

Delandistrogene Moxeparvovec Micro-Dystrophin Expression and Safety in 2–3-year-olds with Duchenne Muscular Dystrophy in ENDEAVOR and ENVOL Studies

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Background

- Delandistrogene moxeparvovec is an rAAVrh74 vector-based gene transfer therapy that delivers a transgene encoding delandistrogene moxeparvovec micro-dystrophin, which has been shown to slow disease progression in ambulatory patients with DMD^{1–4}
- Delandistrogene moxeparvovec is approved in the USA for ambulatory patients (aged ≥4 years) and in other select countries^{5,6}
- Given the irreversible muscle loss in DMD, gene therapy may have greater potential benefit when administered earlier in the disease course, slowing disease progression at a higher peak function^{7–9}
- In the 3–4-year-old patient population, robust delandistrogene moxeparvovec transduction, micro-dystrophin expression, and sarcolemmal localization were observed 12 weeks post-delandistrogene moxeparvovec infusion. Safety was manageable with appropriate monitoring, with no new signals, and was consistent with the known safety profile of delandistrogene moxeparvovec in other age groups of ambulatory patients (≥4-year-olds)¹⁰
- Here, we assessed the expression and safety of delandistrogene moxeparvovec administered in ≥2- to <3-year-old patients with DMD

Objectives

- To report delandistrogene moxeparvovec transduction efficiency, expression, and sarcolemmal localization, as well as preliminary safety outcomes, in ambulatory patients with DMD aged ≥2 to <3 years receiving delandistrogene moxeparvovec in Cohort 6 of the ENDEAVOR study and Cohort B of the ENVOL study

Methods

- ENDEAVOR is an ongoing, multi-cohort, open-label, Phase 1b clinical trial (NCT04626674; [Figure 1](#));¹¹ Cohort 6 enrolled ambulatory patients aged ≥2 to <3 years
- ENVOL is a multi-cohort, open-label, Phase 2 clinical trial (NCT06128564; [Figure 1](#));¹² Cohort B enrolled ambulatory patients aged ≥2 to <3 years
- Patients were treated with a single IV infusion of 1.33×10¹⁴ vg/kg (by linear qPCR) of delandistrogene moxeparvovec
- Patients in ENDEAVOR Cohort 6 and ENVOL Cohort B were not receiving corticosteroids at the time of screening but did receive corticosteroids from Day –7 to Day 60 after infusion which were then tapered ([Table 1](#))

Results

- At baseline, patients in ENDEAVOR Cohort 6 (N=6) and ENVOL Cohort B (N=3) had a mean (SD) age of 2.6 (0.3) and 2.1 (0.2) years, respectively ([Table 2](#))

Table 2 Baseline characteristics in the ≥2- to <3-year-old ambulatory patient population

Characteristics Mean (SD) (min, max)	ENDEAVOR Cohort 6 (N=6)	ENVOL Cohort B (N=3)
Age, years*	2.6 (0.3) (2.2, 2.9)	2.1 (0.2) (1.9, 2.3)
Dosing weight, kg	14.8 (1.8) (12.4, 17.8)	13.4 (1.3) (12.0, 14.6)
BMI, kg/m ²	18.5 (1.4) (17.2, 20.4)	18.3 (0.8) (17.3, 18.8)
Time since DMD diagnosis, months	20.9 (11.0) (5.6, 38.4)	16.6 (4.5) (11.9, 20.7)
LVEF, %†	63.1 (2.6) (61.0, 68.0)	67.7 (1.2) (67.0, 69.0)

*Age at screening. The patient aged 1.9 years at screening in the ENVOL study was aged ≥2 years at infusion. †Measured by ECHO.

