Comparative analysis of long-term effectiveness of vamorolone vs standard of care glucocorticoid (SoC-GC) treatment in boys with DMD

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Background

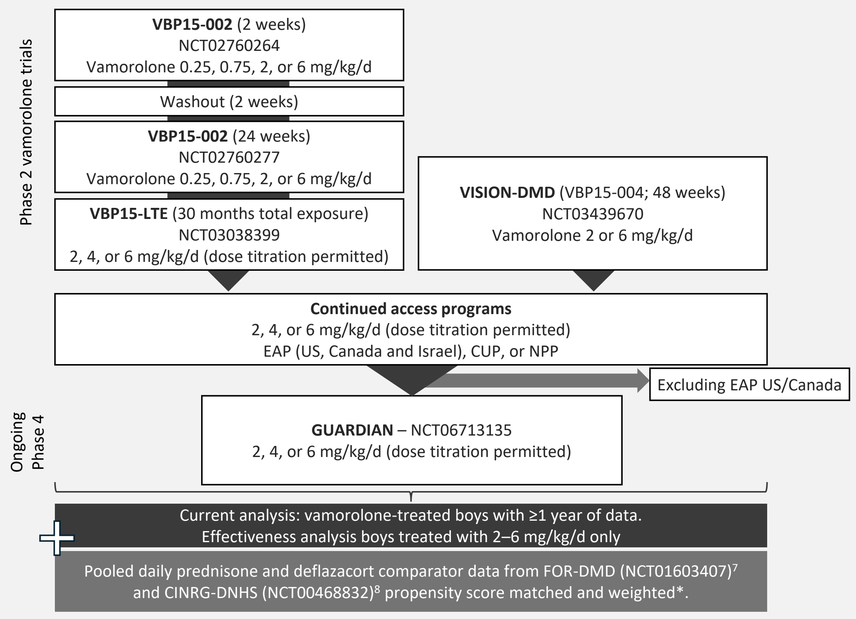
- Vamorolone is a first-in-class dissociative steroid approved for the treatment of Duchenne muscular dystrophy (DMD), including in the United States, the European Union, and the United Kingdom.[1–3,a]
- To date, the safety and efficacy of vamorolone has been well established in treatment-naïve boys with DMD up to 30 months of treatment in Phase 2 trials.[4–6]

Objective

- To assess long-term vamorolone effectiveness, via time to loss of ambulation, and anthropometric changes using longitudinal data from patients enrolled in Phase 2 studies who continued to receive treatment in continued access programs up to inclusion in the Phase 4 GUARDIAN trial, compared with historical data for daily classic corticosteroids (CS; deflazacort or prednisone).
  - *Additional bone health outcomes are presented at Poster 62 S.*
  - *See Poster 66 S for more information about GUARDIAN.*

Methods

Figure 1. Data sources

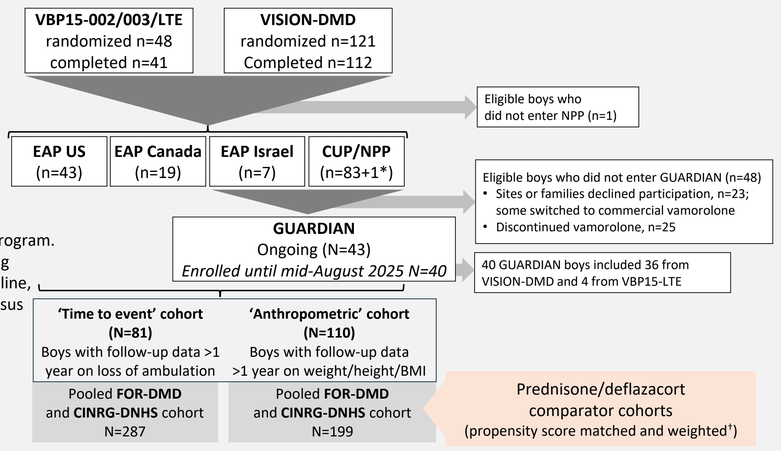


*Propensity score matching criteria: age at start of treatment, age at baseline, and geographical location (North America versus Europe).
CINRG-DNHS, Cooperative International Neuromuscular Research Group Duchenne Natural History Study; CUP, compassionate use program; EAP, expanded access program; FOR-DMD, Finding the Optimum Regimen for Duchenne Muscular Dystrophy; NPP, named patient program; US, United States.

- **Time to loss of ambulation** was calculated from treatment initiation to time of event.
- Due to differences in study designs and data collection, loss of ambulation was defined as the first of the following:
  - Exact date of loss of ambulation defined as:
    - For vamorolone, the date of 'inability to walk independently' assessed by parent or physician.
    - CINRG-DNHS: participant- or caregiver-reported age at continuous wheelchair use, approximated to nearest month and verified by inability to perform 10-meter walk/run test.
    - FOR-DMD did not collect the exact date of ambulation loss.
  - First occurrence of North Star Ambulatory Assessment rating of 'unable to walk'.
  - Inability to complete the 10-meter walk/run test.
- **Anthropometric outcomes** were calculated as z-scores using the Centers for Disease Control growth charts for unaffected males aged 2 to 20 years.[9]
  - Slope analyses from treatment start with random-coefficient models and assumed linear trajectories were used to assess inter-group differences.
- **Cataract prevalence** was defined as new cataract occurrence in boys with an ophthalmological assessment at GUARDIAN baseline and included ophthalmological data from VISION-DMD and adverse events from previous studies (VBP15-002/003/LTE).
  - Vamorolone cataract prevalence was compared with classic CS data using a logistic regression analysis, accounting for follow-up time and weighted based on propensity score matching.
- All studies were conducted according to good clinical practice.

