

Chilvana Patel:

Hello everyone. Welcome. This is Chilvana Patel. I'm a Professor of Neurology at University of Texas Medical Branch Galveston and I'm a neuromuscular expert. Today I am co-hosting a session with Dr. Sanka. I will give Dr. Sanka a chance to introduce herself.

Ratna Bhavaraju-Sanka:

Hello everybody, and welcome to this program. My name is Ratna Bhavaraju-Sanka. I'm an Associate Professor of Neurology at UT Health in San Antonio, and the Chief of the Division of Neuromuscular Disorders in San Antonio.

Chilvana Patel:

I have no disclosures.

Ratna Bhavaraju-Sanka:

Yeah. And here you see the disclosures. I do have disclosures. I'm a consultant with Argenx and Amgen. And you can also see the learning objectives of this program. This program is being sponsored by a educational grant from Argenx and UCB, and you can review the learning objectives in this slide.

Chilvana Patel:

So today, we are going to discuss about updates in the field of myasthenia gravis. It has been exciting time in this world. The AAN 2026 meeting featured a remarkable number of important updates ranging from new analysis of approved therapies to promising late stage clinical trials and real world experience as well as the healthcare utilization. So we will be discussing these updates and providing you some important clinical pearls that we can utilize in our practice.

Ratna Bhavaraju-Sanka:

Thank you, Chilvana. And again, I'm going to start with some of the existing approved medications in the world of myasthenia gravis and some new indications that were presented at the meeting in Chicago in 2026. First, let's talk about efgartigimod, the FcRn inhibitor. There was data presented on the ADAPT trial that was ongoing open label extension of the subcutaneous efgartigimod. And as expected, we did see that long-term efficacy and safety profile of this medication was shown in this data.

But the other newer data that is a little bit more exciting is the ADAPT NXT trial that was looking at different dosing formats. We all know that the initial ADAPT trials used this four weekly doses followed by a four-week inter treatment interval and the re-initiation of therapy based on the symptoms that the patients were noticing. But in this ADAPT NXT trial, they did try every two-week dosing and some of the patients were also moved to every three-week dosing and it still showed that there was sustained benefits in these dosing periods with similar symptoms or side effect protocols.

So I think basically what we see that there are multiple ways of utilizing the efgartigimod sub-Q, and even at every two weeks dosing or every three weeks dosing, we did see sustained efficacy with minimal symptom expression and good tolerability in the medications. Chilvana, do you want to add anything about the ADAPT or the ADAPT NXT trials?

Chilvana Patel:

I think it gives the clinician flexibility to Q2 to Q3 regimen, which might be also improved the compliance for the patient and flexibility as long as it also shown that there is efficacy and safety same time maintained here.

Ratna Bhavaraju-Sanka:

Right, and that's what some of the clinical in the clinics, what we see is these patients are wearing off in the inter-treatment period, and this is a good alternative way of dosing for sustained efficacy in these patients.

The next trial that was really important in my perspective was the ocular myasthenia trial that actually looked at efgartigimod for ocular only myasthenia, and this is a gap in the care because there are not any approved therapies. And I think the preliminary data does suggest that it is helpful in ocular MG, and this is for both seronegative and seropositive patients. And the other interesting part of this trial is this is the first trial that I can think about that used the MG Impairment Index that has a six-point ocular screening, which is based on both patient reported outcomes, and some examination. So this is a new index that we can utilize, especially when using MG-ADL, the amount of scores we get in the ocular subcategory are limited that can prevent us from evaluating improvements. So that's an interesting part of this trial.

The other efgartigimod trial was the seronegative. And again, a big gap in what we see in the clinical care because there's not any approved treatment in the new data that did show that seronegative patients do respond to efgartigimod, and this has actually led to the approval of efgartigimod in this population. So Chilvana, what do you think about this data on the seronegative?

Chilvana Patel:

So if I have to be honest, I would see that the paradigm of myasthenia treatment landscape is changing. Typically, so far we have always focused on the antibody positivity and type of the antibody and depending on the treatments were offered. What I'm seeing is now we are switching to a more clinical phenotype, something like ocular myasthenia gravis or something more towards seronegative. Yes, we have done much better with identifying myasthenia gravis with antibody diagnostic sensitivity improvement, but there is still about 3% to 5% of patients who still remain seronegative, and I think this is something to offer to them. So I think there is a paradigm shift in treatment options for these patients changing more towards focus on more clinical phenotype rather than an antibody status. That's what I think. Thanks.

