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Caregiver Global Impressions of Delandistrogene Moxeparvovec in Participants with Duchenne Muscular Dystrophy: Findings from EMBARK 2-year Follow-up

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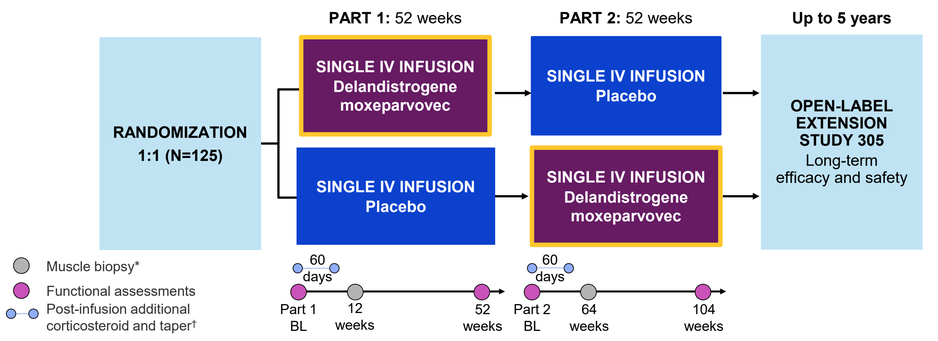
Background

- 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 ambulatory patients with DMD[1–4]
- Delandistrogene moxeparvovec is approved for the treatment of DMD in the USA and in other select countries[5,6]
- EMBARK (NCT05096221) is a two-part Phase 3 study assessing delandistrogene moxeparvovec safety and efficacy in ambulatory patients with DMD aged ≥4–<8 years (**Figure 1**)
  - In EMBARK Part 1, caregivers reported tangible improvements in disease status (specifically DMD symptoms, physical ability, ability to perform daily activities, and overall health) assessed using the CaGI-C and CaGI-S scales,[7] 1 year after delandistrogene moxeparvovec versus placebo infusion[8]

Figure 1 *EMBARK study design*



*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.

Objectives

- To present 2-year caregiver-reported outcomes from the overall population treated with delandistrogene moxeparvovec in Part 1 and Part 2 of the EMBARK study, assessed using the CaGI-C and CaGI-S scales

Methods

CaGI-C: Caregiver Global Impression of Change

- CaGI-C assessments included four separate questions to evaluate: DMD symptoms; physical ability; ability to perform daily activities; and overall health
- Responses were rated on a 7-point Likert scale (no baseline)
- Score values reported by caregivers at Weeks 52 and 104 represented the perceived change from baseline in the CaGI-C domain

CaGI-S: Caregiver Global Impression of Severity

- CaGI-S assessments included four separate questions to evaluate: DMD symptoms; impairments in physical ability; ability to perform daily activities; and overall health
- Responses were rated on a 5-point Likert scale
- Change scores from baseline were computed for each domain and measured the caregiver assessment of change in symptoms and their impact from baseline to Week 52 (Part 1), and from Week 52 to Week 104 (Part 2)
  - Negative scores indicate improvement and positive scores indicate worsening

Analyses

- Analyses were conducted using MDRI, a test for marginal homogeneity, and ordinal regression analyses
- **MDRI:**[9] Analysis of summed response scores (improvement, maintained, deteriorated) across CaGI items
  - Comparison of Part 1 and Part 2 results (paired t-test) separately for the populations treated in Part 1 and Part 2
- **Test for marginal homogeneity (Bhapkar test):**[10] Assessed any differences in the overall distribution of responses between the two groups (matched-pair polytomous data)
  - Delandistrogene moxeparvovec Part 1 versus placebo Part 2 and placebo Part 1 versus delandistrogene moxeparvovec Part 2
- **Ordinal regression analyses (proportional odds model):**[11] Tested if the odds of improving or worsening at Week 104 were linked to treatment (Part 1 vs. Part 2) controlling for age (4–5 vs. 6–7 years) and baseline symptom severity (for CaGI-S)

Results

- Overall, 63 and 60 participants were treated with delandistrogene moxeparvovec in Part 1 and Part 2 of the EMBARK study, respectively
- For CaGI-C, caregiver responses at 2 years were collected for 56 and 52 participants treated with delandistrogene moxeparvovec in Part 1 and Part 2 of EMBARK, respectively
  - For CaGI-S, caregiver responses were collected for 51 and 50 participants, respectively
- Baseline and demographic data from the EMBARK study have been previously described[1]

