

## **Transcript Details**

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New Frontiers in CIDP Care: Exploring Approved and Emerging Therapies

#### Mr. Quigley:

You're listening to *On the Frontlines of CIDP* on ReachMD. I'm Ryan Quigley, and today I'm sitting down with Dr. Chafic Karam to discuss new therapeutic developments for chronic inflammatory demyelinating polyradiculoneuropathy, or CIDP. Dr. Karam is a Professor of Clinical Neurology and Chief of the Neuromuscular Division at the University of Pennsylvania. Dr. Karam, it's a pleasure having you on the program today.

#### Dr. Karam:

Thank you for having me, Ryan.

#### Mr. Quigley:

Now, to start us off, Dr. Karam, how has the therapeutic landscape for CIDP evolved in recent years?

#### Dr. Karam:

Things have progressed. For a long time we had mainly three options, which were steroids, immunoglobulin intravenous, and plasma exchange. These were the more traditional treatments. There's clinical trials supporting their efficacy, and they are recommended as a first-line therapy by the EAN and PNS societies—by the experts.

More recently, subcutaneous immunoglobulin became more widely available, used, and approved in the United States for maintenance therapy in CIDP. So basically, you have people who you start on IVIg, they respond to IVIg after the induction, and now you want to maintain their function. So you can transition to SubQ Ig, which is very helpful because some people may have venous access issues, and instead of putting a port, you can do the immunoglobulin subcutaneous. So that was a welcome addition.

There's two products that are approved by the FDA, but more recently, we have the efgartigimod, which is an FcRn that was very successful in the management of patients with myasthenia and then was studied in CIDP and was also found to be superior against placebo in maintaining the function as well. So because of that, it was approved by the FDA. The challenge is that, first, it's new, so we don't really have a lot of experience with it. Two, it is very specific against IgG. So it lowers the IgG levels. And in some patients with CIDP, now we know the underlying pathophysiology is driven by the IgG, but some other may be driven by IgM or other factors, cells, complement, etc. And in those patients, you don't really expect reaction or improvement.

So this is what's going on right now and what's FDA approved, but there are other medications that are being tested for CIDP. One that seems to be the most advanced at this time is complement inhibition. So following in the steps of myasthenia gravis, if you will, they tried complement, which helped in a lot of refractory myasthenic. And then FcRn is what we're doing in CIDP. It seems that we've tried FcRn. One of them worked. They tried the other one, which didn't work, but that study was flawed, so we don't know. And now, with the complement, we have multiple companies also looking at the role of complement in both refractory CIDP and as a head-to-head comparison against IVIg.

### Mr. Quigley:

Yeah, there's certainly a lot of activity going on in this realm right now. And you actually just spoke on this moment ago, but in particular, what can you tell us about subcutaneous immunoglobulin with enhanced absorption?

### Dr. Karam:

The other way to administer the immunoglobulin instead of IV, which has its limitations—meaning that if a patient has difficult veins or if they had the disease for a long time and this is a chronic disease—most people don't go into remission, so they need maintenance

therapy for a long time—eventually, you would lose access to veins. What we used to do in the past would be, if you want to continue with immunoglobulin, you would put a port, which kind of is an invasive procedure, and people sometimes don't like to do that. And it can get thrombosed and can get infected, so we don't really see that very often, but these are possibilities. And when the subcutaneous Ig became available, it was really welcomed because for these patients, you have an option that doesn't involve putting a port.

You could potentially have less side effects with subcutaneous Ig because technically, you have a slower diffusion into the bloodstream. So people have really bad headache or nausea—they could have less side effects. It does offer more flexibility, so people who want to do it on their own time, they don't want to have a nurse involved, or they don't want to go to the infusion center—that could also be something welcomed with the SubQ Ig because usually, these are done by the patient on their own. So they do it under the skin, and depending on which drug you're using, you can do multiple sites at a time, etc. So these were obviously welcome.