Ratna Bhavaraju-Sanka:

Yeah. Again, I think when it first got approved, there was an increased interest among our patient population who had always been waiting for an approved medication from the FDA. So the other interesting data that we will be looking forward to is the utilization of efgartigimod in patients with juvenile or childhood onset autoimmune myasthenia gravis, so they're looking at both the juvenile and the childhood cohorts. And I think the juvenile cohort so far, the data is showing that it has similar efficacy and side effect profile as in the adult efgartigimod data that we have seen. So hopefully more to come in this, again, another unmet need of juvenile myasthenia gravis, and more data to be looking forward to in the childhood onset autoimmune myasthenia gravis. So that is exciting data about efgartigimod. Now, Chilvana, you want to review some of the other existing medications that were presented at the meeting?

Chilvana Patel:

Thank you, Dr. Sanka. Excellent review for all efgartigimod therapeutic indications. I'm just going to change the gears here and I'm going to start my talk with the RAISE extension trial, which has an open level extension of our standard RAISE trial, which was placebo controlled trial for generalized myasthenia gravis who were acetylcholine receptor positive patient population, and they utilized zilucoplan subcutaneous. As we know that zilucoplan is C5 complement inhibitor, and this open-label extension was 120 weeks, and patients who received zilucoplan or placebo, they were both enrolled in this open-label extension here.

The outcome showed that about 61% patient initially on zilucoplan and about 64% patients who were on placebo achieved MSE, which is Minimum Symptom Expression state, during this period of time. And those who achieved, from that, most of them maintain about 80% of time of MSE during the 120 weeks. So again, I think this points more towards that durable downstream complement inhibition with C5 blockage on acetylcholine receptor positive generalized myasthenia gravis patients. So rather than just the one-time achieving MSE, it is more sustained clinical response. I think that's what I understand from this trial. However, there are 97% of patients do experience treatment-related adverse events. However, they're mild to moderate. So again, there is no major red flag, but it's a good downstream durable response with the zilucoplan.

The other trial which was presented was Vivacity with use of nipocalimab. So again, as we know, nipocalimab is anti-FcRn monoclonal antibody. This was a phase three placebo controlled double-blinded trial. And the patient included in this group was antibody-positive, acetylcholine receptor positive, LRP positive, and MuSK positive patient groups were included. The duration of trial was somewhere about 24 weeks. And what this trial showed that the patient who were treated with nipocalimab, 31% of those patients received MSE compared to 14% in placebo. And those who achieved MSE, 19.5%, so roughly about 20% of patient maintained MSE, which is sustained MSE, which is at least more than eight weeks.

And I think that was an important clinical outpost because it was later translated that the patient who achieved significant sustained MSE actually translated to have a better quality of life scale shown on MG-QOL15r. So I think that would be something important as a future clinical trials too, rather than just once achieving MSE, more focused on sustained MSE because it definitely translated to improved quality of life here. What are your thoughts about it, Dr. Sanka, about these two trials?

Ratna Bhavaraju-Sanka:

Yeah, I think again, as expected, we are seeing sustained improvements in these, and durability is really important for our patient population because the disease control is important for quality of life. And so I think durability and as we've seen in this nipocalimab trial that sustained minimal symptom expression can lead to improvement in quality of life, so I think that's good data to show for keeping these patients on medications for the sustained efficacy.

Chilvana Patel:

I also want to add MINT trial with inebilizumab. And I think this trial brings two important clinical points. So typically, we have utilized in the past for myasthenia gravis patient rituximab, which was targeting anti-CD20 B cells. Inebilizumab is a novel mechanism of action, it is targeting upstream B cell CD19. So it has a broader B cell target population affecting memory cell and mature B cells, but also including plasmablast and some of the plasma cells. So that was a novel mechanism.

