Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/optimizing-the-role-for-corticosteroids-within-the-evolving-dmd-treatment-landscape/37232/

Released: 11/07/2025
Valid until: 11/07/2026
Time needed to complete: 60 minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Optimizing the Role for Corticosteroids Within the Evolving DMD Treatment Landscape

Announcer:
Welcome to CME on ReachMD. This activity titled *Optimizing the Role for Corticosteroids within the Evolving Duchenne Muscular Dystrophy Treatment Landscape* is provided by the France Foundation. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Chrzanowski:
Today, we're going to be talking about *Optimizing the Role for Corticosteroids within the Evolving Duchenne Muscular Dystrophy Treatment Landscape*. My name is Stephen Chrzanowski. I'm a child neurologist, Assistant Professor in the Departments of Neurology and Pediatrics, and the co-director of our Muscular DMD Association Care Center at the University of Massachusetts Chan Medical School.

Dr. Veerapandiyan:
I'm Aravindhan Veerapandiyan, and I also go by Panda. I'm a pediatric neurologist at Arkansas Children's Hospital. I run the Neuromuscular Program here at Arkansas Children's Hospital.

Dr. Chrzanowski:
Today, our learning objectives are such that we're going to identify best practices for the proactive monitoring of corticosteroid-associated side effects in patients with DMD via an interdisciplinary care coordination model. We're going to compare and contrast several corticosteroid-based treatment options for DMD in terms of efficacy and safety from clinical trial data as well as emerging real-world evidence. And lastly, we're going to evaluate real-world patient case scenarios to help optimize corticosteroid use among patients with Duchenne who may also be receiving gene therapy and/or other treatment modalities.

To jump into this discussion, we'll first get a background on Duchenne muscular dystrophy, the gene, the isoform, and the clinical consequences. And we'll spend a couple extra moments just to make sure we have a solid foundation for the rest of this talk. The DMD gene spans 2.4 million base pairs on the X chromosome, containing 79 exons, making it the largest gene in the human body. Because of its size, it is particularly prone to deletions, duplications, point mutations, which explain the genetic diversity that we see across the Duchenne and the Becker phenotypes.

The gene itself encodes the protein dystrophin, a key cytoskeletal protein that links intracellular actin to the contractile elements of the dystrophin-associated glycoprotein complex at the sarcolemma.

There's multiple tissue-specific isoforms driven by internal promoters—in the muscle, in the brain and kidney, and in the central nervous system, and this expression pattern explains why Duchenne not only affects skeletal muscle, but also cardiac, smooth muscle, and central nervous system function.

The image on the right illustrates how the loss of dystrophin disrupts membrane integrity, leading to repeated cycles of damage, inflammation, and fibrosis, resulting in the progressive and irreversible muscle degeneration that we see in Duchenne. So the key takeaway is that loss of dystrophin is not just a muscular problem, but a multi-system problem rooted in the complexity of the DMD gene

and its widespread isoform expressions.

Next, the lack of dystrophin protein leads to progressive segmental necrosis and muscle degeneration. On the left, we can see a schematic of muscle fiber where we see reduced, absent dystrophin leading into mechanically weakened sarcolemmas, causing prone focal tearing during contractile activity, and this leads to a massive influx of extracellular calcium, activation of proteolytic enzymes, and ultimately degeneration. We know that there's a very classic timeline of inflammation, lipid deposition, and eventually scar tissue and necrosis in muscle, leading to the clinical phenotype that we see.

On the right is another schematic showing how the enzyme creatine kinase can be measured in the blood as an indicator of ongoing muscle damage as it leaks through the vulnerable sarcolemmal membrane. This slide here shows the goals of multidisciplinary management across the three major phases of Duchenne: in the ambulatory phase, the early non-ambulatory, and the late non-ambulatory phases.

In the ambulatory phase, our primary goal is to preserve ambulation and delay loss of motor function through corticosteroids, stretching, and physical therapy. At the same time, we aim to delay the onset of nocturnal respiratory support and begin cardiac surveillance and cardioprotective therapy before fibrosis develops. Psychosocially, this is a critical time to maintain school participation, independence for adaptive supports.