## Mr. Quigley:

Now, in regard to the immunoglobulin, what patients would be ideal candidates for this therapy, and how should we approach that decision-making?

#### Dr. Karam:

We know that immunoglobulin works, and it works on most patients, so we always tell our trainees that if a patient doesn't respond to Ig, you have to think about two things. One, do you have the correct diagnosis? And two, do you have the correct dose? Typically, people do respond to Ig. You do have about 15 to maybe 20 percent who don't respond to Ig, and in those patients, you have to consider an alternative therapy.

Who qualifies for it? Basically, you can consider it in any patient. The major issue is the potential of headache and nausea. Sometimes people get rash, and very rarely, you can have a blood clot with this, which obviously is a very concerning thing because it could be something relatively more benign, like a deep venous thrombosis in the leg, but it could lead to a pulmonary embolism or stroke. So obviously, serious complications—less than 5 percent, but definite—and we've seen it in our patients. One way to try to overcome this is to slow down the infusion rate, and that usually can help a little bit with reducing that risk.

### Mr. Quigley:

For those just tuning in, you're listening to *On the Front Lines of CIDP* on ReachMD. I'm Ryan Quigley, and I'm speaking with Dr. Chafic Karam about recent developments in CIDP care.

So, Dr. Karam, if we continue to explore these new therapeutic avenues, what can you tell us about FcRn inhibition?

#### Dr. Karam:

The trial with efgartigimod was a positive trial. The design of that trial was special. So they started with everybody getting the drug first, and those who do respond to the drug are transitioned to a double-blind phase where the drug would be either withdrawn and they would be given placebo or they would continue with the drug. So that way of doing the trial causes a little bit of difficulties on how to interpret and how to apply this in clinical practice. Plus, we don't know compared to IVIg or steroids whether it is the same efficacy, better efficacy, or less efficacious.

So we know that the drug works, but we don't know how it works compared to our traditional medication. And obviously, because it only targets IgG, it may not affect other subtypes of CIDP that are driven by, let's say, IgM or cell or anything else where we know IVIg or steroids or plasma exchange even can work. So probably you're going to be targeting a smaller population of patients, but on the other hand, in those that are driven by IgG, you may have better efficacy, hypothetically speaking. And two, it is much more easier than IVIg. It's an injection under the skin that takes about 90 seconds, and you do it every week. So convenience-wise, it's way better than IVIg or subcutaneous Ig. It's quicker, less side effects, and now they also have an autoinjector, so the patient will be able to do them on their own instead of having a nurse or going to the fusion center to do the infusion. So there's definitely some benefit with the FcRn. The trial helped us understand that a good number of patients also are driven by IgG, which is also helpful because we don't really have a way to test commercially for antibodies in CIDP, and unfortunately, we don't know how we can tell if a patient is going to respond or not.

#### Mr. Quigley:

Now, as we approach the end of our program, Dr. Karam, I have one last question for you. How should clinicians approach shared decision-making when considering these newer treatment options for patients with CIDP?

#### Dr. Karam:

That's a key way to approach this because if you don't have a lot of experience with drugs, you don't know how people are going to react. You want to inform the patient that we're trying this and it's a trial and error. Unfortunately, we have no way to predict who's going to respond to which drug, and you're going to have to try one and see if it works, and if it doesn't, then you can transition to something

else. So, obviously, in milder cases that are very slowly progressive, you do have that option, but in more acute phases or acute disease that result in sometimes people in a wheelchair or are rapidly progressive, you don't really have that option. So you have to make bigger decisions. You may have to go a more traditional route and explore the newer drug at the later time.

## Mr. Quigley:

And with those key takeaways in mind, I want to thank my guest, Dr. Chafic Karam, for joining me to discuss what's new in CIDP treatment.

Dr. Karam, it was great having you on the program today.

# Dr. Karam:

Thank you very much for having me, Ryan.

## Mr. Quigley:

For ReachMD, I'm Ryan Quigley. To access this and other episodes in our series, visit *On the Frontlines of CIDP* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.