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Target Locked in gMG: Why T2T Matters

Dr. Wolfe:

Hello, this is CE on ReachMD, and I'm Dr. Gil Wolfe.

Joining me today is Dr. Christyn Edmundson.

Generalized myasthenia gravis is a chronic, unpredictable disease in which even low levels of ongoing activity can significantly affect function and quality of life. Yet historically, especially prior to the 2010s, treatment decisions in gMG have often focused on short-term symptom control rather than clearly defined long-term goals. Today, that approach is evolving.

With a deeper understanding of generalized MG pathophysiology and the availability of targeted therapies, we now have the opportunity to move toward a treat-to-target strategy, one that emphasizes measurable outcomes, timely reassessment, and individualized care.

Why is it important that we move beyond vague symptom control in gMG and toward clearly defined treatment targets?

Dr. Edmundson:

So that's a great question, Dr. Wolfe. And in this specific case, treat-to-target in generalized myasthenia gravis really means aiming to manage our patients' symptoms with certain prespecified outcomes in mind. In myasthenia gravis, a couple of different outcomes are sometimes used. We'll sometimes talk about complete stable remission, which is someone who has had myasthenia in the past but now has no symptoms of myasthenia and is off all therapy. Obviously, this is a great goal, but not necessarily a realistic one for many of our patients.

There's also pharmacologic remission, which is someone who doesn't have any symptoms or exam findings of myasthenia gravis but remains on myasthenia therapy. Also, it is wonderful to get patients to this target, but not possible for all patients.

More recently in the field, we've used a couple of other targets. The first is called minimal manifestation status in myasthenia gravis, and that describes a patient who typically is on myasthenia therapy and who has no symptoms from myasthenia gravis on a day-to-day basis, but on close neurologic examination does have some findings that suggest the presence of myasthenia gravis.

So essentially, some mild exam findings, but asymptomatic on a day-to-day basis.

And then lastly, we'll sometimes use minimal symptom expression as a target. In minimal symptom expression, patients may have an MG-ADL score of 0 or 1, meaning they either have no or minimal symptoms on a day-to-day basis and may also have some myasthenia gravis findings on exam. Any of these are considered highly desirable outcomes where patients, on whatever therapy they're using, are really minimally affected by their disease on a day-to-day basis.

One of the things that it's important to highlight is that using a target like this can help really push therapy forward for a patient. So, rather than sort of letting a patient linger with a lot of ongoing symptoms that are impacting their day-to-day life, keeping this sort of treat-to-target approach in mind, allowing for escalation in therapy in a way that can bring a patient's symptoms under control more rapidly, avoiding things like high steroid exposure, avoiding the risk of myasthenic crisis, and avoiding the sort of cumulative neuromuscular junction damage that can occur in prolonged uncontrolled myasthenia gravis.

And I have a question for you, Dr. Wolfe. Do you think that setting a target changes the way that patients engage in their care? And if so, why or why not?

Dr. Wolfe:

Oh, I think it does. I mean, you mentioned the minimal symptom expression, and a lot of our patients do have familiarity filling out the MG-ADL form. We've had good success, of late, reaching minimal manifestation status that you spoke about earlier, including patients with gMG. An issue, however, and this is demonstrated in largely retrospective studies that have looked at ultimate outcomes, it could take a good amount of time with conventional therapy, sometimes several years, for patients to reach the minimal manifestation status outcome. I would also mention that in the future, the desired outcome may change from MMS, which is widely applied to the minimal symptom expression outcome, which is readily measurable. It's just a score using the MG-ADL.

What makes this the right moment, would you say, Dr. Edmundson, to add target-driven care in addition to symptoms in gMG?

Dr. Edmundson:

Yeah. So, I would say the biggest thing is that over the last 5 to 10 years, we've seen a really fantastic expansion in the kinds of therapies that are available to treat myasthenia gravis. We now have newer targeted therapies, many of which have sort of a more rapid response time to clinical effect, which allows us to get patients under control more quickly with some of the agents available. So, setting that rapid control, that treat-to-target approach, is more feasible now than it ever was before.

There's also been a shift from the idea of using really broad immune suppression to more mechanism-targeted care. So, I think that this also contributes to making this a good time to really set goals for patients, knowing that we have more targeted agents that can really focus on individual parts of the immune system.

As we use this treat-to-target approach, it really is important to be familiar with some of the outcome measures that we use, some that we've referenced before, the MG-ADL, as well as things like the QMG and MG-QoL15r, which can help us measure our patients' responses over time.

Dr. Wolfe:

Well, this has been a great bite-sized discussion. Our time is up. Thanks for listening.