Delandistrogene Moxeparvovec in Duchenne Muscular Dystrophy: Functional and Safety Outcomes up to 3 Years Post-Infusion in the EMBARK Study

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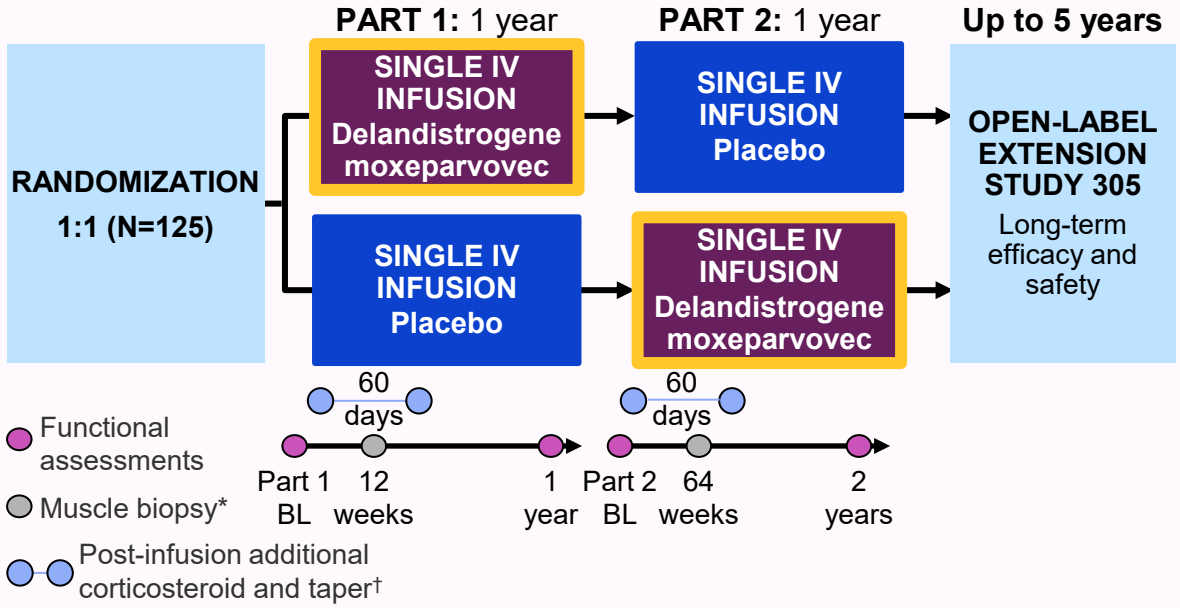
Background and Methods

Delandistrogene moxeparvovec is an rAAVrh74 vector-based gene transfer therapy that delivers a transgene encoding micro-dystrophin, an engineered, functional form of dystrophin shown to slow disease progression in ambulatory patients with DMD[1–4]

EMBARK study design[5]



Pre-defined external control cohort methodology[6]

3-year data were compared with an EC cohort of patients with DMD using propensity-score weighting[6‡]

- Patients receiving only corticosteroid regimens from the FOR-DMD,[7] BioMarin PRO-DMD-01,[8] and CINRG DNHS[9,10] studies were included[§]

EC cohort entry criteria:

- ✓ Aged ≥4 and <8 years
- ✓ NSAA total score ≥14 and ≤32
- ✓ TTR ≤5.75 seconds
- ✓ 10MWR time ≤6.85 seconds
- ✓ Stable dose of oral corticosteroids for ≥12 weeks
- ✓ Had both baseline and at least 1 post-baseline assessment value

- Propensity-score weighting[‡] was based on baseline[‖] age, NSAA total score, TTR, 10MWR, height, weight, and BMI

We report 3-year efficacy and safety outcomes of patients treated with delandistrogene moxeparvovec in EMBARK Part 1 compared with a matched EC cohort

