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The IgG Clock: Redose Using IgG Kinetics

Dr. Wolfe:
This is CE on ReachMD, and I'm Gil Wolfe. Here with me today is Dr. Christyn Edmundson. In this episode, we're talking about what comes after the first cycle. That is, how to time re-treatment with FcRn-blocking therapies.

What does the IgG curve look like for the FcRn agents we use and how does that guide us when we should potentially anticipate symptom return?

Dr. Edmundson:
That's a great question. And just to review quickly, the 3 agents that are FcRn inhibitors that are currently on the market to treat generalized myasthenia gravis are efgartigimod, rozanolixizumab, and nipocalimab. These were all studied in slightly different ways, but you can see here that all of them produce a drop in IgG levels compared with placebo.

You can see the 3 graphs here. On the left is efgartigimod, which is administered in a cyclic fashion, so it's given as 4 weekly doses, followed by a treatment-free interval. And you can see fairly rapidly the green curve here, the efgartigimod-treated patients are achieving a rapid reduction in their IgG levels, then with a gradual return of the IgG during that treatment-free interval.

Very similar in rozanolixizumab, which is the middle pane here, you see a rapid drop in IgG levels in patients treated with both low- and high-dose rozanolixizumab compared with placebo-treated patients, with a gradual return of the IgG levels during that treatment-free interval.

Lastly, on the right here, is nipocalimab. And this nipocalimab is used continuously. So, rather than being used in sort of cyclical fashion as efgartigimod and rozanolixizumab are, nipocalimab is started and then continued every 2 weeks without a treatment-free interval.

Again, you can see the IgG levels dropping rapidly and then maintained at a continuous lower level compared with the placebo-treated patients.

So, how do you tie that pharmacokinetic to treatment targets, and what factors tell you it's time to re-dose?

Dr. Wolfe:
So, it does make some sense. It's not a perfect correlation, but many patients, their symptoms do start coming back as the IgG levels return. This is mostly, as you pointed out, relevant for efgartigimod and the rozanolixizumab, since the way it's given, according to the label, is in a cyclical fashion.

So, when might you re-dose? It could be, if you're following the MG-ADL, when you see that scale rise as far as the number of points, say by ≥2 points. Oftentimes, that's going to be consistent with what the patient's just telling you when you're taking their history, that

they're having certain symptoms return that had been better controlled, say, 1 or 2 weeks prior.

Again, you can often time it to when the symptoms are recurring according to when the last dose of the medication has been given, following the IgG recovery curves that we've seen in studies. This is true whether you're actually tracking IgG levels or not, but we know from the study sort of what that schedule looks like.

So, if the minimum interval has passed where it's actually labeled to repeat the cycle, and there's no concerns as far as different labs, like a really, really low IgG level, and no other clinical flags, such as evidence of a moderate to severe infection, redosing would be very appropriate in that type of scenario. Okay.

If there's evidence of an infection or something else, you may actually want to handle that prior to the retreatment.

Thanks for joining us for another one of these 10 bite-sized episodes on advancing care in generalized MG.