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## Optimizing FcRn Therapy: Addressing and Reducing Adverse Reactions

### Announcer:

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

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### Dr. Silvestri:

This is CME on ReachMD, and I'm Dr. Nick Silvestri. Here with me today is Dr. Chip Howard.

Dr. Howard, the FcRn antagonists are not without their problems. What are the common side effects, and how might they impact the use of these agents as a longer-term treatment option for myasthenia gravis?

### Dr. Howard:

The use of FcRn antagonists in treating MG has only been for the last few years. So I don't think we have a really good handle on what the true side effect profiles are. Commonly, we experience headache that's mild, often treated with symptomatic therapy. We've seen some increase in urinary tract infections and upper respiratory tract infections, and we've seen some diarrhea. Those tend to be the most common.

What is interesting in the ADAPT trial were there were, relative to placebo, modest numbers of UTI and URIs. In the open-label extension, that frequency event per patient-year dropped substantially. So I don't think we really have a handle as to whether or not FcRn antagonists increase infection rates. My own personal belief, looking at some data with chronic plasma exchange that we have, is that the level of IgG does not play a direct role in the ability to become infected with the type of infection that we have. So time will tell us.

I think the difference between a small Fc fragment and a full-size antibody will have an impact on adverse events. We know that some products also inhibit the recycling of albumin and deplete the patient of albumin, and that may be problematic in a patient who is hypoalbuminemic or hypergammaglobulinemic, who has congestive heart failure, etc., that it may be a reason not to administer the drug.

The subcutaneous forms clearly have injection site reactions. The overwhelming majority of these have been very mild. They did not limit the ability to administer the drug. And, in fact, what was seen is that the frequency of these injection site reactions diminished over time with the increased frequency of use. And so we still don't have the full word on that as well. Relative to the current therapies that we use, it's orders of magnitude safer in terms of our experience and my experience in what we see. And these have been well tolerated, very easily manageable in our patient populations.

**Dr. Silvestri:**

Yeah. I agree, Chip. I mean and that's been my own personal clinical experience as well, that whereas the traditionally used agents with broad immunosuppression tended to lead to a lot of problems, I'm seeing fewer and fewer issues with FcRn antagonists. I don't really see a huge increase in infections compared to the traditionally used agents that have been used in the past and still used to a certain degree, so I've been quite pleased with the side effect profile. I mean, certainly these risks exist and we have to counsel our patients appropriately, but with the limited time that we have in terms of follow-up, as you pointed out, I think the side effects seem to be manageable, but obviously we need to have continued vigilance. We need to kind of continue to look at the data, continue to monitor our patients in clinical practice to make sure that we're treating them and we're treating them safely.

And just a quick comment on the subcutaneous injection site. I've definitely seen that at my practice where any patients that have had issues, actually skin injection issues, may have them early on, but they tend to go away with repeated injection, and I think it also affords patients a little bit more in the way of convenience. And I think that will continue to improve with future innovation over the course of time.

**Dr. Howard:**

And the other unique feature is that we don't have to do frequent monitoring of blood work. So we're releasing them from the burden, if you will, that we spoke about earlier as part of their treatment process.

**Dr. Silvestri:**

Absolutely.

Well, great discussion, and with that, our time is up. Dr. Howard, thank you again, and thanks for our audience for tuning in.

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