**Transcript Details**
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/living-rheum/advances-in-axial-spondyloarthritis-how-the-treatment-landscape-is-evolving/13950/

**ReachMD**
www.reachmd.com
info@reachmd.com
(866) 423-7849

Advances in Axial Spondyloarthritis: How the Treatment Landscape Is Evolving

**Dr. Schwartzman:**
Axial spondyloarthritis is a chronic inflammatory rheumatic disease that affects the axial skeleton causing severe pain, stiffness, and fatigue. Advances in its diagnosis and management have vastly improved symptoms and quality of life for our patients. So what exactly are the developments that have been made in the treatment of this disease?

Welcome to *Living Rheum* on ReachMD. I'm Dr. Monica Schwartzman. And joining me today to talk about treatment updates in axial spondyloarthritis is Dr. Joerg Ermann, Assistant Professor of Medicine at Harvard Medical School and physician at Brigham and Women's Hospital.

Dr. Ermann, welcome to the program.

**Dr. Ermann:**
Hello. Thanks for having me.

**Dr. Schwartzman:**
So to jump right in, Dr. Ermann, let's talk about the pharmacological options available for axial spondyloarthritis. Starting with NSAIDs, what new information do we have on the use of this therapy? And does it reduce radiographic progression?

**Dr. Ermann:**
So nonsteroidals have been used in the treatment of ankylosing spondylitis for many years, and they are the first-line treatment when approaching the management of patients with axial spondyloarthritis, or AS, and a number of patients achieve full control of their symptoms by just taking a nonsteroidal. But clearly for many other patients, the pain relief is only partial or they have very little relief from nonsteroidals, and then we move on to biologics and second-line drugs.

The question of whether nonsteroidals have an impact on radiographic progression is somewhat controversial. We don't have a lot of data, but there were two randomized trials that compared either scheduled nonsteroidals versus on-demand nonsteroidals in patients with ankylosing spondylitis, and they came to opposite results. A first study in 2005 showed that scheduled administration of a nonsteroidal had benefit with regard to on-demand treatment, whereas a second study 10 years later using a different nonsteroidal came to the opposite conclusion, so at this point it's really not clear. And if there's an effect, it's probably small.

**Dr. Schwartzman:**
That makes sense. It's important to know that these medications have been around for so long, and a lot of people are comfortable using them for any number of conditions. Just switching gears to focus on new classes of medications, what can you tell us about the efficacy of biologics, and in particular, the IL-17A and JAK inhibitor class of medications?

**Dr. Ermann:**
Yeah. So IL-17A inhibitors were introduced about 5 years ago, and JAK inhibitors have been approved by the FDA for the treatment of ankylosing spondylitis within the last year, so they are relatively recent entries into the treatment field of spondyloarthritis compared to the TNF inhibitors, which have been around for about 20 years. There have been no head-to-head comparisons of these different medications, but if we just compare the outcomes of the individual clinical trials, they all have similar efficacy across the board, so whether that's TNF inhibition, IL-17A inhibition, or JAK inhibition, the outcomes of the clinical trials are very comparable.

**Dr. Schwartzman:**
I think another important class to discuss is the anti-IL-23 class, which are being used for a lot of different indications. Can you tell us a little bit about their role, or perhaps lack thereof, in axial spondyloarthritis and perhaps a biologic basis for this?

**Dr. Ermann:**
Yeah. IL-23 inhibitors are a very interesting phenomenon in spondyloarthritis. So ankylosing spondylitis has an association with polymorphisms in multiple genes in the IL-23 receptor signaling pathway, and so from that perspective, it was expected that IL-23 inhibition would work in patients with ankylosing spondylitis. It also fits into the concept of the IL-23/IL-17A access. So IL-23 is a cytokine that is produced by myeloid cells, macrophages, and dendritic cells, and IL-23 acts on IL-23 receptor-expressing lymphocytes, and these lymphocytes then produce IL-17A and other downstream proinflammatory mediators. But there were two clinical trials—one of ustekinumab, which is an IL12/23 inhibitor, and then risankizumab, which is an IL-23p19 inhibitor—and they both failed and didn't meet their primary endpoints in ankylosing spondylitis or axial spondyloarthritis, which was very surprising.

There has been a number of attempts to explain these results. I personally favor the interpretation that IL-23 plays a role during the initiation phase of the disease, which might take place in the intestine. But at the time when we see the patients because they come to us with back pain, IL-23 is not required anymore to drive the production of downstream cytokines, such as IL-17A. And that's why the IL-23 inhibition at that point is not effective anymore. But it could be that there are a subset of patients that weren't captured in those clinical trials where IL-23 inhibition may still be effective, but that is somewhat speculative.

