCA? **Dr. Dua**

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	Okay, yeah, so, for the patients that were originally in the UPA15 plus 26-week taper group and continuing in Period 2, 87% of those in the continued UPA group and 69% of those in the withdrawn UPA group completed the trial. About 3% of patients in the continued UPA group had prior use of an IL-6 inhibitor, compared to 11% of those in the withdrawn UPA group.[8] The demographics were generally similar across groups. Most of these patients were female, the mean age was around 70 to 71 years old, and about three-fourths of them had new onset disease.[8]
SELECT-GCA efficacy outcomes	**Dr. Dua** And so, let's talk a little bit about some of the efficacy endpoints and starting off with one of the most important ones, which is remission. We know that remission is super important since GCA is a relapsing disease, and up to 50 to 80% of these patients relapse when glucocorticoids are tapered.[1] So these patients in SELECT-GCA entered Period 2 in a state of remission, but the question is, how did they do over this next year? When we think about maintenance of remission from Week 52 to Week 104, we can just briefly review the definitions. Remission was defined as the absence of GCA signs and symptoms and remaining glucocorticoid-free from Week 52 to 104. So 67% of patients in the continued UPA group remained in remission through Week 104, compared to only 28% of patients in the withdrawn UPA group.[8] And when we shift over to complete remission from Week 52 to 104, that's defined as remission, as we just discussed, with the additional normalization of ESR and CRP from Week 52 to 104. In this case, patients in the continued UPA group were more likely to remain in complete remission through Week 104 compared to those in the withdrawn UPA group, with 58% in the continued UPA group maintaining complete remission compared to only 14% of those in the withdrawn UPA group.[9] I think this really is pretty impressive, and kind of aligns with what we thought would happen, but again, important to have the data to show us that, really, continuing patients on this maintenance of targeted therapy with upadacitinib really does improve their outcomes, regardless of kind of which outcome you're looking at of remission or complete remission in the entire second year of their treatment. So, I think this is going to be very important, because, of course, when you withdraw UPA, and if you fall out of remission, then of course, you're re-exposing patients, again, to high doses of prednisone[1,8] So, from a quality-of-life standpoint, and from a re-exposure to high doses of glucocorticoids, I think, this is pretty compelling data that makes us understand the importance of continuing upadacitinib for longer than a year, and at least throughout that second year. **Dr. Boone** Yeah, I agree, for sure. **Dr. Dua**

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	So, in terms of outcomes, SELECT-GCA also looked at disease flare outcomes in Period 2. Dr. Boone, can you tell us a little bit more about the time to disease flare and the relevance of that outcome in your practice? **Dr. Boone** Absolutely. Time to first disease flare was assessed in Period 2 from Week 52 through Week 104. And disease flare was defined as the recurrence of GCA signs or symptoms, or elevated ESR, that required initiation of glucocorticoids.[8] Patients continuing on UPA had a 90% reduction in risk of disease flare compared with those withdrawing UPA, with only 15% in the continued group experiencing at least one flare, compared to 59% in the withdrawn UPA group. And if you look at the Kaplan–Meier curve on the RX update page for this data, you'll see that flares started occurring relatively soon after stopping UPA in the withdrawn group. And I really would encourage you to take a look at this. I think this is probably the most striking visual that shows just how different these groups performed.[8] Dr. Dua, can you talk a little bit about, in SELECT-GCA, how they fared in terms of cumulative glucocorticoid amounts? **Dr. Dua** So in Period 2 of SELECT-GCA, patients continuing UPA had lower median cumulative glucocorticoid exposure of 0 mg—zero, that's amazing—compared to those withdrawing UPA, who had a median cumulative glucocorticoid dose of over 1000 mg.[8] And I know we've touched on this a little bit so far, but the implications of this lower glucocorticoid exposure is huge. I mean, especially after that first, you know, year where they are exposed, so many of my patients are just terrified of having to be put back on steroids. So, the implications of how little steroids, or glucocorticoids, were needed in the second year in patients who continued UPA is really important. **Dr. Boone** Agreed, yeah, it's one of the most important things we can do is try to get steroids down. I mean, we're seeing this in various clinical trials, various disease states. One of the trends is how little steroids can we use while achieving the same or better outcomes?[1,6]
SELECT-GCA safety outcomes	**Dr. Dua** Yeah, of course. And I think that leads us kind of nicely into safety, right? Because we're talking about the safety of these medications. So, in this second year, what is the safety in this population? We know that this is an elderly population[1,3] So, it's important to discuss the benefit:risk equation, especially in this patient population. The key outcomes, in terms of safety, they were tracked over about 2 years for the patients who took UPA15 and for those who received placebo and never took UPA. For patients on UPA, only side effects that happened while they were on UPA or within 30 days after stopping were counted.[8] Overall, the safety profile of UPA in GCA was consistent with the profile in Period 1, and no new clinically significant safety risks were identified with the use of UPA for 2 years.[8]