*Only a subset of patients received a muscle biopsy for expression assessments, based on site experience and feasibility. †Starting the day before infusion, patients received additional corticosteroids (prednisone 1 mg/kg/day) in addition to their baseline stable corticosteroid dose. On Day 60, the additional corticosteroid dose was tapered over a 2-week period, after which patients continued their baseline stable dose for the remainder of the study. ‡Inverse probability of treatment weighting. §Per medical judgement, stable frequency of corticosteroid use includes daily corticosteroid use and all non-daily steroid regimens which have been shown to have comparable functional outcomes to daily corticosteroid use. Daily, every other day, and two-day high dose regimens have been shown to have comparable functional outcomes. However, an intermittent regimen of 10 days on/10 days off was shown to be less efficacious compared with daily steroid use so these patients were excluded from the EC cohort.[2,11–13] As patients had rolled over into the long-term follow-up study, unknown potential confounders related to real-world treatment, including concomitant medications and differences in steroid regimens, are a limitation of this analysis. ‖Propensity-score weighting involves taking an EC group with similar age and function, but unequal distribution, and ensuring overlap after propensity-score weighting. 10MWR, 10-meter Walk/Run; BL, baseline; BMI, body mass index; DMD, Duchenne muscular dystrophy; EC, external control; IV, intravenous; NSAA, North Star Ambulatory Assessment; rAAVrh74, recombinant adeno-associated virus rhesus isolate serotype 74; TTR, Time to Rise.

1. Mendell JR, et al. *Nat Med*. 2025; 31:332–341; 2. Mendell JR, et al. *Neurol Ther*. 2026; doi:10.1007/s40120-025-00879-8 (Online ahead of print); 3. Vandenborne K, et al. *JAMA Neurol*. 2025; 82:734–744; 4. Mendell JR, et al. *JAMA Neurol*. 2020; 77:1122–1131; 5. ClinicalTrials.gov. NCT05096221 (Accessed March 2026); 6. Mercuri E, et al. Presented at MDA 2025; Poster #P86; 7. ClinicalTrials.gov. NCT01603407 (Accessed March 2026); 8. ClinicalTrials.gov. NCT01753804 (Accessed March 2026); 9. ClinicalTrials.gov. NCT00468832 (Accessed March 2026); 10. Spurney C, et al. *Muscle Nerve*. 2014; 50:250–256; 11. Escolar DM, et al. *Neurology*. 2011; 77:444–452; 12. Fenichel GM, et al. *Arch Neurol*. 1991; 48:575–579; 13. Guglieri M, et al. *JAMA*. 2022; 327:1456–1468.

EMBARK Part 1: Demographics and Baseline Clinical Characteristics

Baseline characteristics were matched between patients receiving delandistrogene moxeparvovec in EMBARK Part 1 and EC patients **after propensity-score weighting***

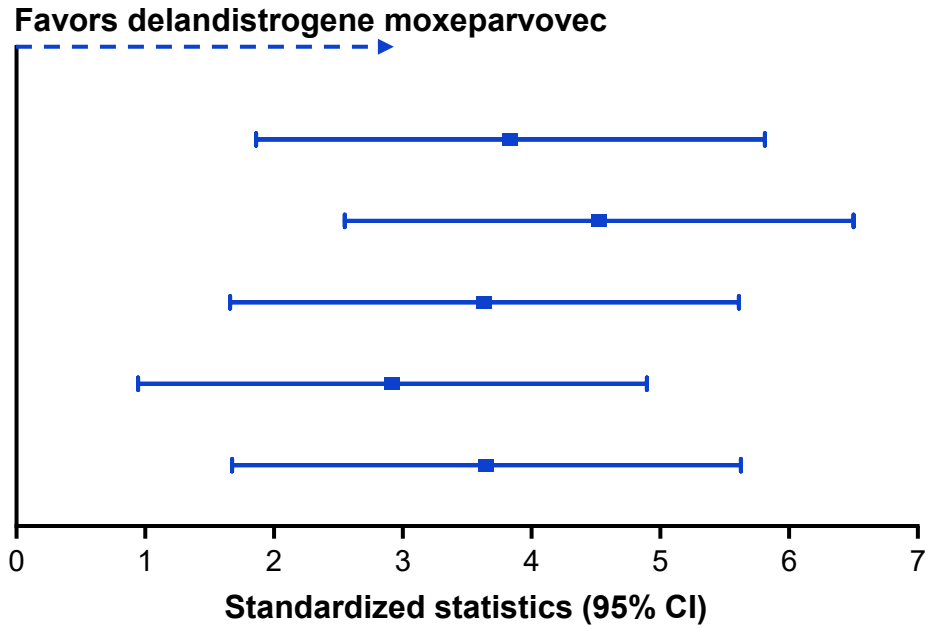
Characteristic, Mean (min, max)	EMBARK Part 1 Delandistrogene moxeparvovec (N=64)	EC cohort (N=143)†	Standardized mean difference after propensity-score weighting*
Age, years	5.98 (4.07, 7.87)	6.24 (4.24, 7.99)	–0.281
NSAA total score, points	23.3 (14, 32)	23.5 (15, 32)	–0.045
TTR, time in seconds	3.51 (1.85, 5.75)	3.52 (1.90, 5.70)	–0.011
10MWR, time in seconds	4.80 (3.20, 6.85)	4.78 (3.00, 6.70)	0.034
Weight, kg	21.20 (13.5, 37.4)	22.18 (14.0, 36.0)	–0.198
Height, cm	108.65 (93.5, 127.0)	110.60 (94.9, 131.1)	–0.285
BMI, kg/m^2	17.80 (13.69, 24.92)	17.90 (13.74, 23.64)	–0.042