Once the boys begin the early non-ambulatory phase, the focus shifts to preserving upper limb function, keeping the ability to reach overhead, bring the hand to mouth, and other functional activities. We continue to delay respiratory decline and prevent cardiac dysfunction. Education and independence remain central, often requiring environmental or assistive adaptations.

Lastly, in the late non-ambulatory phase, the emphasis becomes preserving hand dexterity, for example, controlling a power chair, using a computer to play games, and in addition, maintaining cardiac and respiratory stability with advanced support as needed. This is when we transition to adult care, providing psychosocial planning for autonomy.

And so the key message of this is that our goals evolve but never diminish, and at each stage, we target what's most important to the individuals.

So corticosteroids are the standard of care for Duchenne and the single most effective disease-modifying therapy currently available. Why corticosteroids? Decades of clinical trials and large natural history studies consistently show that corticosteroids improve outcomes in Duchenne. In the short term, they increase muscle strength and function and support the heart and the lungs. In the long term, steroids provide prolonged ambulation by 2 to 5 years, reduce the need for spinal fusion, delay cardiac and respiratory failure, and increase overall survival.

Now that we have multiple new molecular therapies, corticosteroids still continue to serve as the foundation for all modern Duchenne care, setting the baseline for every intervention that we build it upon. This slide summarizes the steroid options for Duchenne and the balance we aim between efficacy and tolerability. Traditionally, we've used prednisone or prednisolone for DMD, with their long history of efficacy in prolonging ambulation and delaying cardiac and respiratory decline. Deflazacort became the first steroid to receive formal FDA approval in 2017, offering similar efficacy to prednisone but tending to cause less weight gain and possibly fewer behavioral side effects, though it may increase the risks of cataracts and bone fragility.

Vamorolone represents a new class of steroid analogs, often considered a dissociative steroid, retaining the anti-inflammatory benefits of corticosteroids but engineered to minimize the side effects related to growth, bone, and metabolic health. It was approved in 2023 for boys 2 years and older. And overall, the evolution of prednisone to deflazacort and now to vamorolone reflect our ongoing effort to preserve muscle, prolong function, and reduce treatment burden and toxicity.

This figure shows how long-term steroids translate to better overall outcomes in Duchenne. We start to typically see motor and speech delays as early as 18 months, followed by gait difficulties and the classic Gowers maneuver. And this is about when corticosteroids are typically introduced.

Once therapies begin, the benefits are seen early on. Steroids slow muscle degeneration, delay loss of walking, and preserve heart and lung function. As shown by the purple bar, consistent steroid use in early childhood through adulthood shifts the entire disease trajectory, prolonging ambulation by several years, delaying ventilatory and cardiac decline, and improving survival.

And here we outline the timeline of Duchenne through the later stages of life, emphasizing how early and sustained steroid use changes the outcome. In this stage, the boys are often becoming quite used to the steroids. Their function is doing quite good—they're ambulating, going upstairs, getting off the ground—but they start to see some of the side effects—the Cushingoid side effects of weight gain, mood behavior, mood disturbances, and some of the other side effects of steroids.

And lastly, as it transitions into the advanced stages of the disease, we see that steroids continue to delay the decline in upper limb function, which is paramount for individuals with advanced disease because this retains the impactful quality of life that they have.

This slide summarizes the mechanisms of prednisone and deflazacort, the mainstays in DMD. First, the anti-inflammatory effects—these drugs bind the glucocorticoid receptors, which move into the nucleus, suppressing NF-kappa B signaling, decreasing inflammatory cytokines and immune cell activation, which, in a big approach, reduces the ongoing muscle inflammation. Because of this, there's a pro-survival effect. Activation of the anti-inflammatory genes limits protein degradation within the muscle fibers. So rather than just suppressing inflammation, steroids also actually help to maintain cellular integrity and slow atrophy.

And lastly, most importantly for Duchenne, is the muscle stabilization. The corticosteroids support membrane repair, reduce leakage of intracellular enzymes and calcium, preserving the fiber stability over time, preventing eventual breakdown of it.

Together, these explain why corticosteroids delay degeneration and functional decline, acting both at the immune and cellular levels to protect dystrophic muscle.