And second, during this trial design, they used strict rigorous steroid taper protocol. So the patient were tried to reduce their daily dose of prednisone five milligram or less during the period of time. So this was, again, 52-week trial and it was phase three placebo controlled double-blinded trial. Patients were

offered placebo versus inebilizumab. The dosing was done either on standard dosing with day one, day 15, and somewhere around six months around 183 days. The patients were on median dose of prednisone anywhere from 15 to 20 milligram in both inebilizumab group as well as the placebo group. And by 26 weeks, about 87% patients from the inebilizumab group and 84% patient from the placebo group reached to the level of prednisone five milligram or less.

The outcome of this trial showed that there is improvement in MG-ADL score. There's improvement in QMG score also. CD20 positive B cell reduction, about 93% were achieved within two weeks and it was maintained throughout the trial. And then anti-drug antibodies were minimum only seen in 4.2%. So with all this data, I think it gives us two important point that this was an example of upstream B cell depletion strategies in patient with myasthenia gravis. And second, patient maintained clinical improvement while on this treatment, particularly when we try to taper off the steroids. So I think this were promising that we can taper off the patients from the steroids, and avoid long-term steroid-related side effects.

Ratna Bhavaraju-Sanka:

I agree. I think this is probably the first myasthenia trial where a steroid taper was included as an endpoint, and it showed that though both placebo and the inebilizumab group were able to taper the steroids, the inebilizumab group had improvements in their MG-ADLs and QMG even with the steroid taper. And knowing the long-term side effects of these steroids, this is something all of our patients or most of us want for our patients is ability to reduce the dose of steroids to reduce the long-term side effects.

So I think these are all exciting data showing that what we have available in the market for myasthenia do produce sustained improvements and are being well tolerated. And some of these also are looking at newer indications, especially the seronegative and the ocular myasthenia gravis patient population, and they may be effective in these populations also.

So I think now, we'll move on to what is in the horizon, right? We are all looking forward to some more newer therapies and newer treatments. And I think what we have coming up in the horizon are also looking at patients who are refractory myasthenics. These are our hard to control patients that we are always worried about and that keep us up at night. So the ones that I want to focus on are the two CAR T trials, the chimeric antigen receptor T cell therapy trials, both. The presentations were based on CD19 CAR T therapies, but they did utilize different, the marker for the identification of the antibody.

So again, the first one is the rese-cel, or I know they have longer names, so I'm going to try to spell it correctly. Resecabtagene autoleucel or the rese-cel CD19 CAR T therapy. And here, as I mentioned before, the co-stimulator is 4-1BB. And from my education from the oncology group, the 4-1BB co-stimulant has a lower risk of ICANS and the CRS. So they looked at both antibody-positive AChR antibody-positive and antibody-negative patients. And this was a single dose of the CAR-T therapy. All these patients had to be preconditioned with lymphodepletion therapies.

And so far, early results do show that one patient achieved MSE from MG-ADL 17 to zero, and the second patient did have a 50% drop in MG-ADL and just with a single dose of the CD19 CAR T therapy. And they also noticed that the B cell depletion was achieved by day eight. And there was one grade two CRS, no ICANS. So, so far potentially safe and effective immune reset option with these CAR-T therapies with a single dose. So that's the exciting part, and this study is fully enrolled and we are awaiting some more data to see if this is something we can look forward to for our refractory patients.

The second CAR-T therapy that they presented on was the KYV-101. Again, this is also a CD19 CAR-T therapy and they utilized it in refractory myasthenia, and they utilized it in AChR and MuSK-positive

myasthenics here. And even this here, the co-stimulation is CD28-based co-stimulation, and that is the difference between the last rese-cel and this CAR-T therapy.

Here again, they utilized refractory myasthenics and no eye cancer CRF, so a good safety profile. And it did show that of the six dosed, 100% achieved a three-point improvement in MG-ADL, and half of them achieved MSE. And five of the six patients enrolled were able to come off their immunosuppressive medication, so exciting data. And again, just single dose of medication causing long-term benefits and improvements and showing that it is safe. So we are evading more data from phase two, and then there's also a phase three trial ongoing with these two CAR T therapies. So other newer therapies you want to highlight, Dr. Patel?

