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Treatment Escalation in Axial Spondyloarthritis: A Look at How and When

Announcer:

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Here's your host, Dr Ethan Craig.

Dr Craig:

There are several factors to keep in mind when considering how to escalate treatment for patients with axial spondyloarthritis, including considerations of how to apply treatment escalation to possible outcomes, therapeutic options for patients, and evidence supporting the role of treatment escalation and disease modification. On today's episode, we're going to focus on how to apply outcome measures in axial spondyloarthritis to decisions on treatment escalation, available therapies, and how to apply the idea of treat-to-target to patients with spondyloarthritis.

This is ReachMD MD, and I'm Dr Ethan Craig. Joining me to explore this idea of treatment escalation for patients with axial spondyloarthritis is Dr Lianne Gensler. Dr Gensler is a rheumatologist and the Director of the UCSF Spondyloarthritis Clinic at the University of California San Francisco Medical Center. Dr Gensler, thanks for being here today.

Dr Gensler:

Thank you for having me.

Dr Craig:

So maybe a good starting point would be just a brief overview of some of the devices we use for measuring disease activity in patients with axial spondyloarthritis. So, Dr Gensler, what tools do you typically use in practice to measure this?

Dr Gensler:

Yeah, so I mean, obviously, when a patient comes in to see you in clinic, you always start with an open-ended question, how are you doing? I think that crude assessment sometimes gets you to a place where a patient may say, "I feel fantastic, I have no symptoms." That's really helpful to me. "I have more pain, I have stiffness," those also helpful because it allows you then to ask more questions. I do like to quantify patient's disease activity. And I use the same outcome measure every visit so that I'm able to look at it over time with an individual patient.

So, for me I use spondyloarthritis-specific indices and, in particular, use the Bath Ankylosing Spondylitis Disease Activity Index, or BASDAI. I also like to measure function, I think functional impairment, we know if people are very impaired, it will have an impact on their long-term outcomes. And so, I measure the BASFI, or the Bath Ankylosing Spondylitis Functional Index. And then because we know in axial spondyloarthritis, that disease activity is actually better measured by an ASDAS, the Ankylosing Spondylitis Disease Activity Score, I do use the ASDAS, which draws from the BASDAI, and includes the patient global and C-reactive protein.

In general rheumatology practice, the RAPID3 is used, because it can be used generically across patients of many disease states, and so I know that is being used in the community. And I think the point is that if you're measuring something, you can compare it within an

individual patient over time. So those are the measures that I like to use, and other measures that people are using. But I think measuring something is helpful for the individual patient.

In particular, for axial spondyloarthritis, patients often come into clinic, and they give you a gestalt of how they're doing. But actually, when you measure it quantitatively, it may actually look different. And that's because these patients tend to accommodate over time. They've had their disease a long time, and so there is a new normal for them, that you may not get to the burden of disease by just asking them, how are you doing today? And I find by being able to quantify their symptom burden, gives me a little bit of a better sense than what they are sometimes telling me.

Dr Craig:

And if we're going to ultimately kind of ask the question of treating to target, maybe the next question is to pivot a little bit and ask, what do we know right now, as far as what are therapeutics like NSAIDs and biologics, what kind of impact do they make on long-term outcomes for patients with axSpA?

Dr Gensler:

Yeah, so, we didn't really talk about whether we should treat patients to target, but just in terms of what are our tools in our toolbox. So, I think the first thing in axial spondyloarthritis is to consider that not all the tools need to be pharmacologic. This really requires a very holistic approach to treatment, including both pharmacologic treatments and non-pharmacologic interventions like physical therapy, exercise, counseling on healthy weight management, smoking cessation, all of those things are really important to a patient's outcome.

If we focus on the therapeutics with the pharmacologic angle, then NSAIDs are the first-line therapy. And that's because they actually work very well. And I think there's a lot of, you know, rheumatologists that, compared to immunomodulatory treatments, NSAIDs feel like they are really small fry. And I actually think the return for the investment is quite good. And I have many patients that are on NSAIDs alone and have been on these agents for many years and have done very well. I think, as we use NSAIDs in the news in the last decade or so, we've had to consider cardiovascular risk. And so, you have to take an individual patient with axial spondyloarthritis and take that into account as you think about using NSAIDs, particularly high dose and continuously. And so, I am more cautious in older patients. Certainly, a patient with known cardiovascular disease, we wouldn't use an NSAID in. In a patient with cardiovascular risk, for example, uncontrolled hypertension, I'm also a little bit more cautious. And then taking into account the bleeding risk is an important, especially as patients get older, and certainly effects on renal function. So those are the like short-term benefits, I think they work very well, but long-term risk, something to consider, particularly in our older patients or patients with comorbidities.

So, I think the other question that comes up for NSAIDs is do they modify the course of disease? And in particular, do they prevent damage from occurring in patients with axial spondyloarthritis? And this has been looked at in a couple of studies.

Some other follow-up studies from observational data, including my own and from the cohort out of Germany has shown that maybe COX-selective NSAIDs may have differential benefit, but I think the jury's a little bit out still in terms of whether NSAIDs will actually modify the course of disease.

Dr Craig:

And still having symptoms, and you're thinking about transitioning that patient with axSpA over to a biologic, Dr Gensler, how do you decide first of all, when to kind of throw in the towel on NSAIDs when you feel like they've not had a good response? And how do you decide whether or not to switch therapies in this situation?