*Inverse probability of treatment weighting.
†Prior to propensity-score weighting, there were 155 patients in the EC cohort who met the entry criteria and had at least one post-baseline visit (FOR-DMD, n=89; BioMarin PRO-DMD-01, n=41; CINRG DNHS, n=25).
10MWR, 10-meter Walk/Run; BMI, body mass index; EC, external control; NSAA, North Star Ambulatory Assessment; TTR, Time to Rise.

EMBARK Part 1: Functional Outcomes at 3 Years

At 3 years, Part 1-treated patients demonstrated **clinically meaningful, durable, and statistically significant functional benefit** versus a propensity-score-weighted EC cohort

Delandistrogene moxeparvovec, N=64*
EC cohort, N=143*



	LSM mean change difference (95% CI)†	*P*-value
NSAA	Δ 4.39 points (2.13 to 6.65)	*P*=0.0002
TTR	Δ –6.05 seconds (–8.69 to –3.41)	*P*<0.0001
RFF velocity	Δ 0.06 rise/second (0.028 to 0.097)	*P*=0.0004
10MWR	Δ –2.70 seconds (–4.51 to –0.88)	*P*=0.0039
10MWR velocity	Δ 0.36 meters/second (0.164 to 0.550)	*P*=0.0003

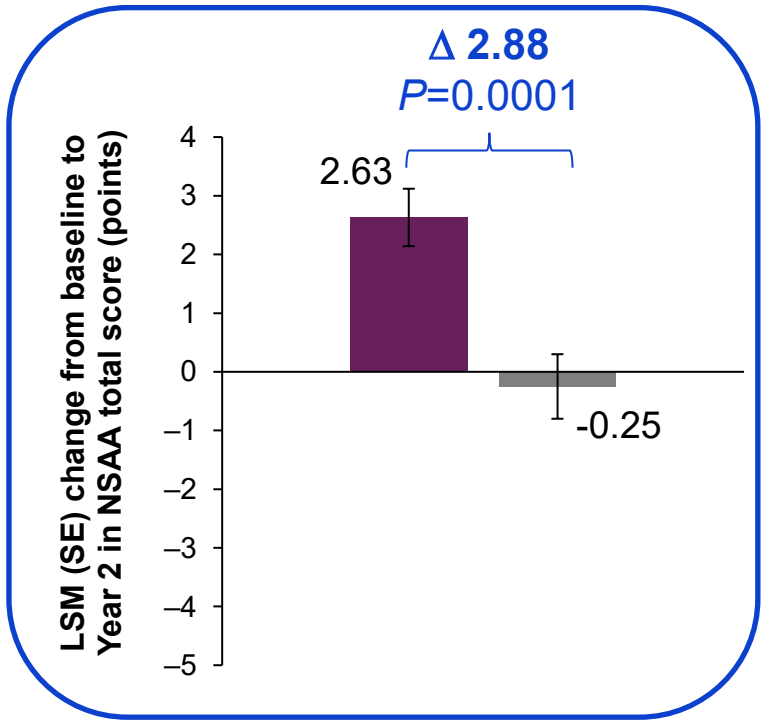
While the primary endpoint of change from baseline in NSAA total score versus placebo was not met at Year 1, both 2- and 3-year follow-up of Part 1-treated patients showed slowing of DMD disease progression versus a matched EC cohort[1,2]