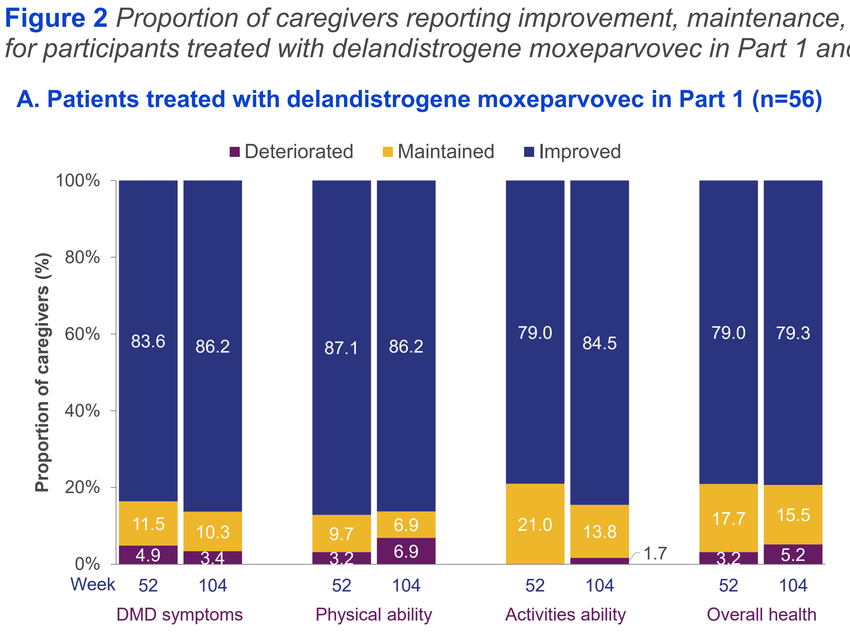
CaGI-C scores between Week 52 and Week 104

- **For participants treated with delandistrogene moxeparvovec in Part 1 (n=56),** caregivers observed that the benefits seen with delandistrogene moxeparvovec persisted up to 2 years post-infusion (**Figure 2A**)
  - CaGI-C scores across all domains indicated persistent and stabilized benefits between Weeks 52 and 104
  - There was no nominally significant difference in the summed response scores across all CaGI-C domains at Week 104 versus Week 52 (difference: –0.1; 95% CI –0.6–0.4; *P*=0.61)
  - The Bhapkar test showed no nominally significant difference in the caregiver response distribution between Week 52 and Week 104
- **For participants treated with placebo in Part 1 and delandistrogene moxeparvovec in Part 2 (n=52),** caregivers reported improvements across all CaGI-C domains 1 year post-delandistrogene moxeparvovec infusion (**Figure 2B**)
  - When comparing CaGI-C scores at Week 104 (52 weeks post-infusion) versus Week 52 (baseline), there was a nominally significant improvement in the summed response scores across the four domains from Week 52 to Week 104 (difference: 1.5; 95% CI 0.6–2.4; *P*<0.001)
  - The Bhapkar test showed a nominally significant difference in caregiver response distribution between Week 52 and Week 104
- Across all CaGI-C domains, 1-year changes reported by caregivers were similar for participants treated with delandistrogene moxeparvovec in Part 1 and Part 2 (**Figure 3**)
- Across all CaGI-C domains, the odds of caregiver-reported improvement were similar between participants treated in Part 1 and participants treated in Part 2 (OR 1.0–1.6) (**Table 1**)

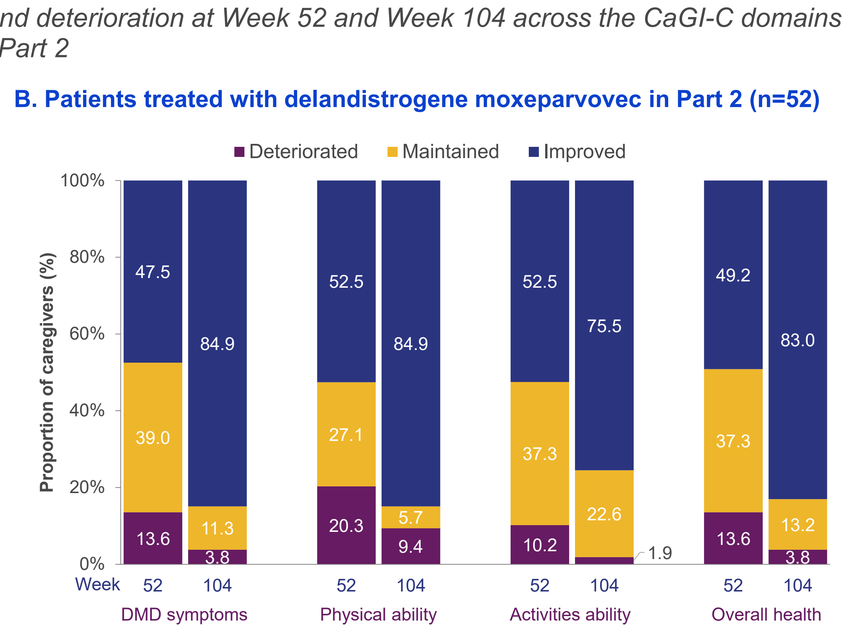
CaGI-S scores between Week 52 and Week 104