Vamorolone represents the next generation of steroid therapy for Duchenne, a dissociative steroid designed to preserve efficacy while minimizing side effects. Traditional corticosteroids like prednisone and deflazacort act through both transactivation and cis-repression of these mechanisms. This combination gives us the anti-inflammatory benefit but also drives many of the metabolic and growth-related toxicities.

In contrast, vamorolone works primarily through selective trans-repression, meaning it inhibits NF-kappa B–mediated inflammation without activating the many genes that cause the negative side effects that we see. So we retain the anti-inflammatory and muscle-protective effects but see less growth suppression, less bone fragility, and less behavioral changes.

Further, vamorolone acts as a mineralocorticoid receptor antagonist, which may confer cardiac benefits—an important consideration in this disease, where cardiomyopathy is a major cause of morbidity and mortality.

In short, vamorolone keeps what's good about steroids and leaves behind what's not, making it potentially a more tolerable long-term option for Duchenne management.

So how do we select a steroid? Prednisone or prednisolone remain the traditional standard of care, slowing muscle weakness, improving pulmonary function, and prolonging ambulation by several years. However, it has a number of drawbacks, including weight gain, behavioral changes, growth suppression, and bone fragility. However, this is the steroid that we know the most about. So there's the most literature published, and we just have the best history and comfort with it.

Building on that, deflazacort offers similar or even greater efficacy with a lower risk of weight gain, potentially reduced scoliosis, which is why many families and clinicians prefer it. But the negative of deflazacort are that it can increase the risks of cataracts and potentially behavioral changes, but the data remains mixed at this point.

And most recently, vamorolone represents the newest and potentially most tolerable option, maintaining comparable functional benefit with less growth stunting, better preservation of bone health. Because it also acts as the mineralocorticoid receptor antagonist, it may support cardiac protection. The main limitation is that it cannot be used for stress dosing, and long-term real-world data still accumulates.

So the choice of steroid really depends on the individual's side-effect profile, tolerance, and family priorities—all sharing the same goals of preserving muscle, delaying decline, and improving long-term outcomes.

So when do we start steroids? And Duchenne timing really does matter. The goal is to begin ideally before the child enters the plateau phase of the disease—the period when strength stabilizes but before measurable decline begins. And for most boys, this window is about 4 to 5 years of age. Starting therapy during this time preserves the fibers before their loss, establishes the anti-inflammatory and membrane-stabilizing benefits early on. And multiple studies confirm that starting steroids before substantial decline leads to longer ambulation, improved pulmonary function, and better long-term outcomes.

Practically, the process begins with family discussion, followed by initiation after nutrition, side effects, endocrinological counseling. The starting dose is typically prednisone 0.75 mg/kg/day or deflazacort 0.9 mg/kg/day, but gradual adjustment based on tolerance. Even in the non-ambulatory phase, continued steroid use remains valuable for cardiac and pulmonary preservation.

And it’s so important, and we try to emphasize this with all of our families, that steroids should never be abruptly stopped. Dose adjustments may be needed for side-effect management, and non-ambulatory patients should continue to delay further loss of functional abilities. As you can see, the acronym STRESS, aptly named, the importance of stress-dose steroids here.

The PJ Nicholoff Protocol has become publicized of recent, particularly from Parent Project Muscular Dystrophy, highlighting the

protocol for stress-dose steroids at a glance. We refer you to Parent Project Muscular Dystrophy for more information regarding this. But in brief, they describe moderate stress and severe stresses that would be managed either by additional daily corticosteroids or emergency stress doses as recommended by one's doctor.

There is growing evidence to continue steroids after loss of ambulation. In the MD STARnet study shown on the left, boys that continued steroids for at least a year beyond losing ambulation experience significant delay in pulmonary decline, as shown by higher percent predicted FVC over time compared to those who stopped or never used steroids.

Similarly, the PRO-DMD study on the right found that in non-ambulatory patients who continued steroid therapy, whether it be prednisone or deflazacort, was similarly associated with slower decline in pulmonary, cardiac, and upper limb function, measured by better preservation of the left ventricle ejection fraction.