*All 64 patients treated with delandistrogene moxeparvovec and all 143 patients in the EC cohort were included in the analyses; MMRM methods account for missing data in these analyses. Twelve patients treated with delandistrogene moxeparvovec in Part 1 did not have 3-year follow-up data. In the EC cohort, 70 patients had missing Year 3 data for NSAA, 10MWR, and 10MWR velocity assessments, and 65 patients had missing Year 3 data for TTR and RFF velocity assessments. †LSMs (of change from baseline) and CIs were standardized in the forest plot by dividing by the SE. Negative values for timed function tests (TTR and 10MWR) show an improvement in the time taken to achieve these endpoints. LSM differences are on original scale (without SE adjustment). Signs of timed function tests were reversed in the forest plot to align favorable directions among endpoints. Numerical results of LSM difference kept the original signs. All *P*-values are nominal and have not been adjusted for multiple comparisons. 10MWR, 10-meter Walk/Run; CI, confidence interval; DMD, Duchenne muscular dystrophy; EC, external control; LSM, least-squares mean; MMRM, Mixed Models for Repeated Measures; NSAA, North Star Ambulatory Assessment; RFF, rise from floor; SE, standard error; TTR, Time to Rise. 1. Mendell JR, et al. *Nat Med*. 2025; 31:332–341; 2. Mendell JR, et al. *Neurol Ther*. 2026; doi:10.1007/s40120-025-00879-8 (Online ahead of print).

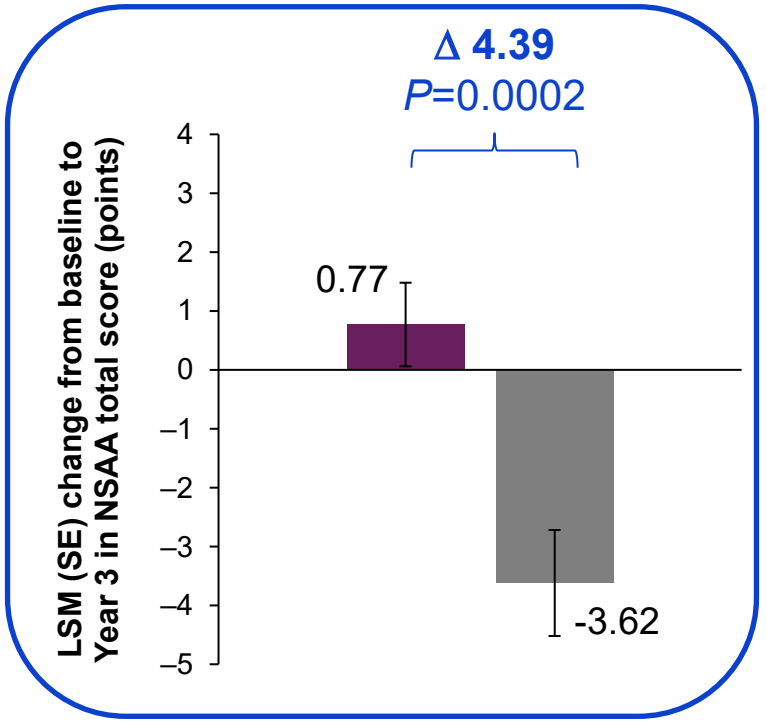
EMBARK Part 1: NSAA Outcomes at Year 2 and Year 3

The difference in NSAA total score between EMBARK Part 1-treated patients and the external control (EC) cohort increased from a **2.88-point difference at Year 2** to a **4.39-point difference at Year 3**

