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Initial and Subsequent DMT Choices in the Management of Multiple Sclerosis

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Initial and Subsequent DMT Choices in the Management of Multiple Sclerosis” is provided by Prova Education and is supported by an independent educational grant from Biogen, Bristol Myers Squibb, and EMD Serono.

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Dr. Coyle:
Treatment goals for patients with MS continue to be refined as more and improved disease-modifying therapies, or DMTs, emerge from clinical trials or continue to accrue real-world data. Notwithstanding, the decision to match a patient with a particular drug agent is not a simple one defined by drug class alone. It is, in fact, far more complex.

This is CME on ReachMD, and I’m Dr. Patricia Coyle. Today, I’m talking with Dr. Jiwon Oh about how clinicians can best approach the short- and longer-term medical management of patients with MS. Our goal is to optimize our patients’ disease course while improving their personal and social quality of life.

Dr. Oh, welcome to the show.

Dr. Oh:
Thank you, very much, Dr. Coyle.

Dr. Coyle:
Dr. Oh, let’s dive right in. Before we discuss how to select therapeutic agents for each particular patient with MS, could you describe for us the NEDA concept, No Evidence of Disease Activity? And in addition, can you clarify what is meant by “treat to target”?

Dr. Oh:
Sure. So NEDA is a concept that actually has evolved from large clinical trials, and what it means is no evidence of disease activity based on the typical clinical measures that we use as well as MRI measures of disease activity. So the traditional version of NEDA that’s really been widely used in clinical trials, and actually many people have adapted to use in clinical practice, essentially refers to patients having no evidence of any clinical relapses or new MRI lesions. And by new MRI lesions, we typically mean new T2 lesions or enlarging lesions, or if you give gadolinium contrast, gadolinium-enhancing lesions. So this is traditionally what the concept of NEDA has meant in clinical trials and also the concept that many people apply in clinical practice. But in recent years, because NEDA essentially has evolved into the target of therapy in clinical practice, there is a school of thought that we should be adding on to the concept of no evidence of diseased activity to include some more advanced MRI measures or some additional clinical measures, possibly measures like brain atrophy. And we can also consider, when they are widely available, adding on fluid biomarkers such as serum neurofilament, which has recently emerged as possibly a very useful biomarker of disease activity in people with MS.

Dr. Coyle:

So I think it's important to have a treat-to-target, what's acceptable, what's not. NEDA seems to be a pretty high bar. I know people talk about minimal evidence of disease activity, or MEDA, perhaps allowing one or two T2 MRI lesions, for example, and I think this is something that we're just going to have to work out with further studies.

Let's turn now to making first-line treatment choices for our patients with MS. What are the key factors that help make that decision? First, let's consider patients who might be managed with moderately effective agents, and then we'll shift our focus to those patients who may require a highly effective agent as their first-line therapy.

Dr. Oh:
So with treatment initiation there are a number of factors that one needs to consider, and unfortunately, accurately predicting how an individual patient will do is one of the greatest challenges that we have in MS clinical practice because we don't have, say, a single fluid biomarker or a single MRI measure or a single clinical feature that tells us exactly who will have really aggressive disease versus who will have mild disease.

But what we do have are a variety of clinical demographic as well as MRI features that allow us to take these factors all into account to try to decide who is somebody that we may be worried about and therefore needs to start on high-efficacy therapy from the very beginning. Some of these factors include demographic features, so men tend to do worse than women; older patients at onset tend to do worse than younger patients, and clinical features also come into play. People who I would be worried about include those who have had frequent relapses in the last two years, those who have had incomplete recovery from their relapse, and those who have presented with motor symptoms or cerebellar symptoms. So these clinical features in various studies have been shown to be associated with a poor prognosis in MS. Finally, the baseline MRI is also quite helpful, and we do know that individuals who have a heavy baseline MRI lesion load tend to have a worse prognosis, and specifically individuals with spinal cord lesions also tend to have a worse prognosis.

So the trick is taking all of these clinical, demographic, and MRI features into account to try to decide if the patient in front of you has concerning features. And if that is the case, then from the very beginning, you would initiate treatment with an agent that you think falls into a higher or highest efficacy category amongst all of the options that we have available.

And I should also mention that family planning – if this is a goal for a female patient in the next few years, that also does influence the treatment decision that you make initially.

Dr. Coyle:
I really believe very strongly in shared decision-making. It's important to elicit what are the concerns of the patient, but as the expert, if I feel strongly, I'm going to try to be as persuasive as possible with regard to what is their optimized treatment choice. However, I'm also going to be very supportive, and I think the key thing is follow them very closely.

For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Patricia Coyle, and here with me today is Dr. Jiwon Oh. We're discussing the management of patients with MS. Our emphasis is on how we can best approach our short- and longer-term medical management of individuals with MS, thereby optimizing their disease course while improving their personal and social quality of life.

We've talked about initial treatment decisions for patients with MS and efforts to individualize these decisions, make them patient-centric while adhering to NEDA and treat to target. Most if not all patients require a modification in their therapy over time. How is that best accomplished?