- For CaGI-S, similar results were observed to those seen for CaGI-C (see the **Supplementary Information** at the QR code)
- Across all CaGI-S domains, 1-year changes reported by caregivers were similar for participants treated with delandistrogene moxeparvovec in Part 1 and Part 2

Figure 2 *Proportion of caregivers reporting improvement, maintenance, and deterioration at Week 52 and Week 104 across the CaGI-C domains for participants treated with delandistrogene moxeparvovec in Part 1 and Part 2*



No nominally significant difference between Part 1 and Part 2 for summed response scores across all four domains: **M=–0.1 (95% CI –0.6–0.4); *P*=0.61**



Nominally significant difference between Part 1 and Part 2 for summed response scores across all four domains: **M=1.5 (95% CI 0.6–2.4); *P*<0.001**

Figure 3 *Proportion of caregivers reporting improvement, maintenance, and deterioration across the CaGI-C domains 1 year post-infusion for participants treated with delandistrogene moxeparvovec in Part 1 versus Part 2*

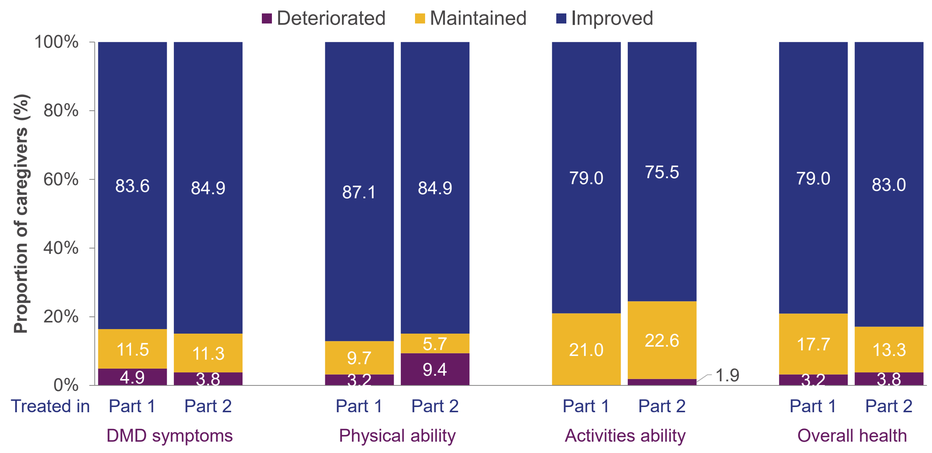


Table 1 *Odds of improvement across the CaGI-C domains at 1 year post-infusion for participants treated with delandistrogene moxeparvovec in Part 1 versus Part 2*

CaGI-C domain	OR* (95% CIs)	*P*-value
DMD symptoms	1.2 (0.6–2.3)	0.6482
Physical ability	1.0 (0.5–2.0)	0.9757
Ability to perform daily activities	1.6 (0.8–3.1)	0.2026
Overall health	1.2 (0.6–2.3)	0.6240

*OR for treatment with delandistrogene moxeparvovec in Part 1 versus treatment with delandistrogene moxeparvovec in Part 2.