So these findings enforce what we see clinically—even after loss of ambulation, steroids remain crucial for maintaining respiratory and cardiac support. Older studies by Connolly and Daftary confirm these effects, showing increased peak flow, respiratory muscle strength, and FVC in patients aged all the way from 7 to 20 remaining on long-term steroids.

And so the take-home message is clear that steroids shouldn't be stopped after loss of ambulation. Continued use preserves multi-system function and improves long-term outcomes in Duchenne. And so this slide summarizes the steroid dosing regimens most commonly used in Duchenne. For classic prednisone, we use 0.75 mg/kg/day, whereas deflazacort is 0.9 mg/kg/day as standard doses. These remain the evidence-based starting points as recommended by major care guidelines. The newer dissociative steroid vamorolone is dosed at 6 mg/kg/day, with a maximum of 300 mg daily for patients over 50 kg. This higher numerical dose represents pharmacologic differences, not greater potency.

Alternative dosing schedules, such as weekend-only or 10 days on/10 day off, may help mitigate side effects like weight gain or behavioral changes, though daily dosing continues to provide the most consistent functional efficacy. Patients with hepatic impairment may need dose adjustments, and steroid doses are often changed over a patient’s life depending on function and, more importantly, tolerance.

So the key takeaway is that one size doesn't fit all; all steroid regimens ought to be individualized to maintain long-term functional benefit while balancing side effects.

When managing long-term corticosteroid therapy, growth and development monitoring remain essential components of one’s care. We regularly track height, weight, and BMI, because we know that steroids cause linear growth suppression. These datapoints help adjust dosing, guide nutrition counseling to prevent excessive weight gain, as well as discuss growth hormone and testosterone.

Bone health remains another major concern. We monitor bone mineral density at baseline and periodically, ensuring all patients receive adequate vitamin D and calcium supplementation. And if osteopenia or fractures are identified, we coordinate early with endocrinology for management, typically with bisphosphonate care.

We also know that steroids delay puberty, so beginning around age 9 or so, we start assessing for pubertal signs. And if puberty remains delayed beyond age 14, we consider testosterone therapy to support growth, bone health, and psychosocial well-being.

The take-home of the is that steroid management in Duchenne isn’t just about muscle, but it’s about supporting overall growth, bone health, and healthy development through adolescence and beyond.

In regards to monitoring strategies for cardiovascular and renal health, we also have to be proactive in these systems. Cardiomyopathy remains a major cause of morbidity and mortality in Duchenne, so early and regular cardiac surveillance is essential. We obtain baseline echocardiograms or cardiac MRIs by age 6 to 7, repeating annually or more frequent if abnormal. We start ACE inhibitors, or if not tolerated, ARBs prophylactically by age 10 or earlier if cardiac dysfunction is detected. And corticosteroids may cause fluid retention, hypertension, and so monitoring blood pressure, renal function, and electrolytes remain essential.

This is a collaboration between neurology, cardiology, and, if needed, nephrology as to optimize cardioprotective and steroid-sparing therapies. For renal health, monitoring the BUN, creatinine, and urinalysis, particularly when ACE inhibitors, ARBs, or nephrotoxic agents are used concurrently, is essential. So steroids extend survival in Duchenne by maintaining cardiac support, but long-term management does require close monitoring of the heart and the kidneys.

In monitoring strategies for metabolic health, we know very clearly that chronic steroids lead to weight gain, glucose intolerance, and dyslipidemia. And so tracking BMI but also the fat percent that individuals have at regular visits remains essential, as does counseling on diet, exercise, and portion control. We screen annually for glucose, A1c, and insulin, and if needed, start agents that can address this such as metformin or other medicines like that. We address obesity early not only to mitigate the cardiometabolic risk but also to support

motor and respiratory function. And simply put, extra weight is extra stress on muscles.

Managing the musculoskeletal components while on glucocorticoids remains important. So in regards to osteoporosis and skeletal fragility, we perform DEXA scans every year to every two years to track bone mineral density. If vitamin D and calcium are inadequate, we supplement as appropriate for individuals on chronic steroids. And we're quite vigilant regarding vertebral compression fractures, especially those with back pain or height loss. Using a multidisciplinary approach between endocrinology, orthopedics, and ourselves helps to prevent fractures and treat them when they happen.

