Podcast Transcript

A Phase 3 Trial of a JAKi in Patients With Giant Cell Arteritis
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Welcome	**Host:** Welcome to RheumNow! This podcast is sponsored and developed by AbbVie US Medical Affairs + Health Impact. Today, we will discuss key outcomes from the Phase 3 SELECT-GCA trial. This trial compared the efficacy and safety of upadacitinib, an oral selective JAK inhibitor, to placebo, both in combination with a glucocorticoid taper, for the treatment of patients with active giant cell arteritis, or GCA. Upadacitinib is indicated for the treatment of adults with giant cell arteritis. Limitations of Use: Upadacitinib is not recommended for use in combination with other JAK inhibitors, biologic DMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine Joining me today to review the SELECT-GCA trial is Dr. Andrea Rubbert-Roth, senior physician and rheumatologist at Kantonsspital St. Gallen in Switzerland. Dr. Rubbert-Roth is one of the investigators in the SELECT-GCA trial. To view the data being discussed today visit the latest RX update at RheumNow.com: “A Phase 3 trial in patients with Giant Cell Arteritis.” Welcome to the podcast, Dr. Rubbert-Roth.
Welcome	**Dr. Andrea Rubbert-Roth:** Hello. I’m very glad to be here. Thanks for the invitation. And I’d like to say hello to the colleagues who listen to that podcast, in particular of the RheumNow audience.
Question: GCA introduction	**Host:** To get us started, could you give us an introduction to GCA and the current treatments?
GCA introduction	**Dr. Andrea Rubbert-Roth:** GCA is a well-known disease. It’s a vasculitis, giant cell vasculitis, it’s called sometimes. It may involve cranial arteries that may eventually even lead to blindness, if it’s mainly cranial, or it can also involve large vessels, meaning the aorta, as well as some of the arteries that descend from the aorta like the carotid, the subclavian arteries, and others. Current treatment options for GCA are quite limited, I think that’s fair to say. And the main stone of treatment are glucocorticoids. However, we all know that the glucocorticoid treatment comes along with a significant risk of glucocorticoid-related toxicity. So, efforts have been made to look for glucocorticoid-saving drugs.
Question: SELECT-GCA trial design	**Host:** Dr. Rubbert-Roth, could you tell us how the SELECT-GCA trial was designed?

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SELECT-GCA trial design	**Dr. Andrea Rubbert-Roth:** Well, the SELECT-GCA trial was designed in a way that patients were able to be enrolled if they were at least 50 years old. It was possible to enroll patients who were either experiencing relapsing disease or patients with newly diagnosed disease. Once GCA is diagnosed, the patients are starting on a certain dose of glucocorticoid. It's going to be decreased, and while the patients are hopefully off symptoms and feeling better, then they are screened and eventually randomized in the trial, meaning that the patients who were receiving upadacitinib that was used in 2 different doses versus placebo, that some patients were able to reduce the corticosteroids relatively quickly after around half a year. The other patients were maintained on glucocorticoids for a whole year, and the primary outcome was a proportion of patients on sustained remission. And so, some patients were having longer time period and higher doses of glucocorticoids, whereas the patients on upadacitinib had a lower amount of glucocorticoids in a shorter time period. And the question, of course, was, "Is it possible to substitute for glucocorticoids, with all the well-known toxicities in particular, the elderly patient population? Is this possible? And can we ultimately achieve sustained remission?" And we do have now the results of the first part of the trial. The trial concept was over 2 years. It's now the first part of the trial. It will be very interesting to move on also in the second year, and some patients stop the upadacitinib, and others are going to be continuous. But, I think it's worth to look at the first part in that regard right now.
Question: Enrollment and baseline characteristic	**Host:** Before we get into the study findings, could you give us an overview of the patients enrolled in SELECT-GCA, including baseline demographics and disease characteristics?
Enrollment and baseline characteristics	**Dr. Andrea Rubbert-Roth:** A total of 428 patients were randomized and treated. Most of these patients were female over the age of 65 and had not been previously receiving IL-6 inhibitors. That's important, only 5% had those. We know that there may be a common pathway between IL-6 inhibitors and JAK inhibitors. Seventy percent had new onset disease. Thirty percent had relapsing disease, and the mean baseline glucocorticoid dose by the time that the patients were enrolled in the trial was around 35 mg per day.
Question: Key endpoints	**Host:** Thank you for that overview. Can you also give us an overview of the endpoints in the SELECT-GCA trial?
Key endpoints	**Dr. Andrea Rubbert-Roth:** Overall, upadacitinib 15 mg together with a 26-week glucocorticoid taper met its primary endpoint. There were a variety of secondary endpoints. These were grouped in a hierarchical order, and 9 of the 11 endpoints were also achieved. And unfortunately, we don't have the time to go over this in detail, but I think that's also a significant success.

