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**MS Learn Online
Feature Presentation
Disease Modifying Therapies – Part One
Fred Lublin, MD**

Tracey>> Welcome to MS Learn Online, I'm Tracey Kimball.

Tom>> and I'm Tom Kimball. Disease modifying therapies help many individuals with relapsing forms of MS as well as those with secondary-progressive disease who continue to have relapses.

Tracey>> Dr. Fred Lublin from Mt. Sinai Hospital in New York City talks to correspondent Rick Sommers about some of the different agents available that can reduce disease activity and disease progression.

>>Dr. Lublin: So, for the past 16 years we have had what are called disease-modifying therapies, that is, therapies that alter the course of multiple sclerosis. And so we now have six that are marketed in the United States for treatment of the disease, primarily for treatment of the relapsing forms of the disease, and treatment of the disease in its earliest stage, which is after you've had your first attack, when in fact we can't even fully diagnose you yet.

So, these therapies are primarily immunomodulators, or immunosuppressants its effects on the immune system. And we have interferon beta 1-a, two types of that, interferon beta 1-b, glatiramer

acetate, natalizumab and mitoxantrone. And they work by different mechanisms, but ultimately what they're doing is cutting down on the number of attacks people have, and decreasing the chance of individuals developing disability.

We use them in somewhat different ways. At least we use the interferons and glatiramer acetate primarily as first-line therapies for early stage disease, the relapsing form of the disease. Natalizumab can be used as first line, but more often is used on individuals who haven't responded or don't tolerate other interferon or glatiramer acetate.

And then mitoxantrone is saved for those who really aren't responding to much of anything, perhaps entering the progressive phase. But it's a little more challenged agent because it has more side effects.

>> **Rick Sommers:** Now, are they all known by brand names as well?

>>**Dr. Lublin:** So, the brand names would be Betaseron, Avonex, Copaxone, Tysabri, Rebif and Novantrone.

>> **Rick Sommers:** I'm a new patient, I've been diagnosed. We've looked at the MRI. How do you pick from the six? Do you throw a dart at a board and say, "All right, let's try this one?"

>>**Dr. Lublin:** There is no standard way of determining. The way we do it is interactively with the individual to see what we think would be the most appropriate agent for them, and what they think would best fit into their lifestyle.

So, usually early on we would start with either an interferon or glatiramer acetate, Copaxone. And there you're talking about an injectable therapy. So, it is injected subcutaneously or intramuscularly, and it may be injected once a week or three times a week, or every other day or daily, depending on which agent is chosen.

And so those are all considerations. Efficacy-wise, there's a great similarity between what we see with interferons and what we see with glatiramer acetate. So, it revolves around other things: lifestyle, number of injections, side effect profile. Interferons tend to produce flu-like symptoms. That we can mitigate, but nevertheless it's an issue. People who have busy travel schedules may like, for example, once-a-week injection. So, it's an ongoing discussion that we have with the patient to try and pick out what's best for them.

And then once they're on the agent, of course, you're not locked into it. You always can modify it or change it, if there is reason to think that someone would do better with something else.

>> **Rick Sommers:** And somebody may react to one, I don't want to use names, but react to one, and then you'll switch them over and they'll do fine on that. That's a case you've seen?

>>**Dr. Lublin:** Right. So, sometimes people have side effects with one they may not have with the other. Sometimes, and this is harder to gauge, is people maybe respond -- it may not work for them, and so you switch them to another agent to look for better efficacy.

>> **Rick Sommers:** Well, that's an interesting point, because people say to me, "Oh, you're on an MS drug. You look great, it must be working." How do we really know and is it working?

>>**Dr. Lublin:** This is a big question for us. Because it's very hard to know whether a drug is working or not on someone once you start them. For any given individual, you no longer have a control. Once you start them on the agent, you don't know what they would have done had they not. And MS is such a variable disease, that you can't look at what they did last year and say, well, they're better or they're worse this year. To think that that really gives you valid information to tell you how the drug is working, it doesn't.

This is why we go to the great difficulty and expense of doing these clinical trials with control groups and placebos and everything, just to prove that the agents work. Because just switching, for example, one drug to another doesn't tell you that one is working better than another. It's a very difficult concept.

So, when we put people on these agents and they'll say, "Well, how long am I going to take this agent?" We say, "We're going to take it until something better comes along." What we're really looking at is that they tolerate it and that they do well on it. But we have not yet as a community determined whether they should be allowed to have one attack, or should they be allowed to have any new MRI activity? All of our agents are partial therapies, they're not cures. So, one wouldn't reasonably expect to have nothing more happen once you started it. So, it is a difficult issue for us to figure out when it's working.

>> Rick Sommers: And the concept of being diagnosed, absorbing that diagnosis, and then being told you have to start on one of these therapies, which is terrifying to some people. In a recent MS Viewpoint survey [it was] shown that a lot of patients are apt to defer any kind of therapy for a while because they want to wait until something orally comes out. Do you see that?

>>Dr. Lublin: Well, there are two aspects of that. One is dealing with the initial impact of being diagnosed and being told you have to take an injection. And it does take a lot of discussion, a lot of counseling not only with the physician, but we also utilize social workers and nurses and nurse practitioners as a team concept, to help people get comfortable with the idea.

The reason we do that is we don't necessarily have a luxury of time, because our studies show us that the earlier we start treating individuals, the better they do. So, we want to let people adjust to the changes that are

coming for them, but we don't want to wait too long, because that puts them at risk. So, we like to get them started on therapy very early.

There are some people who don't want to take injections, and we understand that, and so we have a number of pills in the developmental pipeline. We've seen recent data on two of them that have shown positive results moving forward. And so I expect we will see those on the market, hopefully, in the not too distant future. It won't be in this calendar year, but perhaps next.

But then we have to go through the whole process of evaluating and looking and seeing what their side effect profile is, who are they most appropriate for. And I expect we're going to be having long discussions with our people already on injectables, whether it's appropriate for them to switch to a pill if one comes around or whether they should stay with what they're doing.

>> **Rick Sommers:** So, it's not a slam-dunk, quid pro quo, we're going to have an oral drug, let's move everybody over.

>>**Dr. Lublin:** No, it's not, because these are different agents. It's not in oral form. At least there's nothing in the pipeline right now, that I'm aware of, that's an oral form of what we already have. You know, there are different agents, different mechanism of action, and different side effect profiles.

>>**Rick Sommers:** How long have you been involved in the MS community?

>>**Dr. Lublin:** Oh, I guess about 26 years.

>> **Rick Sommers:** So, you've seen, I mean, just incredible breakthroughs.

>>Dr. Lublin: Well, we went from having no therapy to having therapies. This was an incredibly exciting thing, 1993, when the first therapy came along. So, professionally, it doesn't get much better than working in an area when its first therapy comes through.

Tracey>> I remember when the first disease modifying therapy was approved just over 15 years ago because I was diagnosed just a few months later.

Tom>> And today there are six disease modifying therapy options and more will be coming. Staying informed about these therapies and other developments is important.

Tracey>> So join us again as Dr. Lublin continues his discussion on the available therapies for MS.