**Dr. Schwartzman:**
With all the new treatments in our therapeutic armamentarium, when and how do we know which treatment option is right for our patient?

**Dr. Ermann:**
Yeah. So I think there's a number of things to consider. One, has the patient been on certain treatments before? For instance, in case of a patient who was treated with a TNF inhibitor and then after a couple of years the efficacy was lost here, it would be very reasonable and is also recommended by the ACR/SAA/SPARTAN treatment recommendations to just switch to an alternative TNF inhibitor because this is a secondary loss of efficacy most likely due to formation of antidrug antibodies, and it's very likely that another TNF inhibitor will be effective. But there is also primary nonresponse, and then it would be more appropriate to switch immediately to a different mechanism of action.

A second aspect that needs to be considered is other disease manifestations. For instance, in a patient who has very prominent psoriasis, I would favor an inhibitor of IL-23 if it's predominantly peripheral arthritis or IL-17A if the patient has axial disease because IL-23/IL-17A inhibitors are better in treating plaque psoriasis than the TNF inhibitors.

**Dr. Schwartzman:**
I think you speak to a lot of really important points in terms of how we have a few different classes of medications available to us that really help us tailor the medications to the patient's individual disease manifestations.

For those just tuning in, you're listening to *Living Rheum* on ReachMD. I'm Dr. Monica Schwartzman, and today I'm speaking with Dr. Joerg Ermann about treatment updates in axial spondyloarthritis.

Something that often comes up with patients is whether medications used for axial spondyloarthritis are lifelong. Dr. Ermann, should we be tapering or discontinuing medications, and if so, when?

**Dr. Ermann:**
Yeah, this is indeed a question that comes up quite frequently, often even before we start the medication: "Is this something that I have to do for the rest of my life?" It's something that has been looked at in a number of studies over the last few years. So there were four trials that used a very similar design with different medications, so patients were first treated to get into remission, and then those who achieved remission were randomized to either continue with the medication or switch to placebo, and then they were followed for about a year. And the results were pretty consistent. So in the course of this one year, about 50 to 75 percent of patients who switched to placebo relapsed and had to be retreated. Now, does that mean that drug withdrawal is something that makes no sense at all? That's a bit difficult to say because it's a glass half full, half empty situation because it also means that about a third of patients were still in remission after one year of placebo. So I think that is something that needs to be discussed with the patient, whether he or she is willing to try and how strongly they wish to discontinue the medication.

**Dr. Schwartzman:**
So something that always comes up with my patients is diet. Are there any dietary interventions we can counsel our patients on to help manage their symptoms?

**Dr. Ermann:**
So I don't think that we really have good information specifically for axial spondyloarthritis or ankylosing spondylitis. Patients probably ask more about diet than they ask about exercise, but we have more and better data on the role of exercise in managing axial spondyloarthritis than we have on dietary interventions. I would expect diet plays an important role and probably could help to achieve remission or stay in remission simply based on the insight that dysbiosis in the gut plays an important role in the disease process. And obviously, with what we eat, we feed the bacteria, and we can change the composition of the microbiota in the intestine. But whether this is really true and what kind of dietary interventions would be helpful requires further study.

**Dr. Schwartzman:**
So before we come to a close, are there any additional treatment options on the horizon?

**Dr. Ermann:**
There's ongoing research in this field. We clearly lack knowledge about some of the cytokines that play a role in the disease process. JAK inhibitors do not work by inhibiting the TNF or IL-17A receptor signaling pathways, so there must be additional cytokines. There are some data to suggest that GM-CSF plays an important role, and there are some studies ongoing to look at this mediator. And then there are some additional cytokines that have not advanced yet to trials in human beings. A recent study in mice found that a cytokine called MIF, macrophage migration inhibitory factor, was critical in a mouse model of spondyloarthritis, so that is also a potential target for human disease.

**Dr. Schwartzman:**
Thank you for that update. With those forward-looking thoughts in mind, I'd like to thank my guest, Dr. Joerg Ermann, for sharing treatment updates for our patients with axial spondyloarthritis. Dr. Ermann, it was great speaking with you today.

**Dr. Ermann:**
Thanks for having me.

**Dr. Schwartzman:**
For ReachMD, I'm Dr. Monica Schwartzman. To access this episode and others from the series, visit ReachMD.com/LivingRheum—that's R-H-E-U-M—where you can Be Part of the Knowledge. Thanks for listening.