Conclusions

- Treatment-related benefits were observed when using caregiver reports of participants' DMD symptoms, physical activity, daily activities, and overall health after receiving delandistrogene moxeparvovec
- At 2 years post-delandistrogene moxeparvovec infusion, caregivers reported maintenance of clinical improvements reported at 1 year post-infusion
- Consistency in caregiver-reported improvements was observed for participants treated with delandistrogene moxeparvovec in Part 1 and Part 2
- Parental perceptions provide insights beyond clinician-reported and performance-based outcomes, offering a complementary perspective on treatment impact

Acknowledgments & Disclosures

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Abbreviations

BL, baseline; CaGI-C, Caregiver Global Impression of Change; CaGI-S, Caregiver Global Impression measures of Severity; CI, confidence interval; DMD, Duchenne muscular dystrophy; IV, intravenous; MDRI, multi-domain responder index; OR, odds ratio; rAAVrh74, recombinant adeno-associated virus rhesus isolate serotype 74.

References

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.** US Food and Drug Administration. ELEVIDYS® Highlights of prescribing information. https://www.fda.gov/media/169679/download (Accessed March 2026); **6.** Jolly H, et al. *Lancet*. 2025; 405:1572–1573; **7.** Staunton H, et al. *Health Qual Life Outcomes*. 2021; 26:184; **8.** Audhya I, et al. *Neurol Ther*. 2026; 15:41–60; **9.** Tandon PK, et al. *Orphanet J Rare Dis*. 2021; 16:183; **10.** Bhapkar VP. *J Am Stat Assoc*. 1966; 61:228–235; **11.** McDonald CM, et al. *Neurol Ther*. 2025; 14:211–225.

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Supplementary information

CaGI-S scores between Week 52 and Week 104

MDRI

- For participants treated with delandistrogene moxeparvovec in Part 1 (n=51), caregivers reported marginal progression of severity of impairments and impacts over Part 2; however, the difference in the summed scores across the CaGI-S domains did not reach nominal significance (difference: –0.9; 95% CI –1.8–0.0; *P*=0.051) (**Supplementary Figure 1A**)
- For participants treated with placebo in Part 1 and delandistrogene moxeparvovec in Part 2 (n=50), caregivers reported reduction in severity of symptoms and impacts following treatment with delandistrogene moxeparvovec compared with Part 1; however, the difference in the summed scores across the CaGI-S domains did not reach nominal significance (difference: 1.0; 95% CI –0.1–2.1; *P*=0.07) (**Supplementary Figure 1B**)
- Across all CaGI-S domains, 1-year changes in severity reported by caregivers were similar for participants treated with delandistrogene moxeparvovec in Part 1 and Part 2 (**Supplementary Figure 2**)

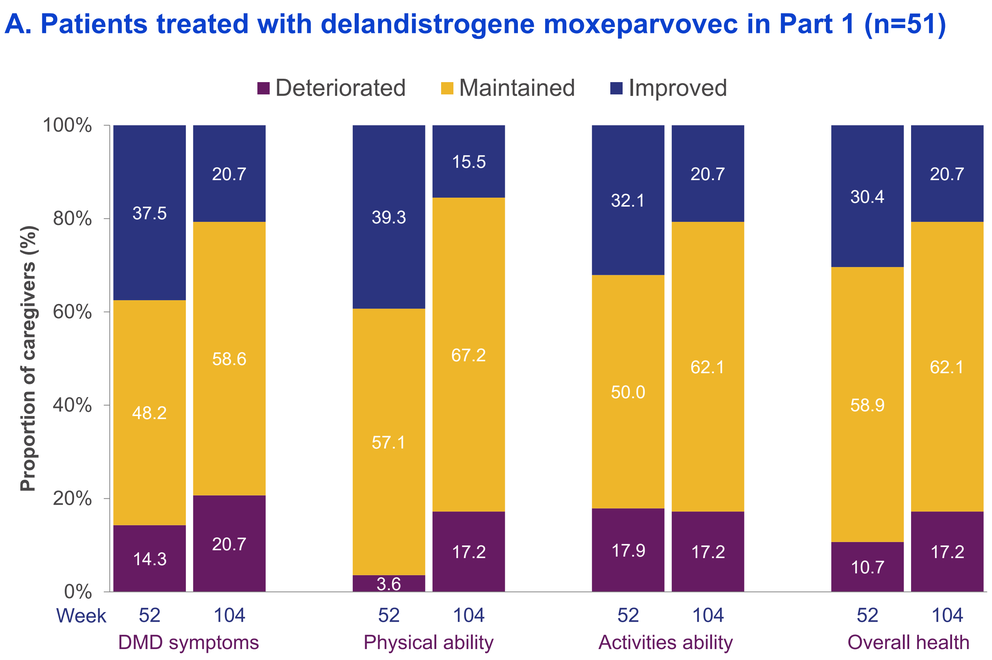
Bhapkar

- For participants treated with delandistrogene moxeparvovec in Part 1 or Part 2, the Bhapkar test showed no nominally significant change in the caregiver response distribution between Week 52 and Week 104