Dr. Oh:
So when it comes to switching treatment or treatment escalation, there are a number of factors that come into play, and this is actually where NEDA can become very useful. So as you said earlier, Dr. Coyle, NEDA is often the ideal target that we strive for in clinical practice, but in reality, this may be too high of a bar. And I do think this minimal evidence of disease activity is most likely more practically a useful goal to have in clinical practice. So in general, when an individual patient has started on a treatment, things that would make me consider other treatments are either evidence of disease activity that is concerning – so whether it's a clinical relapse – or MRI lesions over time. And the number of MRI lesions, you know, depending on the individual situation can vary. But generally, if an individual develops 3 or more new MRI lesions while on treatment in the last year, for me, that is high concern. And that is enough evidence of disease activity, even if there is not any clinical evidence of disease activity, that would make me want to escalate that patient's treatment to a disease-modifying therapy that I think has a higher efficacy than the one that the patient currently is on.

There are also many other reasons why patients may need to switch therapy. One of them is related to an adverse event with their current disease-modifying therapy. And if this is something that is not reversible and that bothers them quite a bit, this would be reason to change therapy. And in this setting, one could consider either a lateral switch or a treatment escalation, if needed. In addition, if there are serious tolerability issues – and the reason tolerability issues become a concern is that they directly impact a patient's adherence to therapy if this is a concern over time, because these are typically chronic therapies that require a regular dosing, this

would be another reason why we would want to switch therapy.

Finally, again, as I alluded to earlier, for a female patient, if she is considering family planning, this would also influence treatment choice, and there are a number of treatment options available that, you know, based on data that have been collected for many years as well as existing studies, we know are safer than others during the time when a woman is planning to conceive. And so in that situation, a discussion needs to be had about her current therapy, whether she can continue on it during the time she is trying to conceive, and what to do when she becomes pregnant.

Dr. Coyle:
So I think my take-home from this is that there are multiple reasons, potentially, to switch a disease-modifying therapy, and therefore, it's good news that we have multiple choices. And it really means we need to keep open lines of communication to make sure our patients are doing well and a switch is not indicated.

Dr. Oh, current MS therapeutic options have significantly increased treatment algorithm complexity. For many patients, the burden of their disease is actually made worse by the burden of therapy. One outcome is poor therapeutic adherence by patients, leading to worsening disease and quality of life outcomes, often measured by an escalating EDSS [Expanded Disability Status Scale] disability score. As part of our desire to maintain patient-centric care for MS, how do you approach this issue to keep your patients fully engaged in treatment decisions and adherence to therapy?

Dr. Oh:
Well, that's a great question, Dr. Coyle, and it really is a challenge in MS clinical practice. And this is because many of the medications that are available, they need to be taken daily and sometimes even twice daily. And I have to say, on occasion when I have had to take medications, I actually am somebody that is very bad at remembering to take a daily medication. And so I completely understand how in some situations having a medication that you need to take like clockwork daily or even twice daily may not necessarily be compatible with certain patients' lifestyles and schedules.

And so, you know, adherence, especially for a chronic disease that lasts decades like MS is a major issue because, ultimately, adherence is what determines a disease-modifying treatment's efficacy. And so I think this is really an issue that needs to be discussed actively with patients at every clinical visit. And if there is an issue with adherence, fortunately, because of the number of treatment options that we have available – and we also now have available therapies that are administered very infrequently. And there are even induction-type therapies where therapies are administered in short cycles, and in some people, they can go for many, many, many years without requiring any chronic continuous therapy and are able to achieve disease control. So I think the bottom line is adherence is something that in real life really needs to be considered. Chronic therapies over time are not easy to take for many patients, particularly if there are some side effects or tolerability issues, and so this is something that should be actively discussed. And if it is clear that it's a problem, fortunately, we have many options and particularly options that do not require frequent dosing. And in particular patients, this may be a very useful treatment option for them.

Dr. Coyle:
Well, this has certainly been a fascinating conversation, but before we wrap up, Dr. Oh, can you share your one take-home message with our audience?

Dr. Oh:
It's hard to; there's many messages I'd like to share. But I would say the one thing is more options is always a good thing, and so I think this, as neurologists, it gives us the opportunity to really tailor treatment appropriately for individual patients, whether it's for disease activity or tolerability or lifestyle. So I would say that is my one take-home message.

Dr. Coyle:
And I would say treat-to-target is important. Determine what's acceptable or not acceptable as a response. Make sure patients are going to be followed. We're doing surveillance MRI scans – make sure they're done under an MS protocol, ideally at the same facility so an optimum comparison can be made.

Unfortunately, that's all the time we have today, so I want to thank our audience for listening in and thank you, Dr. Jiwon Oh, for joining me today and for sharing all of your valuable insights. It was great speaking with you today.

Dr. Oh:
Thank you very much. It's been a pleasure.

Announcer:
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