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	There were some higher rates of herpes zoster observed in those on UPA15 compared to placebo, and that was 5.9 vs 3.0 events per 100 person-years, respectively.[8] And, you know, in terms of the herpes zoster data, we know that this is something we are concerned about in an elderly population in general, in those on glucocorticoids, and then also in those who are getting JAK inhibitors.[1,7] So, I think, this really does sort of highlight the need to discuss vaccinations in our patients, right? So, we have to make sure we have good strategies in place, or good alerts, when we're in a busy clinical practice to try to make sure we're discussing vaccinations in our patient population. Do you have any thoughts, Dr. Boone? **Dr. Boone** Yeah, I mean, I think this reinforces our need to make sure our patients are getting vaccinated against zoster when they're going on JAK inhibitors.[7] And now, it's not just zoster that we need to think about, but there's other adverse events we need to think about when it comes to JAK inhibitors, and so let's talk about VTE and MACE.[1,7] Rates of thromboembolic events were similar in those in the UPA15 group compared to the placebo group, with 3.3 vs 3.0 people per 100 person-years experiencing a thromboembolic event, respectively.* Looking at the major adverse cardiac events, there were no reports of MACE in the UPA15 group, but there were two in the placebo group, and these both occurred during Period 1, when people were on higher doses of steroids.[1,9] *(*Data represents all thromboembolic events, including DVT, PE, and arterial thromboembolic events. Rates of venous thromboembolic events, including DVT and PE, were 3.0 in the UPA15 group vs 3.0 in the placebo group)* So, Dr. Dua, how did these patients fare in terms of malignancy or serious infections? **Dr. Dua** Yeah, again, really important questions in terms of things that come up in clinic a lot. So, the rates of malignancy, excluding non-melanomatous skin cancer, were similar between UPA15 and placebo with 1.9 vs 1.5 people per 100 person-years experiencing a malignancy, respectively. UPA15 had lower rates of serious infections compared to placebo, with 5.9 vs 10.5 events per 100 person-years, respectively.[9] And so, you know, in terms of how this impacts patients and their tolerability. These are important discussions to have with the patients, right? These are kind of scary new concepts to them. So, discussing, these are the risks of clots, these are the risks of cancers, these are the risks of prolonged glucocorticoid exposure, these are all really important clinical conversations to have with our patients, but I think this data is really reassuring, that in, you know, over a 2-year period, we really weren't seeing new safety signals in this continued UPA arm.[8] Dr. Boone, do you have any other thoughts on the safety data that's come up here? I know it's a huge question that patients are always asking about. **Dr. Boone** Yeah, I like the way you talked about these sorts of trade-offs that we face. That's actually one of the things that I often tell my patients, especially when they have a

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	disease that requires more intense therapy. I say, there's no solutions, there's only trade-offs, and so weighing these trade-offs is super important. And, it's tough with rare diseases to generate huge numbers of patients over a long period of time, but I think we have a good amount of patients here, and it's reassuring that we aren't seeing any obvious signals from any of these major adverse events compared to placebo, with the exception of zoster.[8] **Dr. Dua** Yeah, and patients are used to hearing the word, you know, steroids or prednisone -and they're not familiar, necessarily, with a lot of these other sort of targeted therapies, and so being able to really explain that even though you've heard about steroids before, it doesn't mean that it's safe, and that there is actually an associated risk of infection[3] is really important to be able to communicate that message, and having the data behind it, having this information is really critical in terms of educating our patients.
Final thoughts	**Dr. Dua** So I think those are all super important points, and just to summarize what we know now from this Period 2 data, the continued use of upadacitinib was associated with maintenance of remission, a lower likelihood of flares, and reduced cumulative glucocorticoid exposure in Period 2. And, as we just talked about, no new safety risks were identified.[8] I think, you know, this is a new mechanism of action that has been approved for this disease, and it's being increasingly used across practices. And I have patients on the treatment, and they ask me, "How long am I going to be on it?" And now we have good information that lets us know that, you know, if we stop it after that first, you know, year, there's a concern for flare that happens pretty quickly after stopping it.[8] And so, what about you? What do you think? **Dr. Boone** Yeah, I agree. I mean, kind of similar themes here. We knew from the Period 1 data and the *New England Journal* [*of Medicine*] publication that UPA is an effective steroid-sparing therapy for GCA, and while we had some reassuring safety data at the time, the 1-year timeframe had us wondering whether over 2 years we would start to see some new signals of concern, especially, and as you said, this older population that has more comorbidities, and they're at higher risk for complications.[1] So, this 2-year data really provides some reassurance to me. My biggest takeaway otherwise is just how impressive the sustained benefit of UPA was during Period 2. Eighty-five percent of patients having no flares over a whole year is just a really compelling number to me and probably impacts my desire to use UPA in GCA the most. This flare rate was also expressed by the continued use of UPA reducing the flare rate by 90% compared to withdrawing UPA.[8] We would probably have been pretty impressed if this number was about 50% reduction, but such a big relative reduction by 90% really speaks highly of the durability of response to this drug. And when we're talking about such a high-stakes disease like GCA that many people need treatment for, for several years, this durability of response is just so important to how I think about treating my patients.