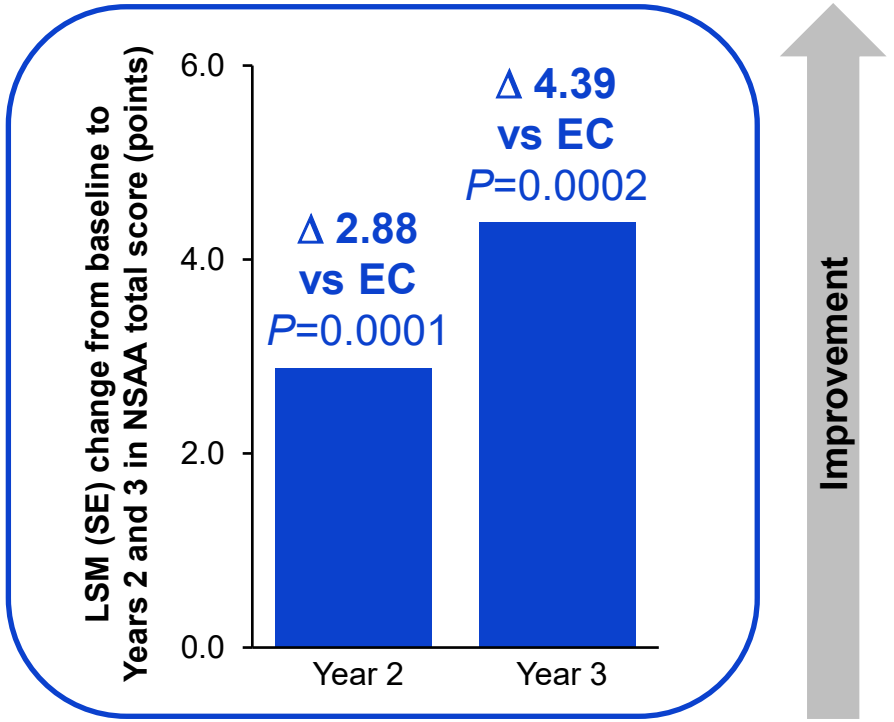
Year 2 versus EC[1]



Year 3 versus EC



Difference between treated and EC



Delandistrogene moxeparvovec, N=64* EC cohort, N=143*

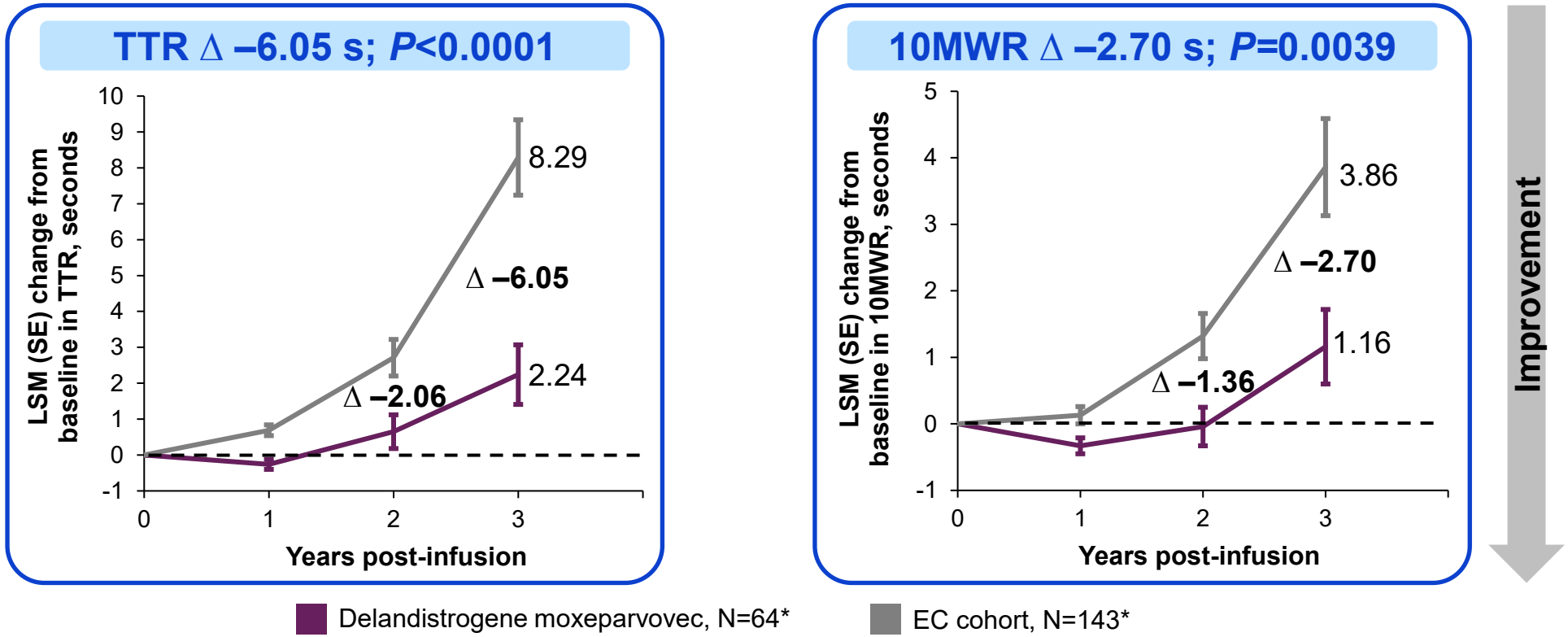
*All 64 patients treated with delandistrogene moxeparvovec and all 143 patients in the EC cohort were included in the analyses; MMRM methods account for missing data in these analyses. Twelve patients treated with delandistrogene moxeparvovec in Part 1 did not have 3-year follow-up data. In the EC cohort, 70 patients had missing Year 3 data for NSAA. All *P*-values are nominal and have not been adjusted for multiple comparisons.