In regards to monitoring infections with glucocorticoids, we know that glucocorticoids do cause immune suppression and potentially reduce the efficacy of vaccines. So what's important is that live vaccines are given prior to the onset of steroid initiation, and this is a coordination with one's primary care provider that they get what they needed. Also, we encourage and support the use of pneumonia vaccine, as this is a high-risk population who is quite vulnerable to respiratory infections at the appropriate ages.

Psychiatric monitoring remains a critical component of our interdisciplinary care for individuals with Duchenne, particularly because we know that steroids can worsen and cause psychiatric health problems, so we monitor and watch for mood changes, irritability, depression, which are very common with corticosteroid use. If needed, we can switch the steroid to try either deflazacort if on prednisone, or vamorolone if on one of the other two. We use validated behavioral rating scales for both patients and their caregivers to track changes over time. And if or when needed, we work with our psychiatry colleagues to best manage and support individuals, to give them the best quality of life from a psychiatric standpoint.

So what should patients do if they miss a dose? It's of the utmost importance that patients religiously continue to take their glucocorticoids without missing, but missing doses do happen. We do our best to educate families that missing dose for greater than 24 hours can precipitate adrenal crises. Sharing the symptoms of adrenal crisis, we reinforce adherence and carry the PJ Nicholoff Protocol card with our families for emergency guidance. During illness or surgery, we increase the steroid dose, i.e., stress dosing as directed by care protocols, and we, with a very low threshold, encourage families to seek immediate medical attention if symptoms of adrenal crises develop.

So the section takeaways from this are as such: initiate early, ideally before the plateau phase; monitor continuously looking at growth, bone, cardiac, metabolic and behavioral domains, pulling in the respective specialists as to give the kids the best interdisciplinary care. We manage proactively; we never stop steroids abruptly. We continue steroids after a loss of ambulation. And lastly, as we've described multiple times, we coordinate care and the communication across specialties ensures safety and longevity, ultimately for the best interest of the patients.

Dr. Veerapandiyan:
Okay, we just heard about the overview of Duchenne and the different steroids, the pros and cons. Let's dive into the literature, the evidence out there to talk about the effectiveness of different steroids.

The first slide that you look at here is the early evidence of use of prednisone in Duchenne muscular dystrophy. This clinical trial dates back to 1989 and it is looking at two different doses of prednisone in patients aged 5 to 15 years old. As you could see here, both doses actually show significant improvement in the muscle strength and function compared to placebo. The most frequent adverse events that were seen here included weight gain, excessive hair growth, and Cushingoid appearance.

Since this study, there were several studies, including real-world, that were published to talk about the efficacy of steroids, including prednisone and others, in slowing down the disease progression as well as delaying the onset of cardiomyopathy and respiratory dysfunction in patients with Duchenne muscular dystrophy.

So one of those studies here is a study from the CINRG which was looking at deflazacort and prednisone comparison. As you could see here, this was done between 2006 and 2016, and the study enrolled over 440 patients with Duchenne muscular dystrophy aged between 2 and 28 years. And they were followed up for up to 10 years. In this one, they compared the use of deflazacort versus prednisone, and deflazacort was associated with statistically significant preservation of function compared to prednisone. As you could see here, the preservation of function was across three key milestones, including the ability to stand from supine, age at loss of ambulation, as well as age at loss of hand to mouth function.

And there was most recent study that was presented in March 2025, from the ImagingDMD group. So here they again looked at the boys with Duchenne on deflazacort versus prednisone. And the age at loss of ambulation was significantly higher in participants on deflazacort compared to prednisone, and the muscle disease progression was also slower in deflazacort-treated subjects compared with prednisone-treated subject.

We heard about different dosing regimens that's being used in these boys—you know, daily versus weekend dosing versus 10 days on

and 10 days off intermittent dosing. So here this trial, FOR-DMD clinical trial looked at the efficacy of the different corticosteroid dosing regimens. They looked at daily prednisone, daily deflazacort versus intermittent prednisone, specifically focusing on the 10 days on and 10 days off regimen. So this study has showed that both daily prednisone and deflazacort were more effective than intermittent prednisone in their composite primary outcome.