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Closing	**Dr. Dua** Thank you for joining us to learn more about SELECT-GCA. And listeners, if you would like to learn more about SELECT-GCA Period 2, take some time to visit RheumNow.com and view the therapeutic update on this data. And thank you, Dr. Boone, it was really fun talking with you about this. **Dr. Boone** Absolutely, yeah, I'm glad to be here, this was great. **Voiceover** 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. The most common adverse reactions in GCA, greater than or equal to 5%, are upper respiratory tract infections, headache, fatigue, peripheral edema, cough, anemia, rash, herpes zoster, and nausea. Please also read the additional safety information within AbbVie's November 2025 Rx update on RheumNow.com 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

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INDICATION

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

Adults with giant cell arteritis (GCA).

> **Limitations of Use for GCA:** 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 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

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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 GCA: The most common adverse reactions (≥5%) are upper respiratory tract infections, headache, fatigue, peripheral edema, cough, anemia, rash, herpes zoster, and nausea.

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; CRP, C-reactive protein; DMARD, disease-modifying antirheumatic drug; DVT, deep vein thrombosis; ESR, erythrocyte sedimentation rate; GCA, giant cell arteritis; IL, interleukin; JAK, Janus kinase; MACE, major adverse cardiovascular event; PE, pulmonary embolism; UPA, upadacitinib; UPA15, upadacitinib 15 mg once daily; VTE, venous thromboembolism.

References:

1. Blockmans D, Penn SK, Setty AR, et al. A Phase 3 Trial of Upadacitinib for Giant-Cell Arteritis. *N Engl J Med.* 2025;392(20):2013-2024. doi:10.1056/NEJMoa2413449
2. Alba MA, García-Martínez A, Prieto-González S, et al. Relapses in patients with giant cell arteritis: prevalence, characteristics, and associated clinical findings in a longitudinally followed cohort of 106 patients. *Medicine (Baltimore)*. 2014;93(5):194-201. doi:10.1097/MD.0000000000000033
3. Gale S, Wilson JC, Chia J, et al. Risk associated with cumulative oral glucocorticoid use in patients with giant cell arteritis in real-world databases from the USA and UK. *Rheumatol Ther.* 2018;5(2):327-340. doi:10.1007/s40744-018-0112-8
4. Broder MS, Sarsour K, Chang E, et al. Corticosteroid-related adverse events in patients with giant cell arteritis: A claims-based analysis. *Semin Arthritis Rheum*. 2016;46(2):246-252. doi:10.1016/j.semarthrit.2016.05.009
5. Chen S, Cui X, Chen Y, Guo X. Biologic therapies for the treatment of large vessel vasculitis: A systematic review and meta-analysis. *PLoS One*. 2025;20(3):e0314566. doi:10.1371/journal.pone.0314566

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6. Maz M, Chung SA, Abril A, et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Giant Cell Arteritis and Takayasu Arteritis. *Arthritis Rheumatol*. 2021;73(8):1349-1365. doi:10.1002/art.41774
7. RINVOQ (upadacitinib) [package insert]. North Chicago, IL: AbbVie Inc.
8. Schmidt W, Setty A, Dejaco, C, et al. Efficacy and safety of upadacitinib in giant cell arteritis: 2-Year results from the re-randomized, double-blind SELECT-GCA Phase 3 trial. Oral presented at: American College of Rheumatology Convergence 2025; October 24-29, 2025; Chicago, IL.
9. Data on file, AbbVie Inc. ABVRRTI81873.