EC, external control; LSM, least-squares mean; MMRM, Mixed Models for Repeated Measures; NSAA, North Star Ambulatory Assessment; SE, standard error.

1. Mendell JR, et al. *Neurol Ther.* 2026; doi:10.1007/s40120-025-00879-8 (Online ahead of print).

EMBARK Part 1: Other Functional Outcomes at 3 Years

At 3 years, Part 1-treated patients demonstrated **clinically meaningful, durable, and statistically significant functional benefit** versus a propensity-score-weighted EC cohort



*All 64 patients treated with delandistrogene moxeparvovec and all 143 patients in the EC cohort were included in the analyses; MMRM methods account for missing data in these analyses. Twelve patients treated with delandistrogene moxeparvovec in Part 1 did not have 3-year follow-up data. Two patients in EMBARK Part 1 lost ambulation between Year 2 and Year 3. In the EC cohort, 70 patients had missing Year 3 data for 10MWR assessments, and 65 patients had missing Year 3 data for TTR assessments. All *P*-values are nominal and have not been adjusted for multiple comparisons.

10MWR, 10-meter Walk/Run; EC, external control; NSAA, North Star Ambulatory Assessment; SE, standard error; TTR, Time to Rise.

EMBARK Part 1: Cardiac Data at 3 Years

LVEF and LV fractional shortening **do not indicate any cardiac safety signals** over 3 years of follow-up in EMBARK Part 1-treated patients

Mean (SD)	N	Baseline	Year 1	Year 2	Year 3
ECHO LVEF, %	50	65.3 (5.7)	65.2 (5.0)	64.5 (6.9)	60.5 (3.6)
ECHO LV fractional shortening, %	49	35.5 (4.5)	36.1 (6.4)	36.8 (8.2)	35.5 (3.6)

ECHO, echocardiogram; LV, left ventricular; LVEF, left ventricular ejection fraction.