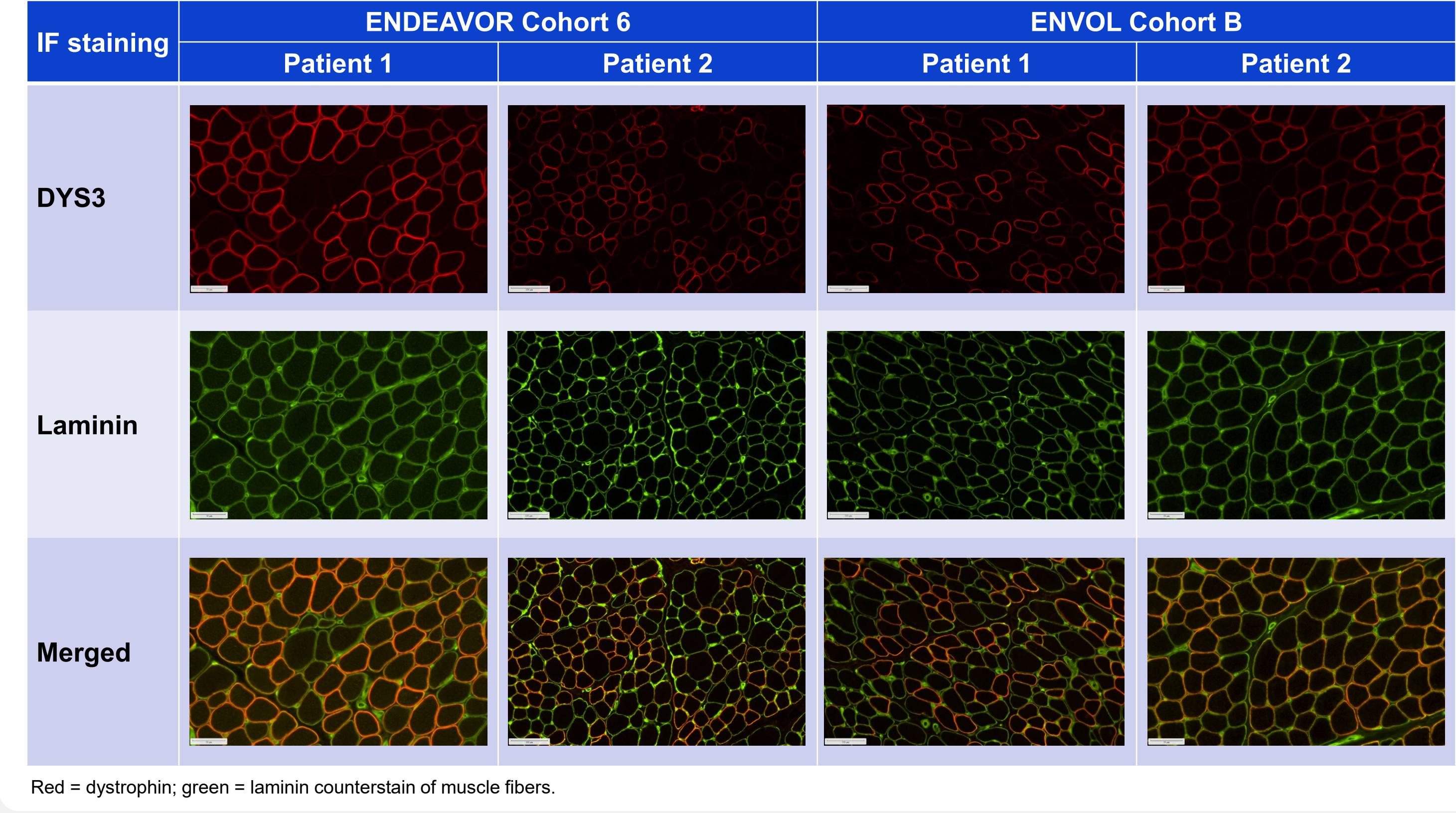
Delandistrogene moxeparvovec transduction efficiency, micro-dystrophin expression, and sarcolemmal localization

- For patients aged ≥2 to <3 years, in both ENDEAVOR Cohort 6 and ENVOL Cohort B, Week 12 muscle biopsies showed robust delandistrogene moxeparvovec transduction efficiency, micro-dystrophin expression, and localization to the sarcolemma ([Table 3](#); [Figure 2](#))

Table 3 Week 12 muscle biopsy outcomes in ambulatory ≥2- to <3-year-olds

Week 12 Mean (SD) (min, max)	ENDEAVOR Cohort 6 (N=6)	ENVOL Cohort B (N=3)
Vector genome copies, number per nucleus	4.5 (1.6) (2.0, 6.6)	5.3 (1.9) (4.0, 7.0)
Western blot, % control	93.9 (38.2) (48.6, 161.0)	72.8 (16.9) (56.0, 90.0)
PDPF, %	79.9 (19.8) (43.9, 98.4)	64.7 (8.6) (56.3, 73.5)

Figure 2 Examples of IF staining showing micro-dystrophin expression in ambulatory ≥2- to <3-year-old patients treated with delandistrogene moxeparvovec



Acknowledgments & Disclosures

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Figure 1 Study designs for ENDEAVOR Cohort 6 and ENVOL Cohort B