This slide shows the primary outcome measures that they were used, including the velocity of the time to rise from the floor, forced vital capacity, and the global satisfaction subscale score. Again, the daily prednisone and the deflazacort group showed an improvement compared to the intermittent dosing group.

Alright, so here we talk about the study on vamorolone, which is one of the newer steroids. Just to highlight here, vamorolone is also a steroid. If you look at the FDA prescribing information, they talk about how different side effects that they typically include in the corticosteroid. That is one of the key takeaways that I wanted to emphasize—that vamorolone is also a steroid.

Now, in this study, they have included 121 boys with Duchenne muscular dystrophy aged between 4 and 7 years, and they were randomly assigned to one of these four groups, either placebo or prednisone or vamorolone these two different doses. They looked at 2 mg/kg/day versus 6 mg/kg/day. And patients receiving either placebo or prednisone were able to cross over to either doses of vamorolone.

So the primary outcome here was the time to stand, and they also looked at the time to run/walk at 10 meters as well as 6-minute walk test. So the primary outcome was done at 24 weeks, and then they also continued to follow these patients till 48 weeks. At 24 weeks, boys treated with vamorolone 6 mg/kg/day have shown improvements in their time to stand velocity, 6-minute walk test, as well as time to walk/run 10 meters. As you look at the 48-weeks follow-up, again, vamorolone at 6 mg/kg/day improved motor outcomes as well as improved patient growth compared to prednisone.

So when we look at the safety of vamorolone from this clinical trial, they have compared that with the prednisone, and what they have found was the behavior problems were reduced in the vamorolone group. Similarly, gastrointestinal symptoms were also reduced in the vamorolone group. And Cushingoid features were decreased in patients treated with vamorolone as well.

I just wanted to talk about these three different options, as was pointed out earlier, they all have pros and cons. There are slight differences in the adverse effect profile that you would see. From a vamorolone standpoint, the two things that stand out are: one, the growth—it doesn't affect the growth compared to the other steroids, prednisone or deflazacort—and they have seen reduced number of vertebral fractures with vamorolone.

One of the things that was pointed out was the long-term data for vamorolone; we have used prednisone and deflazacort now for years, and in the clinical experience, we have long-term data, either as a study or from our clinical experience. However, vamorolone, that long-term data is missing, and that's where the SUMMIT clinical trial comes into place. It's a multicenter, observational, prospective, longitudinal registry design to collect information from boys with Duchenne that are treated with vamorolone. The study plans to follow up to 250 participants who are taking vamorolone for the treatment for up to 5 years. The study is collecting key information, including medical assessments, some of the tests that we do, questionnaires, including quality of life questionnaires, as well as labs and imaging, mainly to focus on the safety as well as efficacy of vamorolone.

Alright, from here, so we talked about the three different steroid options for Duchenne muscular dystrophy: prednisone, deflazacort, and vamorolone. Like we highlighted before, there are some similarities and also important differences between each one of them. You know, all steroids, from prednisone and deflazacort experience that they slow down the disease progression. They delay the loss of ambulation, delay the onset of scoliosis surgery, delay cardiomyopathy. We also looked at the real-world and natural history data that's showing deflazacort might be slightly superior from an efficacy standpoint compared to prednisone. And we also reviewed the safety of each one of them, including the newer steroid, which is vamorolone.

The clinical trials show comparable muscle function improvements to prednisone and improved safety profile compared to prednisone in certain aspects, including growth stunting, Cushingoid features, and behavior problems.

So in this section, we are going to focus on the use of corticosteroids in the setting of evolving therapeutic landscape for Duchenne muscular dystrophy. So you know, we have gene transfer therapies, we have exon skipping therapy, we have givinostat, and there's also several other upcoming therapies in clinical trials. So how are we placing the corticosteroids in this evolving landscape?

So the first thing I want to focus on here is switching from one steroid to another, especially with recent approval of vamorolone, how are we switching the patients who are already on prednisone or deflazacort?