EMBARK Part 1: Overview of 3-Year Safety Results

No new safety signals were observed between Years 2 and 3; AEs typically begin within the first 90 days post-infusion[1,2]

Overview of AEs, n (%)	Baseline to Year 1 N=63	Year 1 to Year 2* N=63	Year 2 to Year 3* N=58
Patients with any TEAEs	62 (98.4)	53 (84.1)	37 (63.8)
Patients with any SAEs	14 (22.2)	5 (7.9)	4 (6.9)
Patients with any TR-TEAEs	48 (76.2)	15 (23.8)	2 (3.4)
Number of TR-TEAEs	235	34	2†
Patients with any TR-SAEs	7 (11.1)	1 (1.6)	0 (0)
AEs leading to study discontinuation	0 (0)	0 (0)	0 (0)
Treatment-related deaths	0 (0)	0 (0)	0 (0)‡

*New events between Years 1 and 2 and Years 2 and 3, respectively (excludes ongoing events that began during the previous time period)

Between Years 2 and 3, there was a lower frequency of TR-TEAEs than during baseline to Year 2, and no TR-SAEs were reported

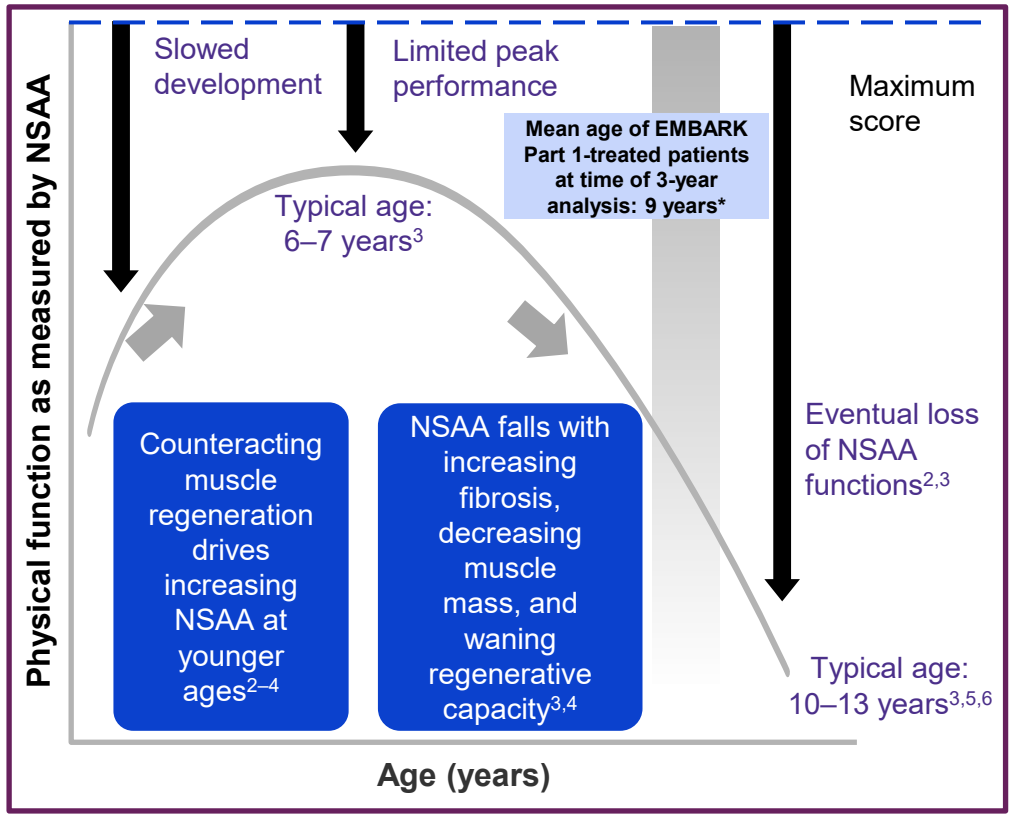
†Two TR-TEAEs of troponin-I increased. ‡One death assessed as unrelated to treatment was reported in a 9-year-old patient 931 days post-treatment.
AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TR-SAE, treatment-related serious adverse event; TR-TEAE, treatment-related treatment-emergent adverse event.
1. Mendell JR, et al. *Nat Med*. 2025; 31:332–341; 2. Mendell JR, et al. *Neurol Ther*. 2026; doi:10.1007/s40120-025-00879-8 (Online ahead of print)

EMBARK Part 1: Conclusions at 3-years post-infusion

Patients **aged 7–10 years** (treated in Part 1 at ≥4 to <8 years of age) demonstrated:

- **Clinically meaningful and durable functional benefits** compared with a matched EC cohort
- Evidence of a **widening treatment effect** between Years 2 and 3, consistent with **increasing divergence from natural history**
- **Slowing of DMD progression**, consistent with earlier observations of **reduced muscle damage** as measured by MRI[1]

- **No new safety signals** between Years 2 and 3
- The delandistrogene moxeparvovec safety profile remained **consistent with prior experience** and **manageable with appropriate monitoring**



*At time of last assessment.

