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Time needed to complete: 1h 04m

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### Transforming MS Management

#### Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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#### Dr. Weinstock-Guttman:

I'm Bianca Weinstock-Guttman, Professor of Neurology at Jacobs School of Medicine and Biomedical Sciences at the State University of New York. And with me here is Professor Mark Freedman, my colleague and friend.

#### Dr. Freedman:

Hi, everyone. I'm Mark Freedman. I'm a Professor of Neurology at the University of Ottawa, a Senior Scientist at The Ottawa Hospital Research Institute, and the Director of the Multiple Sclerosis Clinic here at The Ottawa Hospital General Campus.

#### Dr. Weinstock-Guttman:

So, I would like today to ask Professor Freedman to go a little bit in depth on the question about what therapeutics is he using in the first diagnosed MS patients, versus the ones that do not respond to previous therapy, meaning switching?

#### Dr. Freedman:

Well, nothing like a nice and easy question, Bianca, that I have to be able to answer in just a few minutes. But why don't I just take the overall approach to this and say, every time I see a patient, whether they're newly diagnosed or they've been treated, I try to get some feel for the beginning of their disease. And I may be seeing them well down the road, but I really want to know how the disease started, because that gives me an impression of where therapy should be going.

We're all aware of the fact that some patients are really presenting very early, they're quite fortunate, they have very minimal disease, and they have very little residual to the disease. And there's others who harbor silent disease for who knows how many years, present rather late, have a large disease burden. And you know, time's ticking in terms of being able to gain control over their MS. So, I try to get that perspective. And if I'm dealing with a naive patient with very mild disease, we have a number of medications that we've lived with now for the last 30 years that are considered modestly effective. But some patients with mild disease, that's all they need. And we've seen that they can live very nicely on these therapies with minimal risk for 20-30 years without a problem. We're just, you know, not so accurate at being able to assess who has the mild disease. But I think we – with enough experience, you can really package them in there.

And so, I think of the therapeutics in three categories, and for this particular patient, the early naive patient, the package of immunomodulators is where I would go to, and these are the drugs that some people refer to them as platform therapies. They can control the disease without necessarily immunosuppressing the host. And so, the risks are actually very low in the long run. The patients who run amok with their disease, they get a substantial breakthrough, there's two categories of drugs that I would go to. I would go to the anti-trafficking therapies, those are our S1P receptor agonists and drugs like natalizumab. And then the sort of more definitive therapy, so the cell-depleting therapies, some people refer to those as the highest efficacy therapies because they are cell depleting, but they're also the riskier ones, because when you deplete cells, you're immunocompromising the host. And that's actually true of the

anti-trafficking drugs as well.

So now, if I'm dealing with a patient who's already maybe been on a platform therapy, disease breakthrough is occurring, I try to assess what kind of breakthrough that is. Is it substantial? Did they leave with deficits? Are they repairing with steroids? Is there MRI building lesion burden? Is there residual EDSS on their neurological scale? These are people who are getting into trouble. And so, if I'm really, really worried that things are hot, they've had two or three attacks and numerous enhancing lesions, the anti-trafficking drugs will shut them down very quickly. And so, one of the two categories that I mentioned, the S1P receptor agonists or the natalizumab, would gain hold of their disease for a period of time, but those are not long-term drugs. Those are drugs that you have to be very concerned about you in the long run because of PML issues. And those are things that increase with age. So, there's a sort of finite time that you would use them and then there's some kind of a mitigation strategy to get them off of it and either de-escalate them back to a platform, or if that fails to control them or we're considering escalating further because their disease is still not controlled, you would then go to the cell-depleting therapies.

Now you could go directly – if you had a naive patient on therapy breaking through, you can go directly to the cell-depleting therapies. And in that group of drugs, we have the anti-CD20 therapies, there's two or three of these out there. We have drugs like cladribine. That's known as an immune reconstitution type treatment where you give it for a finite period of time, and then you don't need any more therapy, and then you can just repeat the courses later on if disease continues. We also have a drug that's sort of fallen out of favor, alemtuzumab, is in that immune reconstitution type treatment group. But because of all the side effects that's been associated with it, more people are staying away from alemtuzumab.

And ultimately, you know, what we do up here in Ottawa if things fail to control, we can go right to hematopoietic stem cell treatments, which is fairly definitive, but you only want to do that once in your lifetime.

So, I try to tailor the therapy to what the disease is doing, the burden that the patient brings to the table, be it either at a naive stage or later if they've failed to control with other therapies, and then try to introduce the therapy that's going to be most likely to take care of that disease that's broken through. That's it in a nutshell, unless you have particular questions.

**Dr. Weinstock-Guttman:**

No, I only wanted to indicate our, or my primarily, you know, management in general. We do have pretty much the same, trying to identify specific characteristics of the patients; severity, age, and consider an appropriate therapy, although we're starting to consider as the first therapy often in a patient with the so-called induction therapy with the B cell therapy. We're still waiting for, sure enough, the results of the randomized studies, evaluating the induction therapy, versus the rest of the medication for naive patients. But the retrospective data does support so that eventually starting with an induction therapy may be more efficient. And again, as you said, later on, we have to go and figure out the de-escalation. So yeah, I think that we'll have to wait to learn more about the results of different studies.

And again, in our site, it's also related to the insurance approval. And often as we want to start the medication as early as possible, we don't have time to, you know, to fight with the insurances and go for what is approved first time.

Thank you very much, Dr. Freedman. And thank you very much for listening to our talk. Thank you. Bye.

**Announcer:**

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