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Generalized Myasthenia Gravis: Inside the MINT Trial and CD19 B-Cell Therapy Advances

Welcome to Neuro Frontiers, a series in which Practical Neurology partners with ReachMD to bring you clinical research and advancements that further clinicians' ability to diagnose and treat neurologic conditions. In this episode, Dr. Richard Nowak, professor of neurology at Yale University, discusses the phase three MINT trial, highlighting the efficacy and safety of CD19-targeted B-cell therapy for individuals with generalized myasthenia gravis and its impact on outcomes and steroid reduction in real-world practice.

Hello, everyone. I'm Joe Rusko. I'm the editor-in-chief of Practical Neurology, and it's my pleasure to chat with Dr. Richard Nowak today. Dr. Nowak, please introduce yourself.

So thanks so much for the invitation and the opportunity to have a conversation with you today. I'm Dr. Nowak, from the Yale School of Medicine.

I'm an associate professor of neurology of the study and treatment of patients with autoimmune neuromuscular conditions, including myasthenia.

Excellent. Wanted to talk to you about the MINT study and those study results, and in particular, why targeting CD19 positive B cells is a worthwhile effort.

It's well understood that B cells are integral to the pathogenesis of myasthenia gravis. B cells, in fact, are the factories of antibody production, including autoantibody production. As B cells mature, they start to lose certain, proteins on their cell surface. CD19 continues to be expressed on certain key pathogenic, B cells that produce autoantibodies, including plasmablasts and plasma cells.

Learnings from our prior work in looking at CD20 B-cell depletion therapy, specifically rituximab and a futility study, that we did, called BeatMG, where we declared futility with the use of rituximab in the treatment of generalized myasthenia gravis, particularly those with AchR. Led us to actually examine whether or not we were effectively, efficiently targeting the drivers to autoantibody production and pathogenic autoantibody production in the case of generalized myasthenia gravis.

So the phase three myasthenia gravis inebilizumab trial actually came from learnings from our prior study with rituximab. CD19 B-cell depletion therapy made good sense for us to examine in the setting of an efficacy trial and a safety trial.

Excellent.

Can you tell us a little bit about the enrolled population in this study and how that differs or aligns with the types of patients seen in an everyday neuromuscular practice?

Absolutely. So we enrolled patients with generalized myasthenia gravis, and particularly those with either AchR antibody or MuSK autoantibody-positive disease, and that accounts for approximately eighty-five to up to ninety percent of all patients with generalized myasthenia gravis. The majority of patients with generalized myasthenia gravis would have been eligible to enroll, so long as they also had active disease.

So the patients enrolled were required to have an MGFA clinical classification at time of enrollment between two and four. And also similar to many of the other registrational trials that have been completed to date, they did also have a requirement on active disease. In this case, that was specified as an ADL score of six or higher and a QMG score of eleven or higher.

Again, very much consistent with other clinical trials examining efficacy and safety in individuals with generalized myasthenia gravis. The other thing that aligns with many of the other clinical trials out there is patients could be also on some baseline therapy in- including

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things like baseline corticosteroids or prednisone, as well as some other non-steroidal immunosuppressive therapies.

Again, this is not necessarily a treatment-naive patient population, but a patient population that is very much reflective of what we see in clinical practice. Again, these are patients with generalized myasthenia gravis, as noted, and those with a certain degree of active symptoms somewhere in the mild, moderate to severe range.

Thank you for that. So the study met its primary endpoint in at week twenty-six in terms of some measurements like MG-ADL as well as QMG results. How do you interpret those efficacy signals, and which ones are most clinically meaningful, for a neurologist? Much of the current therapeutic landscape and the clinical trials, that have been completed to date have adopted the use of the MG-ADL score as its primary endpoint.

This is a patient-reported clinical outcome measure typically recommended as a primary endpoint by the FDA. I can't think of any trials in phase three that have not used the MG-ADL, scale. It is reflective of how a patient is doing in terms of patient-reported symptoms, some of which are specific to their condition, such as double vision, eyelid droop, difficulty with chewing, swallowing, weakness in their extremities, for instance, a-among other symptoms.

And we, looked conventionally at a change in the score at week twenty-six compared to baseline and compared that to the treatment arm versus placebo. And as you mentioned, we met the primary endpoint demonstrating a statistically significant difference and greater reductions in MG-ADL score in the inebilizumab population as compared to placebo.

What I will point out here is that MINT is unique in that it differs also from other clinical trials where there was a forced steroid taper that began at week four. It was protocol specified, so patients enrolled in the study were required to reduce or taper their prednisone dose to, five milligrams or less by week twenty-four.

So not only are we observing a clinical, benefit that's greater in the inebilizumab population as compared to placebo, but also participants were able to reduce their corticosteroid dose during the course of the clinical trial. It's very nuanced there because one might say, “If you didn't do that, would you have observed greater differences in the treatment group versus the placebo?"

And the answer is we don't know. The trial was designed to what we would do in clinical practice. So as many of my colleagues know that are treating patients with autoimmune conditions, including myasthenia gravis, once we start a new treatment in those that are on some amount of corticosteroids, we want to lower the prednisone dose.

