Transcript Details

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Rozanolixizumab for Myasthenia Gravis: An Alternative to Corticosteroids

Announcer:
You're listening to *NeuroFrontiers* on ReachMD. On this episode, Dr. Gil Wolfe will discuss rozanolixizumab as a treatment for generalized myasthenia gravis, or gMG. Dr. Wolfe is a SUNY Distinguished Professor of Neurology at the University at Buffalo Jacobs School of Medicine & Biomedical Sciences. Let's hear from him now.

Dr. Wolfe:
Rozanolixizumab is one of quite a few molecules—but only one of two that are approved at this point in time—that are neonatal Fc receptor antagonists. So the neonatal Fc receptor, which is also designated as FcRn, is a receptor that helps salvage IgG. So the half-life of the immunoglobulins are quite different one from the other. IgG is by far the longest—about three weeks because it is salvaged through these receptors. If there is not binding of IgG to this neonatal Fc receptor in these vesicles in the cell, then it ends up going into a pathway of degradation through lysosomes. But if it is binding the IgG—and this is true of IgG1 through IgG4—in an acidic environment in these vesicles, it then gets salvaged back into circulation. So again, IgG half-life is about three weeks, whereas for, say, IgA or IgM, you're talking about four or five days.

If you have a molecule like rozanolixizumab that competitively targets and binds to that neonatal Fc receptor and prevents IgG binding, you're going to send IgG into that degradation pathway, and that's what this does. And so it floods the system, binds to the neonatal Fc receptor, and prevents this IgG recycling. As a result, you have a marked quick reduction in IgG in a matter of days. By a week or two, you see 60, 70, and over time, 80 percent reductions in IgG pretty much across the board. IgG4 is a little bit less, but it's still markedly reduced.

Rozanolixizumab was the second molecule approved by the FDA. It's the first full IgG molecule that was approved by the FDA for generalized myasthenia gravis.

We have five targeted therapies—five different molecules—that have now been approved for generalized MG. We have no head-to-head studies. It is really hard because the populations were somewhat different, especially for eculizumab, because they required a refractory nature before patients were allowed to enter the study. But it's really hard to make comparisons. They all are generally in the same ballpark.

Corticosteroids work pretty quickly in MG, but these newer agents, including rozanolixizumab, probably do work somewhat faster. Obviously, corticosteroids are very inexpensive. You can deliver them a variety of ways, including by mouth. All of these targeted therapies require a needle in some fashion. Rozanolixizumab specifically is a Sub-Q infusion. It's quick—a matter of 10, 15 minutes—and it's done weekly. So it's quite quick, but you don't have an oral delivery system for any of these new targeted therapies. They spare the types of side effects that we see with corticosteroids, which are well known and are very significant, especially when you get to even relatively what we would say moderate doses of, say, prednisone or prednisolone. When you look at the studies, there hasn't been a real significant increase in infections. You might see a slight uptick in upper respiratory infections, upper urinary tract infections, and the like. There have not been a whole host of opportunistic-type infections. Again, it's only reducing IgG. The rest of your immune system is remaining active.

Not all of the trials, but several of them, have clearly shown quality of life improves in patients on these agents. What other benefits could we see? When you really don't want to use corticosteroids—and there's a lot of patient groups where that really is problematic—these agents can come into play. There is a series of patients showing that these drugs can work quite well in patients in myasthenic crisis. I think plasma exchange is getting harder and harder to access in many hospital systems. It's a big deal. It generally requires

large-bore catheters and a specialized staff. Sometimes it's not available on weekends and all these kinds of things. These drugs could help us in that very scenario, and according to the case reports, are already doing that.

Announcer:
That was Dr. Gil Wolfe talking about rozanolixizumab as a treatment for 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!