Real-World Safety Profile of Delandistrogene Moxeparvovec in the US Postmarketing Setting

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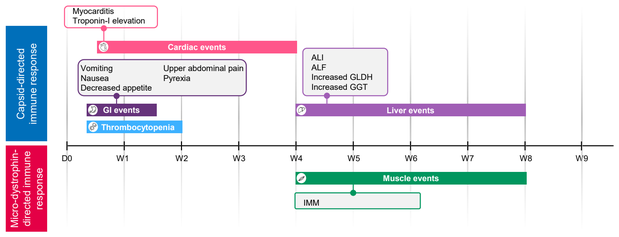
Background

- Delandistrogene moxeparvovec is an rAAVrh74 vector-based gene transfer therapy that delivers a transgene encoding delandistrogene moxeparvovec micro-dystrophin, an engineered, functional form of dystrophin shown to slow disease progression in DMD[1–4]
- Delandistrogene moxeparvovec is approved for the treatment of ambulatory patients with DMD in the US and in other select countries[5,6]
- Clinical trial experience has established a consistent safety profile for the frequency, type and timing of AEs associated with delandistrogene moxeparvovec in patients with DMD (**Figure 1**)[7]
- In a pooled analysis of >200 clinical trial patients, the safety and tolerability of delandistrogene moxeparvovec was manageable with appropriate monitoring and treatment of AEs, which typically occur within 90 days post-infusion[7]
  - This highlights the greatest risk for safety events within the first 90 days after infusion and the importance of close monitoring during this time
- Long-term monitoring of patients treated in clinical trials continues to further characterize the safety and efficacy of delandistrogene moxeparvovec[8]
- Evaluation of real-world data from patients treated commercially with delandistrogene moxeparvovec is important to determine whether the safety and tolerability profile observed in clinical studies is consistent with outcomes in clinical practice
- Real-world data collection is ongoing in the Phase 4, prospective, observational ENDURE study (NCT06270719), which is evaluating the long-term effectiveness and safety of delandistrogene moxeparvovec compared with SoC for patients with DMD in the US. An interim analysis from this study was recently presented[9]
- While Phase 4 observational studies allow for protocol-specified monitoring of enrolled commercially treated patients, complementary spontaneous reporting and other postmarketing sources can provide broader insights into safety in clinical practice in the full commercially treated population

Figure 1 *Timeline of AEs following treatment with delandistrogene moxeparvovec and their association with immune responses[5,10,11]*



Objective

- To evaluate the real-world postmarketing safety of delandistrogene moxeparvovec from commercially-treated patients in the US in patients with DMD stratified by age

Methods

- Patients treated with commercial delandistrogene moxeparvovec who experienced AEs were identified from the Sponsor's database, which identifies AEs from the sources and through the process outlined in **Figure 2** (data cutoff November 2, 2025)
  - The data cutoff precedes the latest delandistrogene moxeparvovec label update, which includes an updated indication for the treatment of ambulatory patients only, a Boxed Warning describing the risk for serious ALI and ALF, updated hepatic monitoring and updated corticosteroid recommendations for patients with liver function abnormalities following delandistrogene moxeparvovec infusion[5]
- The safety database was used to identify the most commonly reported AEs, followed by targeted searches using specific search criteria for AEs of special interest
  - PTs are standardized MedDRA terms used to consistently code and report AEs and medical conditions, to help identify potential safety signals across diverse sources and populations[12]

Figure 2 *Identification and processing of patient cases*

Validity check
Four criteria for a valid case: Identifiable patient, identifiable reporter, AE or special situation, delandistrogene moxeparvovec. Initial or follow-up assessment, seriousness assessment

Data entry and case processing
Structured data entry, narrative writing, event coding (MedDRA)*

Rigorous quality control
Compliance and accuracy check

Medical review
Clinical assessment, identification of data gaps, determination of follow-up questions

Follow-up
Targeted queries sent to the reporter, incorporation of follow-up data into the case and reassessment

Regulatory reporting

*Verbatim terms are identified as their PTs (e.g. "patient threw up" is classified as "vomiting").