And we typically start that at some period of time after a new treatment is initiated. In this case, we started four weeks later, a month later, and we wanted to do what we would do in clinical practice. We felt that it was critically important to do in that, in maintaining moderate to high doses of corticosteroids during the course of a six-month-plus RCP was not what we would wanna do and not what we would typically do in clinical practice.

We felt that was important, and it was built into our clinical trial here. The other things that I will mention, we also not only looked at patient-reported outcomes, but a standard of physician-reported outcomes like the QMG. So the QMG also demonstrated a statistically significant difference compared to the placebo group at week twenty-six in the combined study population.

And, certain other key, secondary outcome measures were, met in terms of their statistical significance, including a change in ADL scores, for instance, in the ACHR and, MUSK subpopulations when we did the subgroup analyses. And that's detailed very clearly in our initial report, which was published in The New England Journal of Medicine in, twenty twenty-five.

Excellent. Appreciate that. What about some of the adverse effects seen in this trial?

In terms of adverse events and safety profile, we didn't find any significant concerns or signals. The most frequent AEs with inebilizumab were things like COVID-19, headache, cough, nasopharyngitis, infusion-related reactions, and UTIs.

Again, we observed this in the placebo group. These were slightly more frequent in the inebilizumab group, but not of great concern. And again, I will point out the trial for the most part was done during the early years of the COVID-19 pandemic, so it's not unusual that we would have observed these.

But no great concerns, and very much in line with the safety profile and adverse event, events observed in the NMOSD and IgG4-related disease clinical trials. Very good and well-tolerated, overall. I would refer my colleagues certainly to the primary manuscript and the package insert, to review in more detail the AEs and safety profile.

So in addition to our primary, readout, which was at week twenty-six for the combined study population, which included both the ACHR and the MUSS groups, and in addition to us looking at week twenty-six, the ACHR and MUSS groups, separately as some of our key secondary outcome measures, the randomized control period went out to fifty-two weeks for the ACHR subpopulation.

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And we did that primarily because we weren't sure whether or not response in the ACHR group was going to be quick or a little bit longer in, in time to observation. So in our fifty-two week data, when we looked at the ACHR subpopulation, we're seeing greater improvements over time compared to week 26.

That's number one. Number two, what was encouraging by us looking at the 52-week data for the ACHR is that there is a sustained effect or a durability of response, that's observed. So not only are patients observed to get better within the six-month or 26-week RCP for the combined study population, when we look out to essentially a year, we're seeing that response is sustained, but also greater responses, over time.

And that would be consistent with the mechanism of action of inebilizumab. Again, this is a CD19 B-cell-directed therapy targeting the factories of autoantibody production. So we wouldn't expect necessarily that there would be an immediate benefit within a week or two or three, but rather that the response would be further along.

That said, we would also expect, based on the mechanism of action, that if you're really targeting upstream drivers to immunopathogenesis, that there would be a sustained response, but also greater responses over time. So the 52-week RCP was critical in us sort of examining that. But to further that sort of thought process, participants were eligible to enroll in an open label period or an open label extension that went up to three years.

Anyone that completed the RCP was eligible for that. And, uh, later this year, we'll have available our first cut at OLP data looking at participants that went a year into their, uh, open label extension study period. So those, those data are forthcoming and likely to present it at an upcoming conference later this year.

So more to come and quite a lot of learnings I think that we'll have from the open label extension period. So the RCP has provided an answer to a fundamental and critically important question. Number one, is CD19 B-cell-directed therapy effective? And the answer is we could say yes based on the pre-specified, uh, efficacy measures that we have.

Number two, is it safe and tolerable in the generalized myasthenia gravis population? And the answer is yes, we could say that. Not only can we say that for generalized myasthenia, but we could say that for both ACHR and MUS groups that it demonstrated efficacy in, uh, safety and tolerability. That, that, through its recent approval back in, uh, December 2025 for the use for our patients.

My general sense is that this offers, uh, an additional therapeutic option for our patients, and it's first in class for patients with a generalized myasthenia gravis. There's no other anti-CD19-directed B-cell therapy for patients with generalized myasthenia gravis approved by the FDA at this time.

So it certainly offers advantages. The other is if you think about the therapeutic burden of, of treatments for our patients, this is a medication that's given, uh, twice a year, so every six months, uh, compared to some others. So it also has some advantages from the perspective of therapeutic burden, and I think those are relevant in evaluating for patients and my colleagues in selecting the treatment for, for our patients.

I think so. I, many of us, uh, can have quite busy schedules, and you're juggling work. You're juggling taking care of kids. You're juggling a lot of things, and so having something that's convenient, that's less often has certain advantages. For instance, if they have to go or have to have an infusion or injection quite frequently.

It can be very impactful. We don't think about these, especially if you don't have options. If you have only one option or two options, and that's what it is, that's just what it is. But in a landscape that has become quite full of options, it's also nice to have an option that is convenient.

Not that that's the main reason to consider, because I think the main reason here to consider is what is an agent doing, what is it targeting, and how well is it working for patients with generalized myasthenia gravis? But it is something that I think patients factor into to deciding on what option is best for them.

And I think that's where medication options and having a, a variety available, come into play.

Thank you, doctor, for sharing your knowledge in this episode of Neuro Frontiers, and thanks to you, our listeners. NeuroFrontiers is brought to you by the editors of Practical Neurology. Be sure to visit practicalneurology.com for more podcasts in the field of neurology.

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