Supplementary Material: Two-year outcomes following delandistrogene moxeparvovec treatment in ambulatory patients with Duchenne muscular dystrophy: Phase 3 EMBARK trial

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[a]Sites were activated but did not enroll any patients. IEC, Independent Ethics Committee; IRB, Institutional Review Board.

Table S1. Corticosteroid entry criteria for the EC cohort

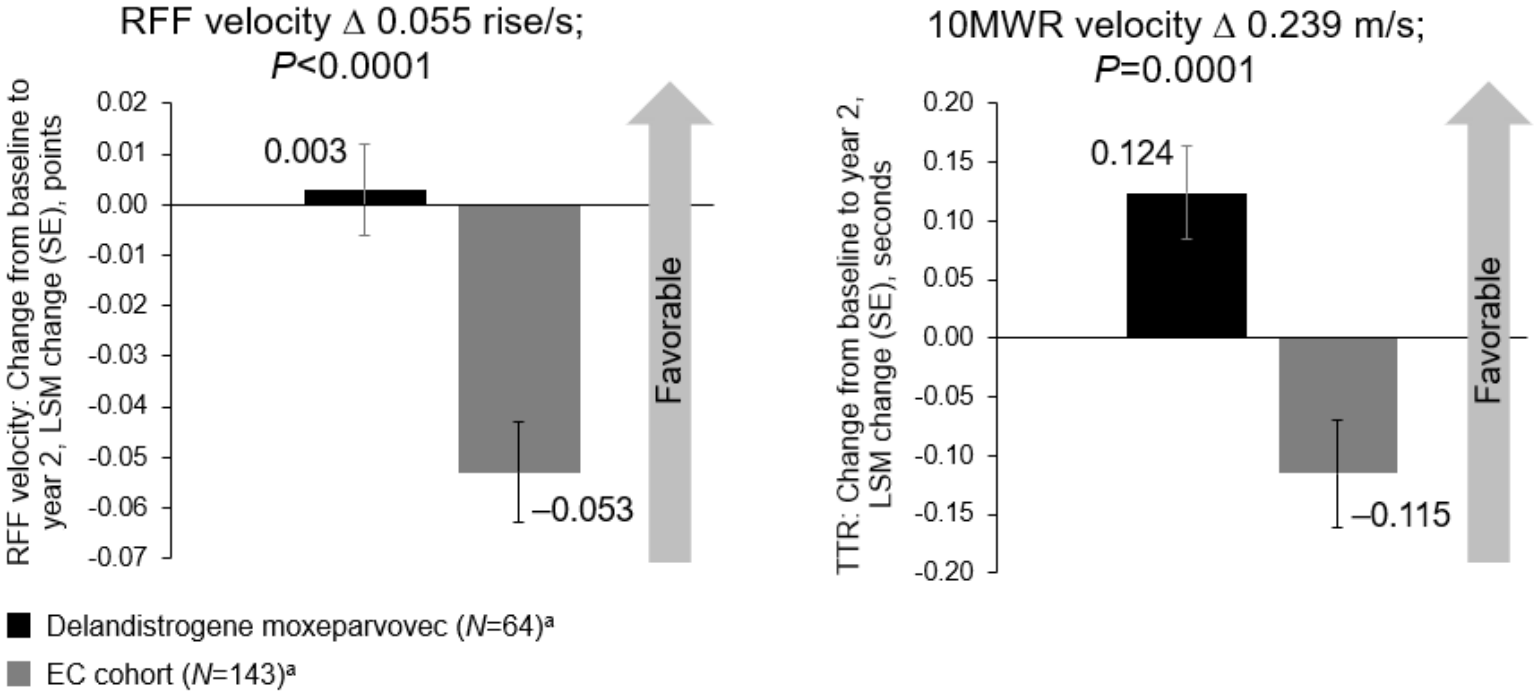
EC study	Corticosteroid entry criterion algorithm
FOR-DMD (NCT01603407)	• Stable use of oral corticosteroid duration ≥12 weeks prior to the re-baseline date • Patients on 10 day on/10 day off regimen were excluded (as not considered as stable dose) • Remaining patients were on stable dose of oral corticosteroids (i.e. daily prednisone [0.75 mg/kg/day], daily deflazacort [0.9 mg/kg/day])
PRO-DMD-01 (NCT01753804)	• Corticosteroid records for DMD use were first identified with medical adjudication • Stable use of oral corticosteroid duration ≥12 weeks prior to the re-baseline date • Any gaps in steroid treatment >30 days were excluded • After above steps, corticosteroid duration was calculated based on start/end study date of medication
CINRG DNHS (NCT00468832)	• Stable use of oral corticosteroid duration ≥12 weeks prior to the re-baseline • All routes were assumed to be oral as route information was not collected • Any gaps in steroid treatment >30 days were excluded • Corticosteroid duration was calculated based on start/end study day of medication

Multiple regimens of corticosteroids (frequency of dosing) have been used as standard of care for patients with DMD. However, published longitudinal studies have shown that not all regimens lead to equivalent changes in functional outcomes. Daily, every other day, and two-day high dose regimens have been shown to have comparable functional outcomes [1, 2].

However, an intermittent regimen of 10 days on/10 days off was shown to be less efficacious compared with daily steroid use [3]. No literature exists supporting comparability of other, less commonly used regimens (e.g. 7 days on 7 days off). Therefore, 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.

DMD, Duchenne muscular dystrophy.

Fig. S1. Change from baseline to year 2 in RFF velocity and 10MWR velocity compared with the EC cohort



[a]All 64 delandistrogene moxeparvovec-treated patients and all 143 EC patients were included in the analyses; MMRM methods account for missing data in these analyses. One delandistrogene moxeparvovec Part 1-treated patient did not have 2-year follow-up data. In the EC cohort, 29, 28, and 30 patients had missing Year 2 data for NSAA, TTR, and 10MWR assessments, respectively.

All *P*-values reported are nominal and have not been adjusted for multiple comparisons.

10MWR, 10-meter Walk/Run; EC, external control; LSM, least-squares mean; MMRM, mixed effects models for repeated measures; RFF, rise from floor; SE, standard error; TTR, Time to Rise.

References

1. Escolar DM, Hache LP, Clemens PR, et al. Randomized, blinded trial of weekend vs daily prednisone in Duchenne muscular dystrophy. Neurology. 2011; 77:444-52.
2. Fenichel GM, Mendell JR, Moxley RT, 3rd, et al. A comparison of daily and alternate-day prednisone therapy in the treatment of Duchenne muscular dystrophy. Arch Neurol. 1991; 48:575-9.
3. Guglieri M, Bushby K, McDermott MP, et al. Effect of Different Corticosteroid Dosing Regimens on Clinical Outcomes in Boys With Duchenne Muscular Dystrophy: A Randomized Clinical Trial. JAMA. 2022; 327:1456-68.