Now a case summary. A 12-year-old boy with Duchenne muscular dystrophy. He was initially started on prednisone 0.75 mg/kg/day. He was on it for a year and then was transitioned to deflazacort at age 7. However, he developed some side effects from deflazacort. Now

the family wants to switch to vamorolone.

So one of the key aspects here is that the approved dose for vamorolone is 6 mg/kg/day. If you're switching from either daily or intermittent dosing of deflazacort or prednisone, the recommendation is to switch to vamorolone 6 mg/kg/day. You can possibly down-titrate up to 2 mg/kg/day, since it was looked at; however, the starting dose has to be 6 mg/kg/day, especially when you're switching from another steroid.

Here, in this particular patient, the main concerns were behavioral problems and a short stature. Now, after switching to vamorolone 6 mg/kg/day, within 3 months family reported improved behavioral problems as well as the growth. The BMI trajectory had plateaued, and the growth velocity has improved.

Now, this experience is going to vary in the real world when you see patients from one patient to other patient. For example, I've had patients who had more behavior problems with vamorolone compared to deflazacort. But I think the key thing here to focus on is the growth velocity. So some of these boys, they're emotionally affected by their growth, especially when they're on prednisone and deflazacort, they are short-statured, and that affects some emotional when they compare themselves to their peers. For that reason, you know, we have switched these boys to vamorolone as well.

I think we talked about it here. The one other thing I wanted to emphasize also is when you're transitioning from again one steroid, either prednisone or deflazacort to vamorolone, make sure we follow them closely to make sure there is no adrenal crisis or any other adverse effect from vamorolone.

Alright. Another concept here is your gene transfer therapy. So how are steroids being used or considered in the setting of gene transfer therapy? We have delandistrogene moxeparvovec, which is commercially approved, and we also have other clinical trials looking at different gene therapy programs.

So we'll look at a couple of cases here. So there's two cases, 4- and 9-year-old, with Duchenne muscular dystrophy. They both received microdystrophin gene therapy while continuing on vamorolone. So here, both patients were started on prednisone 1 mg/kg/day the day before the gene therapy. And their baseline steroid was vamorolone 6 mg/kg/day. And the prednisone was added to vamorolone, and the prednisone was tapered at 7 weeks post infusion, and that was discontinued by 12 weeks post infusion, and the vamorolone was continued. And both patients, they had no significant adverse events from this regimen, use of vamorolone as a background steroid on top of prednisone.

Now, this is also going to be a different experience, varied from one patient to other patient, or also the dose that you are using for vamorolone. Remember vamorolone, the recommended dose if you're switching from one steroid also even starting dose is 6 mg/kg/day.

Alright, let's talk about the considerations for corticosteroids with gene transfer therapy. Like we discussed before, all of these boys, or most of these boys, are on baseline standard of care corticosteroids, either prednisone or deflazacort or vamorolone. Or sometimes they may be on a weekend dosing or 10 days on/10 days off dosing of prednisone as well. So the key is you have to maintain them on the baseline corticosteroids. And then if we need to add another steroid, it's almost always prednisone, because we don't have that on other steroids to be used around the time of gene therapy infusion as an immunosuppressive medication. So they are started around the time of infusion to mainly reduce the reactions against the vectors that's being used and sometimes against the antibodies that are made for against the microdystrophin protein itself.

The current guidelines emphasize maintaining patients on the stable corticosteroid regimens prior to gene therapy administration, and start prednisone one day prior to infusion, and maintain them on that prednisone 1 mg/kg/day for minimum of 60 days, could be up to 120 days. The timing, the duration of that is constantly evolving as we learn more about the safety profile of these gene transfer therapies.

Sometimes we may see adverse effects from the gene therapy, such as, you know, liver injuries, myocarditis, immune-mediated myositis, at which times the dosing of these corticosteroids would be adjusted. Sometimes we use intravenous methylprednisolone. Sometimes we increase the oral prednisone dose. So again, something to keep in mind, and from a steroid standpoint.