- Only evaluable AEs reported to Sponsor Safety were included

AEs of special interest

- **Acute liver injury (ALI) search strategy:** Liver-related Medical Dictionary for Regulatory Activities (MedDRA) (preferred terms [PTs] under these standardized MedDRA queries [SMQs])
  - Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions*
  - Hepatitis, noninfectious*
  - Cholestasis and jaundice of hepatic origin*
  - Liver-related investigations, signs and symptoms*
  - Liver-related coagulation and bleeding disturbances*
  - From the retrieval set (per search strategy above), exclude elevations associated with a laboratory and AE profile suggesting a muscle source of transaminases

*Narrow and broad scope.

- **Immune-mediated myositis (IMM):** All cases identified under the IMM search strategy were assessed using the myositis case definition. Cases meeting this definition were classified as Definite or Possible IMM
  Search strategy: MedDRA high-level term muscle infections and inflammations, and PTs (asthenia, fatigue, malaise [if any of them are grade ≥3/severe])

- **Myocarditis:** All PTs identified under the myocarditis search strategy were assessed as Definite or Probable based on the myocarditis case definition[13,14]
  Search strategy: MedDRA noninfectious myocarditis/pericarditis (PTs under these SMQs):*
  - Troponin I increased
  - Troponin I abnormal
  - Troponin increased
  - Troponin T increased
  - Troponin abnormal
  - Blood creatine phosphokinase-MB increased
  - C-reactive protein increased
  - Red blood cell sedimentation rate increased
  - Fibrin D dimer increased

*Narrow scope.

Results

- This analysis included 715 patients (4 to <8 years, n=338; 8 to <12 years, n=212; ≥12 years, n=165) treated with delandistrogene moxeparvovec in the commercial setting as of November 2, 2025
- The following approximate timeframes were used to categorize specific safety events as treatment-related:*
  - Nausea and vomiting: within ~10 to 15 days post-infusion
  - ALI:† within ~90 days post-infusion
  - IRRs/hypersensitivity: within ~24 hours post-infusion
  - IMM: ~1 month, generally within the first 2 months post-infusion
  - Myocarditis: within 24 hours to more than 1 year post-infusion
- The most common TR-TEAEs (≥15% [events/total exposure]) were vomiting (n=141 [21.0%]), nausea (n=143 [20.0%]) and ALI† (n=132 [18.7%]) (**Table 1**)

*Relatedness was determined by the Sponsor, rather than the PI as in clinical studies, including Phase 4 studies.
†ALI terms includes all PTs within the SMQ mentioned in the methods section.

Table 1 *TR-TEAEs with frequency ≥15%**

TR-TEAE	Number of events	Frequency*
Vomiting	141	21.0%
Nausea	143	20.0%
ALI†	132	18.7%

*Number of AEs/total exposure.
†ALI terms includes all PTs within the SMQ mentioned in the methods section.

- There were 57 (8.0%) events of serious ALIs reported and 50 (7.0%) hospitalizations due to ALIs (**Table 2**)
- Serious ALI frequency and hospitalizations were similar in patients aged 4 to <8, 8 to <12 and ≥12 years (n=26 [7.7%] vs. n=23 [6.8%], n=15 [7.1%] vs. n=14 [6.6%] and n=15 [9.1%] vs. n=12 [7.3%], respectively)
- In the postmarketing setting, there has been one treatment-related death (0.1%) due to ALF at 84 days post-infusion in a non-ambulatory patient of 16 years of age with advanced-stage DMD
  - Six unrelated deaths (0.8%) have been reported in the postmarketing setting, occurring from 34 to 1,816 days post-infusion as of May 2026

Table 2 *US postmarketing ALI/ALF/hospitalizations due to ALI**

	Number of patients	ALI (serious and non-serious)	Serious ALI	ALF†	Hospitalizations due to ALI
All patients	715	132‡ (18.5%)	57 (8.0%)	1 (0.1%)	50 (7.0%)
4 to <8 years of age	338	64 (18.9%)	26 (7.7%)	0	23 (6.8%)
8 to <12 years of age	212	24 (11.3%)	15 (7.1%)	0	14 (6.6%)
≥12 years of age	165	40 (24.2%)	15 (9.1%)	1 (0.6%)	12 (7.3%)

*Criteria for ALI, serious ALI, ALF and hospitalizations were determined/reported by the treating physician.
†Two ALF cases related to delandistrogene moxeparvovec treatment and resulting in death ~3 months post-infusion have been reported in non-ambulatory patients (one in the ENVISION trial and one in the commercial setting) at 15 and 16 years of age, respectively. There was one additional instance of ALF in a 22-year-old non-ambulatory patient. This event was not related to delandistrogene moxeparvovec, and the patient's liver concerns have subsequently resolved. ‡Age not reported in three patients.

