New Frontiers in the Treatment of DMD Across the Age Spectrum

RAPID RECAP

Learning Objectives

- Evaluate real-world, case-based scenarios for patients with DMD to address considerations when assessing candidacy for gene therapy across the age spectrum
- Assess the latest clinical trial data for DMD gene therapy treatments to help inform clinical decision-making
- Describe best practices for ongoing monitoring of patients at various ages who have received gene therapy for DMD

Assessing Patient Candidacy[1,2]

Timing of the Physical Exam to Determine Candidacy

A physical exam should be conducted **1 month prior** to and again **within 48 hours** of the infusion

Timing of Baseline Lab Collection

Baseline labs should be collected twice prior to gene therapy infusion: at the evaluation appointment **(~1 month prior)** and again **within 1-3 days of the procedure**

Communication Strategies

Communication depends on the physician and institution, but patients/caregivers should be **provided with contact options** in case of questions or side effects

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Pre-Infusion Considerations[1,2]

Corticosteroids

- Discuss starting **additional prednisone a day before** infusion and continuing for **at least 60 days**, and need to **adjust dosing** if adverse effects occur
- Explore plans for continuing **corticosteroids after treatment**

Strength/Mobility

- **Check PUL/NSAA scores**
- Discuss potential **impacts to strength** following gene transfer therapy
- State that the goal is **stability of strength** or **slowing decline**
- Review with patient/caregivers that each person with DMD is an individual, and **results will be individual to that person**

Cardiology

Check:

- EKG
- Echo
- Cardiac MRI
- Medications
- Discuss potential **cardiac risks** associated with gene transfer therapy
- Review safety data showing **no increased risk** with delandistrogene moxeparvovec
- Review required post-infusion monitoring
- Emphasize starting at an appropriate cardiac baseline to **optimize tolerability** of systemic stressors

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Pre-Infusion Considerations (continued)[1,2]

Pulmonary

- Check *FVC* and *FEV1*
- Discuss **considerations for airway protection** in the context of nausea/vomiting
- Discuss the potential for treatment to **maintain neuromuscular lung mechanics**

GI/Nutrition

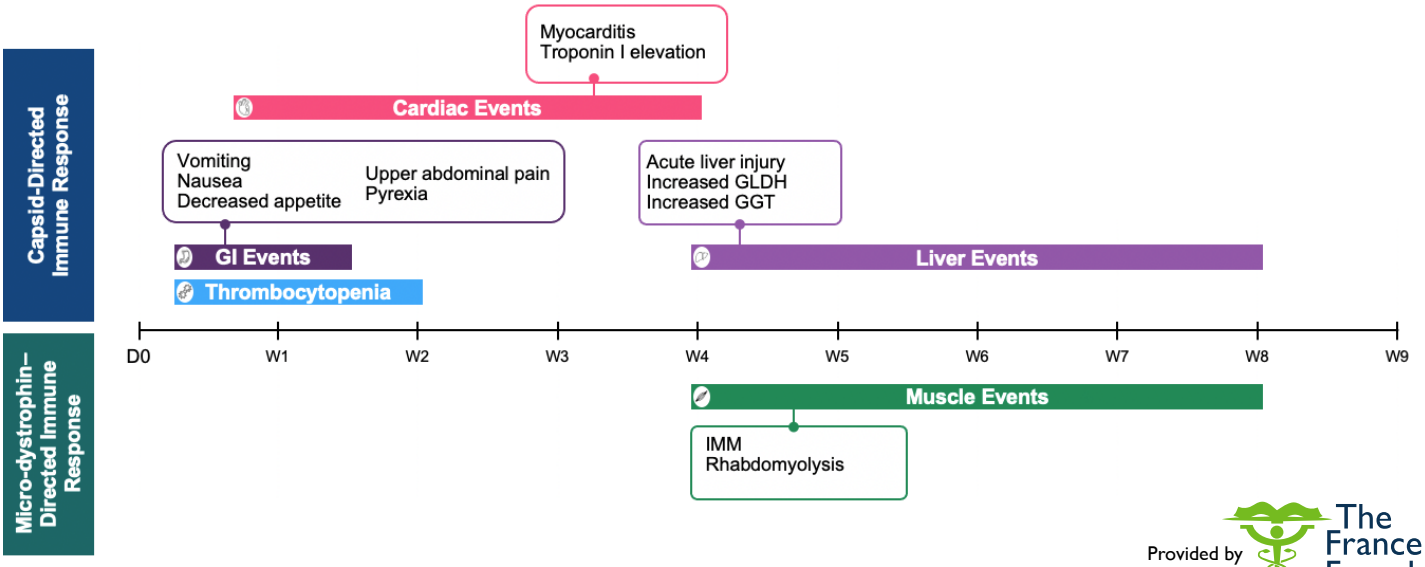
- Check weight
- Discuss **considerations for nausea/vomiting** after delandistrogene moxeparvovec
- Discuss consideration for some individuals to **add famotidine routinely** versus as needed in the context of increased corticosteroid dosing