DMD, Duchenne muscular dystrophy; EC, external control; MRI, magnetic resonance imaging; NSAA, North Star Ambulatory Assessment.

1. Vandenborne K, et al. *JAMA Neurol*. 2025; 82:734–744; 2. McDonald CM, et al. *Lancet*. 2018; 391:451–456; 3. Muntoni F, et al. *PLoS One*. 2019; 14:e0221097; 4. Rooney WD, et al. *Neurology*. 2020; 94:e1622–e1633; 5. Emery AEH. *Lancet*. 2002; 359:687–689; 6. Niks EH and Aartsma-Rus A. *Expert Opin Biol Ther*. 2017; 17:225–236.

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Disclosures

- JRM received study funding from Sarepta Therapeutics, Inc. while at Nationwide Children's Hospital at the time of the study and is currently an employee of Sarepta Therapeutics, Inc. JRM is a co-inventor of AAVrh74.MHCK7.micro-dys technology.
- FM has received honoraria and grants from Sarepta Therapeutics, Inc. for participating in symposia and advisory boards and is involved as an investigator in Sarepta Therapeutics, Inc. clinical trials. He reports participation in advisory boards for Novartis, F. Hoffmann-La Roche Ltd, Edgewise Therapeutics, Dyne Therapeutics, Pfizer, PTC Therapeutics, and Italfarmaco.
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- EMM has received fees from AveXis, Biogen, and F. Hoffmann-La Roche Ltd.
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- CL-A is an investigator in Sarepta Therapeutics, Inc. clinical trials and a sub-investigator in studies sponsored by Pfizer, Solid BioSciences, Edgewise Therapeutics, Italfarmaco, and Genentech/Roche.
- AN has received fees from AveXis, Biogen, and F. Hoffmann-La Roche Ltd.
- CP participates in an advisory board and is a consultant for Biogen, Sarepta Therapeutics, Inc., AveXis/Novartis Gene Therapies, Genentech/Roche, and Scholar Rock; serves as a speaker for Biogen; and is a principal investigator of studies sponsored by AveXis/Novartis Gene Therapies, AMO Pharma, Astellas, Biogen, CSL Behring, Fibrogen, PTC Therapeutics, Pfizer, Sarepta Therapeutics, Inc., and Scholar Rock.
- US-S has received honoraria for counselling and participating in invited talks from Sarepta Therapeutics, Inc. and F. Hoffmann-La Roche Ltd.
- AV has a consultancy/advisory role with AMO Pharma, AveXis, Biogen, Edgewise Therapeutics, FibroGen, Novartis, Pfizer, PTC Therapeutics, Sarepta Therapeutics, Inc., UCB Pharma, Catalyst, and Scholar Rock; has received research funding from AMO Pharma, Capricor Therapeutics, Edgewise Therapeutics, FibroGen, the Muscular Dystrophy Association, Novartis, Parent Project Muscular Dystrophy, Pfizer, RegenxBio, and Sarepta Therapeutics, Inc.; and has other relationship(s) with MedLink Neurology for editorial services.
- CMZ has received research support from Biogen and Novartis and has served on an advisory board for Sarepta Therapeutics, Inc.
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- APM, CR (at time of submission), and COT are employees of Roche Products Ltd and may have stock options in F. Hoffmann-La Roche Ltd.
- MG and MM are employees of F. Hoffmann-La Roche Ltd and may have stock options.
- LRR-K is an employee of Sarepta Therapeutics, Inc. and may have stock options. In addition, she is a co-inventor of AAVrh74.MHCK7.micro-dys technology.