Chilvana Patel:

Yeah, I think as you mentioned, there are so many newer therapies coming currently, so I think I'm going to add pre-well trial, which is a phase three trial using gefurulumab. So again, it's a novel agent, particularly it is a dual anti-C5 binding nanobody. So the interesting part of this agent is that it is a smaller in size, so it has a better tissue penetration. So it allows weekly administration subcutaneous rather than daily. So I think that gives a patient a flexibility. I think that was the initial concept when it was introduced.

Again, the study included acetylcholine receptor positive generalized myasthenia gravis patients. Study was about 26 placebo-controlled one-to-one subcutaneous self-administered injections given in gefurulumab group. The data, the outcome in the form, it shows that there is improvement in MG-ADL, QMG, MG composite score, and the improvement in MG-ADLs is seen by the first week. So again, the safety profile was similar to placebo, and there were no meningococcal infections are seen during this trial so far. So again, it points towards that with the newer novel agents, we can still attain rapid and sustained improvement in clinical status as soon as by the end of the first week while giving a patient a flexibility of injecting self-administering subcutaneous on weekly basis. So very exciting for patients.

The second one I want to talk about is MaGic, which is a phase two trial with claseprubart. Again, a novel mechanism of action. So far we have learned about C5 complement block. This was more upstream C1 complement block in a classical pattern with the hope that we can still preserve our innate immunity by preserving our alternative pathway and lectin pathway.

So again, the design was done for three groups. They used two different groups, two different dosing for claseprubart. One was 300 milligram every two weeks and second was 600 milligram every two weeks. And the third group was of course placebo. Patients were randomized and the initial study was 13 weeks, but then there is an open label extension for 52 weeks with a safety follow-up for another 40 weeks is going on.

So what the initial results again show there is improvement in MG-ADL, same with QMG and the MG composite score. MSE, minimum symptom expression, was achieved somewhere in about 27% to 37% of patient. And again, this improvement seen as fast as by the end of first week with MG-ADL score. No serious adverse reactions, no serious bacterial infection or autoimmune activations are noticed. So again, this provides that, hey, there is a novel pathway, novel agent selectively inhibiting C1 block, complement block, particularly in patients we can offer acetylcholine receptor positive generalized myasthenia gravis patients. And maybe preserving the innate immunity, the risk of infection may be less. But again, this needs to come with more with phase three trials to be confirmed.

And then lastly I want to add is the NIMBLE study. And I think again, this is a phase three trial. It's a combination treatment that was a novel concept and what they used was cemdisiran and pozelimab. So cemdisiran, it has siRNA, so it's a small interfering RNA which reduces the C5 hepatic expression, and

also reducing circulation by, it reduces C5 circulation by slicing RNA. And pozelimab is anti-C5 monoclonal antibody. So with combination treatment, the goal was to complete blockage of C5 to achieve. And during the trial, they achieved somewhere around 99% also. But the trial has four arms and that include isolated cemdisiran arm. Then another was isolated pozelimab arm, and then there was a combination arm, and then there was a placebo.

Interestingly, the outcome shows that, of course, cemdisiran shows more efficacy compared to placebo in the form of MJDL and QMG. But when we achieved 99% C5 complement block with combination therapy versus only isolated cemdisiran arm, did not show major difference in clinical efficacy. So again, that raises the question, do we really need to achieve complete C5 blockage to achieve the clinical efficacy or partial C5 blockage? Still, we can achieve the similar efficacy. So I think that was an interesting concept. And again, hopefully more we will learn about it as we move forward here. What are your thoughts, Dr. Sanka, about this newer treatment?

Ratna Bhavaraju-Sanka:

Yeah, I think a lot of these newer therapies, again, showing effective and safe response to our myasthenic population. And it's actually interesting to see that we don't really need 100% blockage of your C5 to see a response. So cemdisiran data actually showed that it was better in its efficacy compared to the combination with the pozelimab. So again, we want to utilize the minimum needed immunosuppression or C5 blockage for our patients to help reduce the side effects profile. So this is interesting data and I'm also excited to see the classical pathway blockage showing improvement, a little upstream complement blockage showing improvement in the myasthenia gravis scores and being safe.