Baseline Labs

Check:

- AAV antibodies
- CBC
- AST
- ALT
- GGT
- CK
- Troponin I
- Bilirubin

Timing of Adverse Events in Clinical Trials[3]



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Considerations for Managing Adverse Events[1,2]

	Acute Liver Injury	Myocarditis	Immune-Mediated Myositis
Patient presentation	Acute liver injury is diagnosed/confirmed	Suspected or confirmed myocarditis	Physical signs of IMM (weakness, muscle pain/tenderness, difficulty swallowing) that are progressive over days
Patient monitoring	Patient should be seen in person; assess need for hospitalization based on laboratory and exam findings	Patient should be seen for a physical exam; assess need for hospitalization based on laboratory and exam findings	Patient should be seen urgently by the prescribing physician for physical assessment (including neuromuscular strength assessment) Likely will require admission to the hospital for ongoing close observation
Laboratory studies	If not hospitalized, monitor closely and repeat laboratory studies sooner than 1 week	Monitor closely and repeat laboratory studies sooner than 1 week	Monitor closely and repeat baseline laboratory studies sooner than 1 week
Additional diagnostic and laboratory studies	GGT, PT/INR	Complement C3, complement C4, complement total CH50, CK-MB, CK, urinalysis, cystatin C, CRP Perform an echocardiogram and ECG; consider cardiac MRI	ANA, CK, CRP, aldolase, ESR, myoglobin, cystatin C, urinalysis, and urine output Echocardiogram, ECG, swallow study may be performed
Medication and treatment	Increase oral corticosteroid dose to 2mg/kg/day (max 120mg/day)	Increase corticosteroid to 2mg/kg/day (max 120mg/day) Consider short-term pulse of IV methylprednisolone; also consider adding IVIg	Increase steroid therapy to either 2mg/kg/day (max 120mg/day) or 3-day course of high-dose IV methylprednisolone
Consultation	Consult with hepatologist as needed	Consult with cardiologist	Consult with appropriate specialists (consider rheumatology, immunology, and cardiology

Abbreviations: ANA, antinuclear antibodies; CK, creatine kinase; CK-MB, creatine kinase-myocardial band; CRP, C-reactive protein; EKG, electrocardiogram; ESR, erythrocyte sedimentation rate; GGT, gamma-glutamyl transferase; GLDH, glutamate dehydrogenase; IVIg, intravenous immunoglobulin; MRI, magnetic resonance imaging; NSAA, North Star Ambulatory Assessment; PT/INR, prothrombin time and international normalized ratio; PUL, performance of upper limb

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Key Takeaways

- Gene transfer therapy offers a promising treatment for DMD, but requires a thorough evaluation of multiple organ systems before and after treatment
- Researchers are working on identifying the best practices for monitoring and managing patients with risk factors for complications
- Health care providers must establish a reliable system to monitor lab results and manage potential adverse events

References

1. Zaidman CM, Goedeker NL, Aqul AA, et al. Management of Select Adverse Events Following Delandistrogene Moxeparvovec Gene Therapy for Patients With Duchenne Muscular Dystrophy. *J Neuromuscul Dis*. 2024;11(3):687-699.
2. Mendell JR, Proud C, Zaidman CM, et al. Practical considerations for delandistrogene moxeparvovec gene therapy in patients with duchenne muscular dystrophy. *Pediatr Neurol*. 2024;153:11-18.
3. Crystal Proud, MD, et al. Presented at the 29th Annual Congress of the World Muscle Society; October 8-12, 2024; Prague, Czechia and virtual.

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