Now, we talked about the corticosteroid regimen modification. For the adverse effects, this is some guidance in the label for delandistrogene moxeparvovec in terms of, how can we adjust the corticosteroid regimen when you see liver injury or liver enzyme abnormalities. Again, these recommendations are constantly evolving and changing as we are learning more about the adverse effect itself, the timing of the adverse effects, the severity, and what else could be done.

One of the common questions that we get asked in the clinic is, can deflazacort or vamorolone be used instead of prednisone around the

time of gene therapy infusion, or as a peri-infusion steroid? The answer is no, because there is no direct studies using either deflazacort or vamorolone as a peri-infusion corticosteroid, for delandistrogene moxeparvovec. So usually you have to use prednisone and then either on top of the deflazacort or vamorolone, or sometimes some providers actually convert all of the total corticosteroid dose to prednisone or prednisolone, to make it easier. Those are some of the alternate regimens that you could use. However, you have to use prednisone as the peri-infusion corticosteroid.

So now let's jump into exon skipping therapies. As we know, there are several exon skipping therapies that are commercially approved. How do we see the use of corticosteroids with that? I think, as highlighted in the previous section, corticosteroids are the foundation therapy in Duchenne. I don't think we are there yet to say that we don't need corticosteroids. The corticosteroids may increase the available dystrophin pre-mRNA for exon skipping possibly helping overall efficacy. Also have to remember there's limited evidence exists comparing corticosteroid regimens and dosing and long-term outcomes in combination with exon skipping therapies.

Another point to keep in mind is nearly all these exon skipping trials were done on patients who were already on corticosteroids. I think the recommendation here is the corticosteroids should be maintained during exon skipping therapy. I can give you an example of my own patient who was on an exon skipping agent for a year. We tried to stop the steroid because of the side effects to see after discussing the pros and cons, however, after stopping the steroids immediately, within 2 to 3 weeks, we saw decline, so we had to put them back on the steroids. And something to keep in mind also, it is recommended to maintain the corticosteroids with these therapies, including exon skipping as well as the gene transfer therapies.

Another therapy that was recently approved was the givinostat, which is a HDAC inhibitor. Again, this was also done on boys who are already on steroids. Sometimes people perceive this as a steroid alternative; it's not a steroid alternative, but it was the first non-steroidal therapy that was approved for Duchenne muscular dystrophy, but not as an alternative to steroid. So keep that in mind. In the study, the steroids were used at a stable dose for at least 6 months before givinostat initiation. So dual therapy with givinostat and steroid can lead to improved muscle preservation, slow disease progression, and longer duration of ambulatory status in patients.

So takeaways from this section, corticosteroids are the foundation for Duchenne muscular dystrophy. So three different steroids: prednisone, deflazacort or vamorolone in usage with gene therapy, delandistrogene moxeparvovec standpoint, prednisone or prednisolone is the only steroid that could be used as a peri-infusion steroid. You typically start a day before infusion. It is recommended to continue corticosteroids while you're using exon skipping therapy or givinostat.

So key takeaways for this educational session, again, I'm going to highlight corticosteroids are the basic foundational therapy for Duchenne muscular dystrophy. The age of initiation of corticosteroids is typically 4 to 5 years before plateau, as recommended in the care guidelines right now. But the clinical practice largely varies as deflazacort and vamorolone are approved for 2 years and older, and there might be variability in the practice. As you may see, providers may start steroids around age 2 or 3. It is extremely important to monitor for the side effects as well as efficacy of these different steroid regimens, and also important to think about either adjusting the dose or switching steroids if you see any adverse effects. From a gene therapy standpoint, always use prednisone or prednisolone as the peri-infusion steroid. And the dosage can be escalated if you see any adverse effects. And from a combination therapy with exon skipping or givinostat standpoint, it is recommended to continue the stable steroid dose during these therapies. And more importantly, it is always, always important to involve patient and family when you discuss about these therapeutic options, their effectiveness, side effects, and choose what's the best option for that family and for that individual patient.

Thank you for your attention. Please continue to the evaluation to receive your CME credits. Thank you.

Announcer:
You've been listening to CME on ReachMD. This activity is provided by the France Foundation. To receive your free CME credit or to download this activity, go to reachmd.com/cme. Thank you for listening.