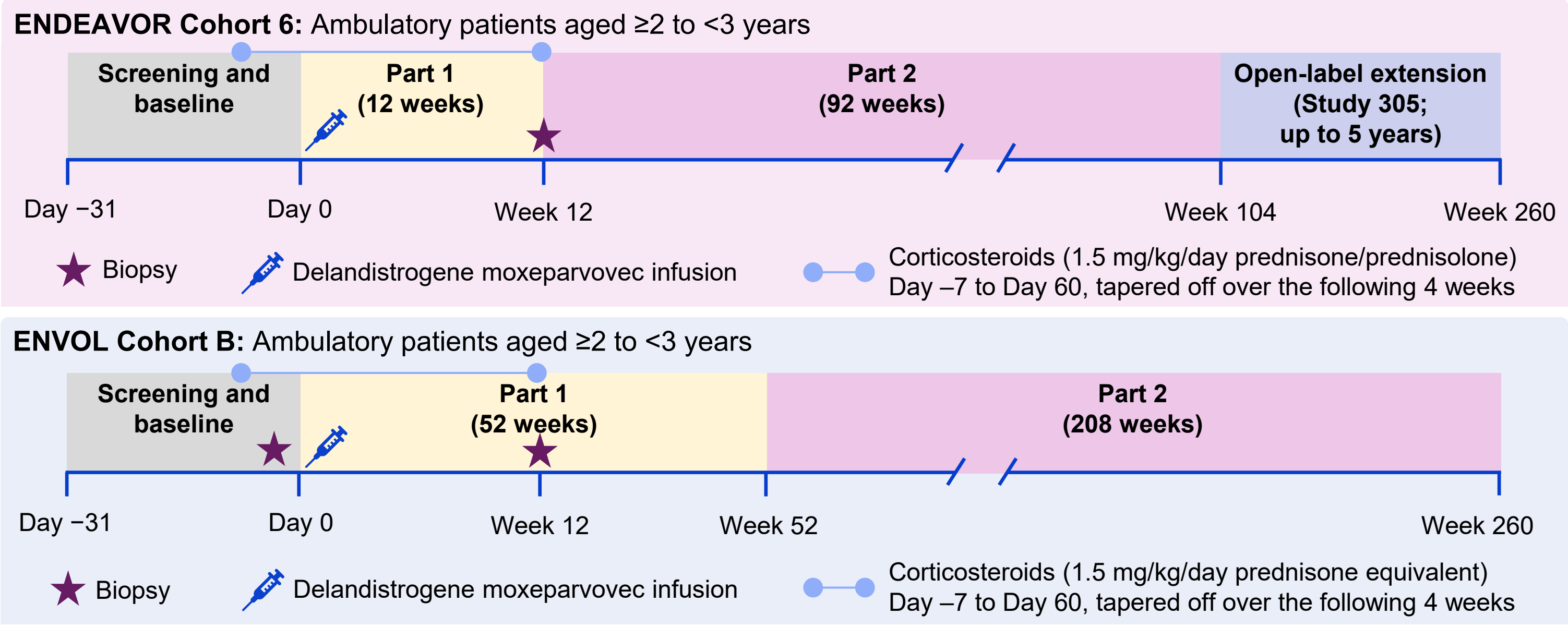


Table 1 Overview of inclusion and exclusion criteria for ENDEAVOR Cohort 6 and ENVOL Cohort B

	ENDEAVOR Cohort 6	ENVOL Cohort B
Inclusion criteria		
Age, years	≥2 to <3	≥2 to <3
Ambulatory status	Ambulatory	Able to cooperate with age-appropriate motor assessment testing
DMD mutations	Fully contained between exons 18 and 79 (mutations between or including exons 1–17 are not eligible)	Fully contained between exons 18 and 79 (mutations between or including exons 1–17 are not eligible)
rAAVrh74 antibody titers/levels	≤1:400	Not elevated
Corticosteroid use	Does not yet require use of chronic corticosteroids and is not receiving corticosteroids at the time of screening	Does not yet receive regular oral corticosteroids and does not plan to receive oral corticosteroids within 1 year of baseline
Exclusion criteria		
LVEF at screening	<40%	<50%

Safety overview

- Mean (SD; range) follow-up was 104.9 (1.6; 103.3–108.0) weeks in ENDEAVOR Cohort 6 (safety data cutoff: April 21, 2026) and 25.1 (1.1; 23.9–25.9) weeks in ENVOL Cohort B (safety data cutoff: August 4, 2025)
- There were no TR-SAEs, treatment-related deaths, or study discontinuations due to AEs ([Table 4](#))
- The first occurrence of most TR-TEAEs was within 60 days of delandistrogene moxeparvovec infusion*
- From Days 60–90, corticosteroids were tapered to mean (SD; range) doses of 0.88 (0.47; 0.56–1.81) and 0.76 (0.05; 0.70–0.79) mg/kg per day administered over mean (SD) durations of 22.3 (3.6) and 29.3 (1.2) days in ENDEAVOR Cohort 6 and ENVOL Cohort B, respectively

*As of April 21, 2026 and January 12, 2026 for ENDEAVOR Cohort 6 and ENVOL Cohort B, respectively.