Again, this comes with by preserving some of the complement pathways, we can hopefully keep that immune response to infections like meningitis and pneumococcal infections and help our patients not have these side effects that could be debilitating and compromising their health. So just a lot of more results to look forward to with the CAR Ts and the newer complement therapies in this population. So more data to come. So moving on to some of the meta-analysis and the real-world data, I know I was very excited to see this study on immune checkpoint inhibitor myasthenia. This is a debilitating disease, so what do you think about that data?

Chilvana Patel:

So I think that immune checkpoint inhibitor use has significantly increased in last couple of decades, and sometime that is the only options that our patients with cancers have it. However, as we are all aware that patients do experience peripheral neuromuscular adverse reaction varying from myasthenia gravis, myositis, as well as GBS. And I think this abstract point, very important fact there that patients who develop overlap syndrome who have a myocarditis myositis and myasthenia gravis combination, they have a much higher risk of mortality. And I think what they suggested, what they illustrated that mortality is about 13%.

Those patients who develop myasthenia gravis, or myasthenia gravis with immune checkpoint inhibitor, ventilatory support and acetylcholine receptor antibody positivity are independent predictors for the death. And troponin T rather than I and CK correlated with the MGFA severity score. So I believe once we start the patient immune checkpoint inhibitor, they need to be closely follow up and monitored through the CCAN. Of course, they need acetylcholine receptor antibody when we are looking for myasthenia gravis in these patients. It's a bad disease, and we don't want to miss considering the mortality being 13%. I think early diagnosis and a close follow-up is very valuable in this group.

Ratna Bhavaraju-Sanka:

Yeah, and working in collaboration with the oncology team. I think that is also really important to help these patients because sometimes these are their last option medications for the cancer therapies.

So again, yeah, there were some meta-analysis and data that was presented. They did show that maybe different approved medications or medications that are being tried do better with different endpoints, like some do better with MG-ADL, some do better with QMG. So I think again, bottom line, all of these medications are effective.

And also, the data did show that earlier initiation of these medications can help control the disease, and even reduce the utilization of prednisone or steroids, corticosteroids. So overall real world data also showing that corticosteroid tapering can be achieved when patients are on medications like rozanolixizumab or other approved medications. So real world data meta-analysis and some of these healthcare utilization data do show reduced hospitalization, reduced steroid use with the approved therapies.

So I think take home points from all the data that was presented is approved medications are still showing sustained efficacy and are safe to be utilized in our patients with myasthenia. And there are different dosing patterns that may be helpful like the ADAPT NXT trial showing different dosing patterns being helpful and newer indications for existing therapies like the seronegative is also helpful. But the upcoming data on these refractory myasthenia patients with single dose CAR T therapies also an exciting time to see in these myasthenia population to see how we can utilize various new medications to help our patients. But I do feel that there are some gaps. So what do you think is missing in what was presented at the academy meeting?

Chilvana Patel:

I think the time is exciting. There are seven new medications came in last seven years. So it's moving in the right direction, but I still feel that we are still away from individualized specialized care. We are still using more generalized concept that this medication we're going to use for the acetylcholine receptor antibody-positive or MuSK positive, but there are so many other comorbidities and other factors actually play a major role about the response to the treatment. So we are definitely missing the biomarkers to determine that which patient would benefit from which kind of targeted myasthenia gravis treatment. So I think that's something hopefully will work in future years and give us a better answer here.

And second, there are so many treatments available, so what we have is more network meta-analysis rather than head-to-head trial. So it is very difficult to choose when we discuss with the patient, "Hey, why you want to go over FcRn treatment versus C5 versus C1 inhibition?"

So I think that part, that algorithm will still take few years to come across because we are still missing one-on-one trials and data. But I do believe that there are registries coming and hopefully we will get more information and that will streamline. But considering that what we used to have in 10 years and what we have now, I think we can offer our patient much better care. And you and I both come across that these patients do much better than what we have seen in the past, so I'm still quite optimistic for the future here.

Ratna Bhavaraju-Sanka:

Right. And I would say more, I'm excited about the future of all these newer therapies and many more to come to help our patients and even the seronegative patients or ocular patients or refractory patients. So exciting times ahead, and hopefully we can chat about many more approved therapies

soon. Thank you everybody for spending your time with us and discussing the data that was presented at the AAN meeting in 2026. Have a good day.

Chilvana Patel:

Thank you everyone.