- Other treatment-related SAEs included myocarditis (n=5), IMM (n=2) and IRRs (hypersensitivity, n=2) (**Table 3**)
- A total of 35 serious infections were observed in the patient population
- The majority of serious infections were assessed as unrelated to delandistrogene moxeparvovec
  - However, a limited number of cases were considered related, primarily based on the absence of an alternative etiology and a time to onset consistent with the peri-infusion corticosteroid treatment period

Table 3 *TR-SAEs of interest*

TR-SAEs of interest	4 to <8 years of age	8 to <12 years of age	≥12 years of age	All patients
Myocarditis	0	1	4	**5***
IMM	0	0	2	**2**
IRRs (hypersensitivity)	2	0	0	**2**

*Three definite cases and two suspected or reported verbatim cases of myocarditis.

Limitations

- Limitations of postmarketing safety data include incomplete or duplicate reporting, difficulties in attributing causality of an AE to treatment, biased or under-reporting, delayed detection of rare events and lack of information on severity of events[15,16]
- Limitations specific to postmarketing reporting in DMD mean that some safety signals may require subsequent validation, due to potentially being confounded by DMD progression, chronic steroid use or other unknown factors[17,18]
- In the current analysis, hospitalization due to ALI rates may not accurately capture the severity of liver events, as patients may be hospitalized in order to receive inpatient steroids or for prompt and early intervention

Conclusions

- The overall safety profile of delandistrogene moxeparvovec in a large population of commercially treated patients in the US is consistent with clinical trial safety results to date
- The frequency of treatment-related ALIs is consistent with interim analysis reports from the Phase 4 ENDURE study
- The frequency of serious ALIs and hospitalizations was comparable in patients aged 4 to <8, 8 to <12 and ≥12 years, highlighting similar safety and tolerability across age groups

Acknowledgments & Disclosures

Sponsorship: Medical writing and editorial assistance were provided by Lucretia Ramnath, PhD, of Nucleus Global, in accordance with Good Publication Practice (GPP) 2022 guidelines (https://www.ismpp.org/gpp-2022) and were funded by Sarepta Therapeutics, Inc., Cambridge, MA, USA.
Disclosures: Delandistrogene moxeparvovec is approved for the treatment of ambulatory patients with DMD in the USA, Japan, Israel, United Arab Emirates, Qatar, Kuwait, Bahrain and Oman. VP, PS and DA are employees of Sarepta Therapeutics, Inc. and may have stock options. RR is a consultant for AveXis/Novartis, Avidity, Biogen, Beren, Dyne, Genentech/Roche, Sarepta, Scholar Rock and Solid Biosciences and is a site investigator for clinical trials with AveXis/Novartis, Biogen, Beren, Genentech/Roche, Ionis and Scholar Rock.

Presented at the 27th Annual Neuromuscular Study Group Scientific Meeting (NMSG); September 25–27, 2026; San Antonio, TX, USA

Abbreviations

AE, adverse event; AEMS, Adverse Event Monitoring System; ALF, acute liver failure; ALI, acute liver injury; D, day; DMD, Duchenne muscular dystrophy; GI, gastrointestinal; GGT, gamma-glutamyl transferase; GLDH, glutamate dehydrogenase; HCP, healthcare professional; IMM, immune-mediated myositis; IRR, infusion-related reaction; MB, muscle/brain; MedDRA, Medical Dictionary for Regulatory Activities; PI, Principal Investigator; PT, preferred term; rAAVrh74, recombinant adeno-associated virus rhesus isolate serotype 74; SAE, serious adverse event; SMQ, standardized MedDRA query; SoC, standard of care; TR-SAE, treatment-related serious adverse event; TR-TEAE, treatment-related treatment-emergent adverse event; W, week.

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