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Question: Efficacy outcomes	**Host:** Can you tell us a little bit more about the key efficacy outcomes from upadacitinib 15-mg group in the SELECT-GCA trial, and why are they clinically important?
Efficacy outcomes	**Dr. Andrea Rubbert-Roth:** The primary endpoint of the SELECT-GCA trial is the proportion of patients achieving sustained remission. The definition of sustained remission is the absence of signs and symptoms of GCA between week 12 and 52 and adherence to the protocol-defined glucocorticoid taper regimen. A significantly higher percentage of patients on upadacitinib 15 mg plus the 26-week glucocorticoid taper achieved sustained remission. These were 46.4% of patients compared to 29% of patients on placebo plus the 52-week glucocorticoid taper. The proportion of patients achieving sustained remission as well as sustained complete remission is very important because it characteristically means that the patients do not experience a relapse. Looking at the proportion of patients achieving sustained complete remission. These were 37.1% on upadacitinib 15 mg compared to 16.1% on placebo. And this was statistically significant. Sustained complete remission was defined as achieving sustained remission together with normalization of the erythrocyte sedimentation rate, the ESR, and high sensitivity C-reactive protein from week 12 to week 52. GCA is a disease that tends to relapse once the corticosteroids are down or even stop. And so, we do see a statistically significant difference, despite the placebo patients had significantly longer and more glucocorticoids.
Question: Ranked secondary outcomes	**Host:** Are there any other ranked secondary efficacy outcomes from SELECT-GCA our audience should be aware of?
Ranked secondary outcomes	**Dr. Andrea Rubbert-Roth:** I'd like to mention some results with regard to the glucocorticoid exposure, and we know that the normal treatment of GCA would cover a 52-week glucocorticoid treatment. And what was measured in the trial was a total cumulative exposure to glucocorticoids within the trial in the different treatment arms. And what was lower, not surprisingly, with upadacitinib 15 mg was the total amount of glucocorticoids. This was 1615 mg versus 2882 mg in patients receiving the glucocorticoids over 52 weeks. In addition, in a post hoc analysis, the median additional glucocorticoid dose at week 52 was greater with placebo. And those patients, to remind you, already received 52 weeks of glucocorticoids taper compared to upadacitinib 15 mg plus the 26-week glucocorticoid taper. And to speak of some numbers, in the placebo group, it was 512.5 mg versus 20 mg in the upadacitinib 15-mg group.

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Question: Safety outcomes	**Host:** Thank you for that review. Now, let's discuss the safety outcomes of SELECT-GCA. What are the key safety outcomes from the trial?
Safety outcomes	**Dr. Andrea Rubbert-Roth:** The safety is very important, in particular in an elderly patient population. I think we are all aware of this. We have to keep in mind that the majority of patients enrolled in SELECT-GCA were newly diagnosed disease. So, those patients didn't have a longstanding history of using corticosteroids. And it's really very surprising that the rates of serious infection were lower with upadacitinib 15 mg plus the 26-week glucocorticoid taper versus the placebo patients who received the 52-week glucocorticoid taper. Namely, 12.7 events per 100 patient-years with placebo compared to 7.9 events per 100 patient-years with upadacitinib 15 mg. We also observed a higher rate of herpes zoster with upadacitinib 15 mg plus the 26-week glucocorticoid taper. That's something that we know is being encountered more frequently with the JAK inhibitors. And in the group of patients receiving upadacitinib 15 mg, we observed 7.3 events per 100 patient-years compared to placebo with 4.2 events per 100 patient-years. Two adjudicated major adverse cardiac events, so-called MACE, occurred in the placebo plus 52-week glucocorticoid taper group. And I think, of note, no MACE was reported in the glucocorticoid 26-weeks group with upadacitinib. Moving to the venous thromboembolism. They were also adjudicated, and rates were similar across different treatment groups. Non-melanoma skin cancer is also very important with these kind of treatments, rates were similar between the upadacitinib 15 mg and the placebo group. Of note, rates of other malignancy without non-melanoma skin cancer were similar between the upadacitinib 15 mg and the placebo group. In addition, no active events of tuberculosis, lymphoma, or gastrointestinal perforations were reported in any of the treatment groups.
Question: Summary and conclusions	**Host:** To wrap up, could you give us some final thoughts summarizing the SELECT-GCA trial?
Summary and conclusions	**Dr. Andrea Rubbert-Roth:** I think SELECT-GCA really shows that it is possible to reduce the amount and the length of glucocorticoid treatment in patients with either a relapse of GCA or patients with a newly diagnosed GCA. And in the context of using upadacitinib 15 mg together with a 26-week glucocorticoid taper, it was even shown that this was superior with regard to efficacy. Also, a glucocorticoid dose reduction compared to patients receiving placebo while on a 52-week tapering. The primary endpoint was sustained remission from week 12 to 52, and 9 out of a total of 11 ranked secondary endpoints were also achieved.

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	We observed an overall higher serious infection rate in patients on placebo, that it's likely due to the higher and longer use of corticosteroids. So, in conclusion, I think the data shows that upadacitinib 15 mg plus 26-week glucocorticoid taper provides a favorable benefit–risk profile and is the first oral targeted therapy for patients with GCA.
Closing	**Host:** Thank you for that summary, and thank you for joining us today to speak about SELECT-GCA.
Closing	**Dr. Andrea Rubbert-Roth:** Thank you for the invitation.
Learn more at RheumNow	**Host:** Listeners, please listen to the following about important safety considerations for upadacitinib. If you would like to learn more about SELECT-GCA, take some time to visit RheumNow.com and view the RX update titled "A Phase 3 Trial in Patients with Giant Cell Arteritis." There, you will find the data we discussed today.
Upadacitinib IMPORTANT SAFETY CONSIDERATIONS AND BOXED WARNING	**Host:** 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 are: upper respiratory tract infections, headache, fatigue, peripheral edema, cough, anemia, rash, herpes zoster, and nausea. Please also read the additional safety information within the RX Update on RheumNow.com titled "A Phase 3 Trial in Patients With Giant Cell Arteritis"

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	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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