Dr Gensler:

Yeah. So, I mean, I think first of all, it's always a shared decision, right? I don't make these decisions unilaterally. It's always sort of getting a sense of where the patient is not just that they're not responding, but what's their preference? There are many patients that are very hesitant to escalate to immunosuppressive medications, especially as we emerge from a pandemic, despite the data that suggests that these don't have a detrimental impact on people with COVID infections. But I think that it’s got to be a shared decision.

So, you know, if we think about what do the guidelines recommend in the situation? Well, they recommend 2 things before even considering escalation. One is, have you given the patient enough time on an NSAID? So, I typically tell patients that it takes about 48 hours to see a benefit from an NSAID, because some of our NSAIDs are longer acting and they're not going to work right away. And you need to give it 2 weeks before you're going to throw in the towel on that particular NSAID, unless, of course, they don't tolerate it. And then that's a separate issue and then factors also into decision to escalation.

The guidelines, both the ACR guidelines from 2019 and also now the EULAR guidelines from 2022, recommend 2 NSAIDs, 2 full doses of NSAIDs before escalating. I think that's reasonable. There is comparative effectiveness data suggest that there's not a lot of

difference between NSAIDs. Sometimes patients come to us on NSAIDs that they've been using over the counter or on their own, and so I will give them credit for that trial, especially if they've used a full dose of that over-the-counter NSAID, and then I prescribe NSAID before escalating to the next stage.

Dr Craig:

And let's say, for the patient that you already have on a biologic that's still having ongoing inflammatory back pain symptoms, you know, clear active disease, how do you go about thinking about how to switch those patients or escalate therapy?

Dr Gensler:

Yeah, so important because we really do not have a lot of treatment options here. So, one thing I really try to avoid in patients is what I call the biologic spiral. And that is treating, you have a patient that's got ongoing disease activity, or perceived disease activity, maybe their CRP is normal, maybe it was always normal. And so, then you decide you're going to switch them to another biologic, and you put them on something either within class or, you know, in another class, and then you keep switching them. And you can imagine the spiraling that happens as you go from one biologic to another.

So, I try very hard to, one, make sure that they have true inflammatory reasons to switch, because the greatest predictor of responding to a biologic is going to be objective inflammation with a CRP being most helpful, and if not that, residual bone marrow edema on an MRI might be important too. So, the first thing I do is labs, and obviously measuring disease activity. But in the setting of a newly elevated C-reactive protein, that is enough for me to say that the patient has disease activity that warrants treatment change. So that's one approach. That's cheap and easy, and we can get that result quickly.

If the CRP is normal, then I typically go on to imaging with an MRI. And that's what's recommended in the guidelines. When you have a patient on a biologic with uncertain disease activity, consider imaging to look for disease activity. And if that is true, then I will go on to switching. If I don't see any of that, but I'm still worried about disease activity, sometimes it's because we're looking in the wrong place. And so, in a patient with established axial spondyloarthritis, say the SI joints don't have inflammation, well, if they're fused in the SI joints, they won't have inflammation there. And then you might need to look in the spine for that residual inflammation. So those are some of the approaches that I use to thinking about whether to switch a patient empirically versus using objective information to help predict that they were going to respond to a switch.

I also like taking a step back in this patient on a biologic with uncertain disease activity, or disease activity that's measuring high, is what else could be driving it? Sometimes it's because they've tapered the biologic themselves. Well, that's an easy one. Sometimes it's because those comorbid conditions that are driving disease activity, in particular, depression and anxiety, are reasons for patients to report higher disease activity. So really thinking about the patient holistically and recognizing that the way we treat patients isn't just about suppressing their immune system, it's about thinking about the driver of the disease activity and then addressing that specifically.

Dr Craig:

And finally, if we step back here a little bit, is there any evidence to support an aggressive, RA-style treat-to-target approach for patients with axial spondyloarthritis at this stage?

Dr Gensler:

Yeah, so I mean, so if we go to TICORA, right, the data is so robust, because it not only shows that by treating to a target you improve clinical outcomes, but you prevent radiographic progression. And so those data are absent in spondyloarthritis in general, actually, and not that radiographic progression has been studied.

We do know that disease activity associates with radiographic progression. So, patients that stay in a high disease state are more likely to progress than patients that are in an inactive state or low disease activity state. So, there's some associative data there. But it doesn't tell us that treating to a low disease activity or less target is going to improve outcomes.

There is a study that was done for treat-to-target in axial spondyloarthritis, TICOSPA, which actually did not meet its primary endpoint, which was looking at an ASAS-Health Index as the primary endpoint, which is a function in health status endpoint. There are several reasons why that study may have been limited, and so, I think the sense is that it may have been the study design and really expert centers that were treating these patients more, perhaps, than we would do in general practice, and also seeing them much more frequently than we might do in a general rheumatology practice.

That said, I don't think we have evidence to say that we should treat patients to an inactive disease state. And I think there are a lot of patients that may not get there, and we could end up over treating patients if we use a specific cutoff.

I do think it's helpful to have treatment goals with patients. And that is dependent on the individual patient. And we can always be aspirational and aim for remission in patients at a group level, even at an individual level. I think patients look to us not just to help improve their disease activity, but to give them hope. And some of the ways we do that are by letting them see light at the end of the tunnel that we can improve their disease activity and at least aim for the stars with a remission.

Dr Craig:

That's great. And aiming for the stars is a nice theme for this program. And as we come to the end here, I want to thank my guest for helping us better understand treatment escalation for patients with axSpA. Dr Gensler, as always, great speaking with you today.

Dr Gensler:

Thank you so much.

Announcer:

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