Transcript Details

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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

The Evolving gMG Treatment Landscape

Announcer:
You're listening to *NeuroFrontiers* on ReachMD. On this episode, we'll discuss recent advancements in treating generalized myasthenia gravis, or gMG, with Dr. Henry Kaminski. He serves as the Meta A. Neumann Professor of the Department of Neurology at the George Washington University School of Medicine and Health Sciences and is also a Principal Investigator for the National Institutes of Health-Supported Rare Disease Clinical Research Network. Let's hear from Dr. Kaminski now.

Dr. Kaminski:
gMG is generalized myasthenia gravis. Patients have ocular symptoms of droopy eyelid and double vision. They'll have swallowing difficulty, speech problems, and weakness of their arms, and they may get easily fatigued when they're walking. And this symptom complex can be highly variable. Some patients have a lot of these ocular symptoms and, in fact, may have purely ocular myasthenia. That's a subtype of myasthenia. The other subtype is gMG—generalized myasthenia gravis—but some people have really predominant swallowing and speech problems, and other patients may really have more limb weakness or respiratory weakness that can be severe, and they end up on a ventilator.

Myasthenia gravis is an autoimmune disease, and specifically, there are antibodies attacking the neuromuscular junction proteins. Predominantly, it's acetylcholine receptor antibodies, and that's an important distinction as we talk about treatments. These acetylcholine receptor antibodies can activate the complement system, they can block how the nerve and muscle communicate, or they can enhance the removal of acetylcholine receptors on the neuromuscular junction. And then there's MuSK myasthenia that doesn't work through the complement system but interferes with how the receptors are clustered at the neuromuscular junction.

We now have a number of treatment options that we've had great experience with over the last several decades. And then really what's exciting in the field is the greater appreciation of the immune system, and autoimmunity in general, which has now educated us on new treatments that have come to the forefront. There's these FcRn inhibitors or complement inhibitors that were identified in the last few years and FDA-approved, so that really comes from a detailed understanding of the pathophysiology. And now with agents in clinical development like CAR T cells, we have an understanding of ways to target these B cells that are producing antibody. There have been attempts also to try to affect the cytokines that we know drive the disease as therapeutic opportunities. The amount of information and understanding of the immune system is growing on a monthly basis, and the tools that we have—for example, multi-omic approaches matched to clinical data—really is very exciting to see how the future goes in myasthenia and developing personalized care for patients.

There's a new class of drug first applied to myasthenia: the FcRn inhibitors. And what's really cool there—it's a beautiful example of how understanding of basic pathophysiology could get translated to the care of patients. This FcRn protein is involved in recycling antibodies. So most of the time, our antibodies are flowing through the body. Endothelial cells pick them up. 95 percent go back into circulation. There's probably a quality control system that eliminates the five percent. But inhibiting that antibody recycling process with FcRn inhibitors dramatically reduces the amount of circulating antibody and in a sense can be considered similar to plasmapheresis. And so patients—the ones that respond—can do very well on this drug.

Going to the next step, there are agents in earlier trials and in development that are going to try to target specifically the pathological antibody-producing cells, and I think that's what I'm most excited about—seeing, in the future, how well we can eliminate those. The past decade has really been remarkable in the history of myasthenia. There's never been this much therapeutic development, so that's just very cool.

We still have a long way to go in treatment of myasthenia. We don't have a treatment that really restores the immune system back to

normal and eliminates myasthenia. We've demonstrated in clinical trials some level of efficacy. Patients are improved, but they're not back to normal. There continues to be an unmet need, and we still have to learn in common clinical practice how we use these agents on an individual patient basis. Once you peel the onion, there's more peels to pull back, and so that's where we are in the field of myasthenia gravis.

Announcer:
That was Dr. Henry Kaminski talking about advancements in the treatment of generalized myasthenia gravis. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!