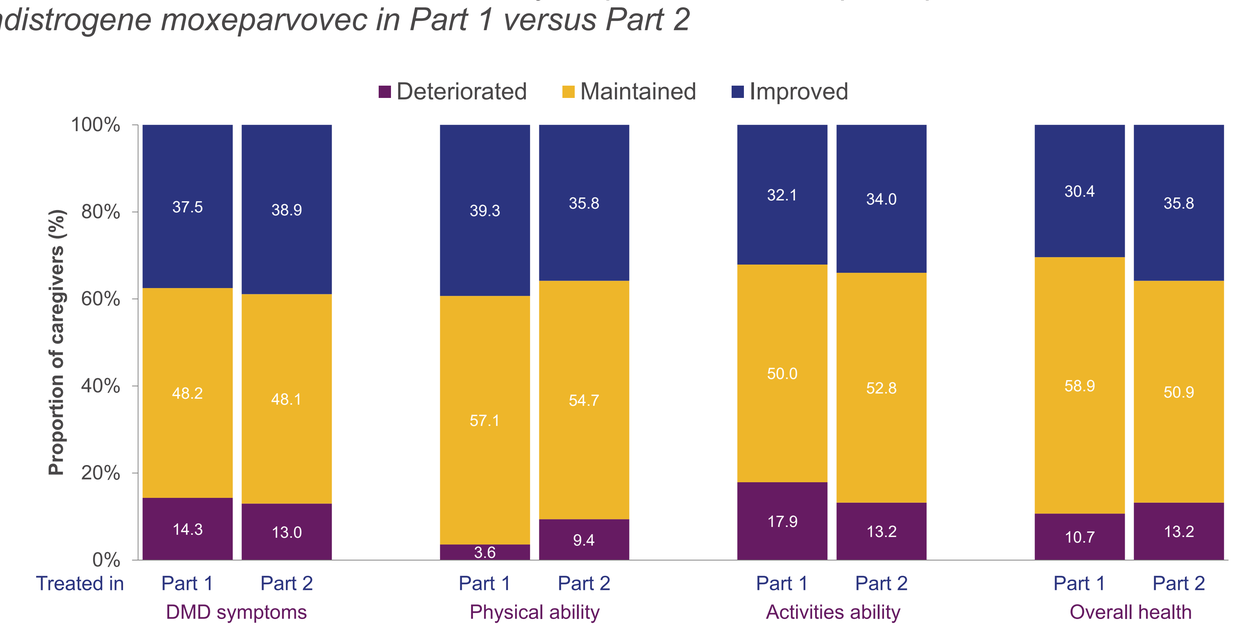
Ordinal regression

- No nominally significant differences were observed when comparing CaGI-S scores 1-year post-infusion in participants receiving treatment in Part 1 versus Part 2 (OR 1.1–1.5) (**Supplementary Table 1**)

Supplementary Figure 1 *Proportion of caregivers reporting improvement, maintenance, and deterioration at Week 52 and Week 104 across the CaGI-S domains for participants treated with delandistrogene moxeparvovec in Part 1 and Part 2*



Supplementary Figure 2 *Proportion of caregivers reporting improvement, maintenance, and deterioration across the CaGI-S domains 1 year post-infusion for participants treated with delandistrogene moxeparvovec in Part 1 versus Part 2*



Supplementary Table 1 *Odds of improvement across the CaGI-S domains at 1 year post-infusion for participants treated with delandistrogene moxeparvovec in Part 1 versus Part 2*

CaGI-S domain	OR* (95% CIs)	*P*-value
DMD symptoms	1.2 (0.6–2.5)	0.6481
Physical ability	1.3 (0.6–2.7)	0.5526
Ability to perform daily activities	1.1 (0.5–2.3)	0.8475
Overall health	1.5 (0.7–3.1)	0.3166

*OR for treatment with delandistrogene moxeparvovec in Part 1 versus treatment with delandistrogene moxeparvovec in Part 2.

Abbreviations

CaGI-S, Caregiver Global Impression of Severity; CI, confidence interval; DMD, Duchenne muscular dystrophy; MDRI, multi-domain responder index; OR, odds ratio.