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From Prescription to Personalization: An HCP's Guide to Tailoring MS Therapeutic Management

Announcer:
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Dr. Freedman:
Hello everyone. My name is Mark Freedman. I'm a Professor of Neurology at the University of Ottawa, and a Senior Scientist at The Ottawa Hospital Research Institute. And I'm here to talk to you today about a little bit of personalizing the treatment of multiple sclerosis.

So, when we think about treatment of multiple sclerosis, it's really important to try to put into perspective where this patient is in their journey. So, in this little cartoon, the threshold here is seen here, and anything above the threshold is something that the patients realize are symptoms, or you can find out that there's signs of the disease. And when demyelination comes and goes, the first time it crosses the clinical threshold, patients are aware of symptoms, you're aware of the signs, but you know, clearly the disease has started before that. And that's why there's evidence of demyelination prior to that.

Now, eventually, the patients will develop an axonal loss. And this is really important. See, you can see when this little green line crosses the line, everybody thinks the patient is into progressive disease. But it's so key to understand that this progressive nature of the disease starts right back here at the origin. And those transections that were seen years ago by Bruce Trapp when he tediously looked at these axonal transections, noted the fact that this disease starts right from the beginning, but you don't realize the buildup of this until the green line crosses the clinical threshold. And at that point, you're aware of the progression, but the progression has been building up all this time. And so, we're trying to prevent this axonal damage.

What drives it? Probably inflammation. You can see that the inflammation comes and goes over time. So, where is the opportunity to treat? Well, you know, the concern is that early on, you have to treat because eventually our ability to compensate for all the axonal loss dissipates. And at some point, the axonal loss exceeds the ability to compensate, and the patient progresses. So, I look at the time window for early treatment is here, probably starting when you're first aware of the disease, and likely ending somewhere out here where these disease-modifying medications that we have today that really address the inflammation are becoming more almost futile, because the axonal loss is irreversible.

Okay, so where is this patient in the window? That's the key here, you've got to use everything at your disposal to figure out, are we dealing with really early disease? Or has this patient built up so much disease that it needs an aggressive treatment now?

Okay, so what are the things that look at? Well, there are three different types of categories I look at here for treatment. And you know, you've got to look at the disease activity, I've just dealt with that. There are certain issues with regards to the drugs and the individual patients that you have to put into consideration. And then finally, you know, you have to talk to the patient. Is this someone planning to get pregnant the next year? Do they have travel? Are they going to be able to adhere to whatever regimen you're going to deal with? So, you've got to look at all those three in order to make a treatment decision. And so, you can see, there's a lot of things that feed into the treatment decision here that all need to be looked at, including even some logistical things like: Am I going to get this drug covered wherever the patient happens to be? Are they going to be able to go and routinely go for their blood test for mitigating any kind of risk

strategy? That's key.

Alright, so how do you put the picture in? How do you know where they are in that window? Here are some elements that probably point to patients who have a poorer prognosis. And of course, you're not going to fill all these boxes. But if you, in general, look at all these things, the more of these things that the patient has, the better the chances that they're an early progressor and you need to be more aggressive.

Alright, so what kind of therapies do we have? I like to put these into about three different categories. The early immunomodulators, they can take care of a lot of early disease, but they're not very powerful drugs, but they are the safest stuff on the planet; you're not going to have to worry about them. I look at the far side and say the cell-depleting therapies are the most effective therapies, but they come with a lot of particular concerns, and those have to be addressed. And then in the middle here are the anti-cell trafficking drugs, which are usually immediately effective, but they have major problems in that you have to follow them for mitigating kind of risk strategies for the PML. Also, if you stop these suddenly, there's a chance for rebound disease that you have to keep in mind. So, there are all sorts of issues.

The disease-modifying immunomodulators are the easy ones. There's almost no risk for PML except for low lymphocytes with DMF. The anti-trafficking drugs are the main ones we have to be concerned about, because of the possibility of PML but also because of rebound. And then finally the cell-depleting drugs are most effective. The immune reconstitution treatments, you only have to give for a limited time. And the anti-CD20s are probably the commonest drug used today, because they're so highly effective but require a little bit of watching.

So, that is it in a sense, but hopefully I've been able to bring some sense of balance to your treatment decision today, and thanks for listening.

Announcer:
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