Table 4 Safety overview in ambulatory ≥2- to <3-year-olds

Event	ENDEAVOR Cohort 6 (N=6)		ENVOL Cohort B (N=3)	
	Patients, n (%)	Events, n	Patients, n (%)	Events, n
TR-TEAEs	6 (100)	18	2 (66.7)	6
TR-SAEs	0 (0)	0	0 (0)	0
Treatment-related deaths*	0 (0)	0	0 (0)	0
Study discontinuations due to AEs	0 (0)	0	0 (0)	0

*Outside of the ENDEAVOR and ENVOL trials, to date, there have been two treatment-related deaths due to acute liver failure approximately 3 months post-infusion in non-ambulatory patients (one in the ENVISION trial and one in the commercial setting) at 15 and 16 years of age and in the advanced stage of DMD.¹³

- In ENDEAVOR Cohort 6, six patients (100%) experienced 18 TR-TEAEs ([Table 5](#))*
- In ENVOL Cohort B, two patients (66.7%) experienced six TR-TEAEs ([Table 5](#))*
- All TR-TEAEs were mild to moderate in severity

*As of April 21, 2026 and August 4, 2025 for ENDEAVOR Cohort 6 and ENVOL Cohort B respectively.

Table 5 TR-TEAEs following delandistrogene moxeparvovec infusion in ambulatory ≥2- to <3-year-olds

TR-TEAEs Events, n (%)	ENDEAVOR Cohort 6 (N=6)	ENVOL Cohort B (N=3)
Troponin I or T increased	1 (16.7)*	1 (33.3)†
Vomiting	5 (83.3)	1 (33.3)
Decreased appetite/hypophagia	3 (50.0)	1 (33.3)
ALT, AST, GGT, or GLDH increased	3 (50.0)‡	1 (33.3)§
Hematoma	–	1 (33.3)
Nausea	2 (33.3)	–
Constipation	1 (16.7)	–
Fatigue	1 (16.7)	–

*In the ENDEAVOR study, only troponin I was routinely measured and one confirmed event of increased troponin was reported at 3×ULN (1.7 µg/L). †In the ENVOL study, troponin I was routinely measured and troponin T was assessed as needed. Confirmed increases of troponin I and T were reported; however, these elevations were mild (maximum troponin I level 1.38×ULN [0.08 µg/L]; troponin T was from a local laboratory). ‡ALT >2×baseline (1053 U/L); AST >2×baseline (316 U/L); GGT >ULN (32 U/L) and >ULN (44 U/L). §Maximum GLDH level of >ULN (7.6 U/L).

Conclusions

- In ambulatory patients with DMD aged ≥2 to <3 years, robust micro-dystrophin expression and sarcolemmal localization were observed 12 weeks post-delandistrogene moxeparvovec infusion
- Higher overall mean and higher minimum delandistrogene moxeparvovec micro-dystrophin expression were observed in the ≥2 to <3-year-old patient population compared with previously observed results in older (≥4 years) ambulatory patients and non-ambulatory patient populations^{1,14}
- The safety of delandistrogene moxeparvovec in ambulatory patients aged ≥2 to <3 years was manageable with appropriate monitoring and consistent with the known safety profile in older ambulatory patients (≥4 years)¹⁴
- The findings of these studies are limited by the relatively small sample size, and assessing functional outcomes over time will provide important context for interpreting the clinical benefit of the observed findings
- Ongoing evaluation of patients treated before the age of 4 years in the ENDEAVOR and ENVOL studies will provide important insights into whether administration of delandistrogene moxeparvovec earlier in the DMD disease course may influence long-term patient outcomes^{11,12}

Abbreviations

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DMD, Duchenne muscular dystrophy; DYS3, monoclonal anti-dystrophin antibody; ECHO, echocardiogram; GGT, gamma-glutamyl transferase; GLDH, glutamate dehydrogenase; IF, immunofluorescence; IV, intravenous; LFT, liver function test; LVEF, left ventricular ejection fraction; PDPF, percent dystrophin-positive fibers; qPCR, quantitative polymerase chain reaction; rAAVrh74, recombinant adeno-associated virus, rheus isolate serotype 1A; SD, standard deviation; TR, SAE, treatment-related serious adverse event; TR-TEAE, treatment-related treatment-emergent adverse event; ULN, upper limit of normal.

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