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Advancing Care: Clinical Innovations on the Horizon

Announcer:
Welcome to CE on ReachMD. This activity is provided by TotalCME. This episode is part of our MinuteCE curriculum.

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Dr. Vissing:
This is CME on ReachMD, and my name is John Vissing. I will be talking to you about some of the disease-specific treatments for limb-girdle muscular dystrophy type R9.

These are interesting times for this disease, because we have fundamentally 2 different treatment options that are ongoing, experimentally, for this condition. One is a substrate-driven therapy, and the other is gene therapy. And if we talk first about the substrate-driven therapy, this is delivering ribitol to the patients. And ribitol is the substrate of fukutin and FKRP. So essentially, when you are overloading the patients with the substrate, you can push more substrate through these defective enzymes to improve the glycosylation on the cell surface, which is what is wrong with this disease.

An important point here is, obviously, that you need to have some functional enzyme to do this. If the enzyme is completely broken, you can't do it. So the more residual enzyme capacity you have, the better the treatment option here. And what we have seen is that there has been a phase 2 trial looking at this.CK levels dropped quite remarkably in the patients, and there were also some nice clinical readouts from this very small trial. And this has led to a phase 3 trial, which is ongoing. It's a very lengthy trial, 72 weeks, double-blind, placebo-controlled trial in more than 100 patients. And as I said, this is ongoing. We have no results yet from this trial. Obviously, this is, although very simple, an interesting approach because it is involving a naturally occurring substrate, ribitol, that we all have in our bodies, just in abundance.

The other treatment option here is gene therapy, and there are 2 companies that are presently looking at this. In one of these trials, which is a phase 1, there were 2 doses studied, and we have results from these 2 doses, especially the lower dose, where patients have been followed the longest. And in those patients, we see that there were some side effects to begin with, like you see with most gene therapy. These were not serious ones, and now all 3 patients are without immune suppressants, doing well, and have almost normal CK values at this point. They also have improvements in their respiratory function and walking capability.

So this looks very promising. Although, of course, this is an open-label trial, so you have to be cautious about this.

Patients at the higher dose had a more mixed response, and therefore the next step will be to go to a phase 2b trial, where patients will be dosed with the lowest dose. Unfortunately, right now there is a temporary hold on the trial due to lack of funding for this one.

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The other approach is essentially delivering the FKRP gene, again in an adeno-associated virus type 9, which was also the case with the first one. This approach also targets the heart, which can be beneficial to the patients. This was not targeted in the first study because there was cardiac toxicity. There can be a problem of overexpressing FKRP in tissues, particularly the heart. So it's finding the balance of trying to correct FKRP, but not too much. Results from the last trial are not known yet. This is still ongoing.

So very interesting times for this disease and thank you for listening.

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