Results

Figure 2. Subject flow from the Phase 2 studies through to the long-term effectiveness and anthropometric analyses



*A single boy was originally in the US EAP and transferred to the UK continued access program.
†Propensity score matching used the following criteria: age at start of treatment, age at baseline, and geographical location (North America versus Europe).

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Conclusions

- **Vamorolone demonstrated similar effectiveness to classic CS up to a median of 5 years.**
- **Vamorolone data show that growth can be maintained without earlier loss of ambulation.**
- **Vamorolone dosage adjustment by clinicians was representative of real-world practice, with a mean dosage of 4.5±1.8 mg/kg/d.**
- **Like classic CS, vamorolone is associated with increased BMI to be monitored and managed according to guidelines.**
- **The long-term effectiveness of vamorolone will continue to be assessed in the GUARDIAN study for 3 additional years.**

Effectiveness Results

Baseline characteristics and dose exposure of the time-to-event effectiveness cohorts

Baseline parameters, mean	Vamorolone 2–6 mg/kg (N=81)	Matched total classic CS (N=287)
Age, years ± SD	5.8 ± 1.0	6.1 ± 1.2
Height z-score ± SD	–0.6 ± 1.0	–0.9 ± 0.9
Weight z-score ± SD	0.1 ± 1.0	–0.3 ± 1.0
BMI z-score ± SD	0.8 ± 1.0	0.5 ± 1.0
TTSTAND, s ± SD	5.7 ± 3.1	6.7 ± 6.3
NSAA score, n ± SD	20.7 ± 6.0	21.1 ± 5.8
Region Europe, n (%) US, n (%)	 49 (60.5) 32 (39.5)	 97 (33.8) 190 (66.2)

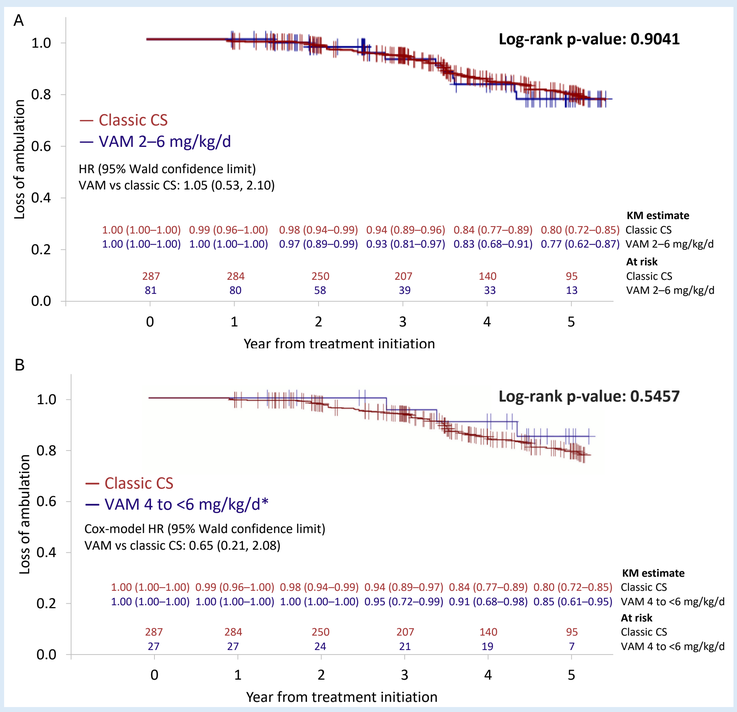
Treatment status at assessment	Vamorolone 2–6 mg/kg (N=81)	Matched total classic CS (N=287)
Mean received dosage, mg/kg/d ± SD	4.5 ± 1.8	N/D
Median treatment duration, years (range)	5.0 (1.0–8.1)	5.7 (1.0–22.5)

BMI, body mass index; CS, corticosteroids; N/D, not determined; NSAA, North Star Ambulatory Assessment; SD, standard deviation; TTSTAND, time to stand from supine; US, United States.

Key Effectiveness Findings

Figure 3. Kaplan-Meier curves of time to loss of ambulation for vamorolone 2–6 mg/kg/d versus classic CS (A) and vamorolone 4 to <6 mg/kg/d versus classic CS (B)

- Time to loss of ambulation was similar for vamorolone 2–6 mg/kg/d pooled dosages versus pooled classic CS (Figure 3A), and deflazacort and prednisone individually.
- In a subgroup of boys treated with vamorolone predominantly at 4 to <6 mg/kg/d (4–6 mg/kg/d, <80% of time on 6 mg/kg/d), time to loss of ambulation was similar to the classic CS cohort (Figure 3B).



Individuals with no events were censored at the last follow-up time with documented information or not having met the milestone event. *The 4 to <6 mg/kg/d cohort were treated with 6 mg/kg/d <80% of the treatment period, acting as a proxy dose for vamorolone 4 mg/kg/d.
CS, corticosteroid; HR, hazard ratio; KM, Kaplan-Meier; VAM, vamorolone.

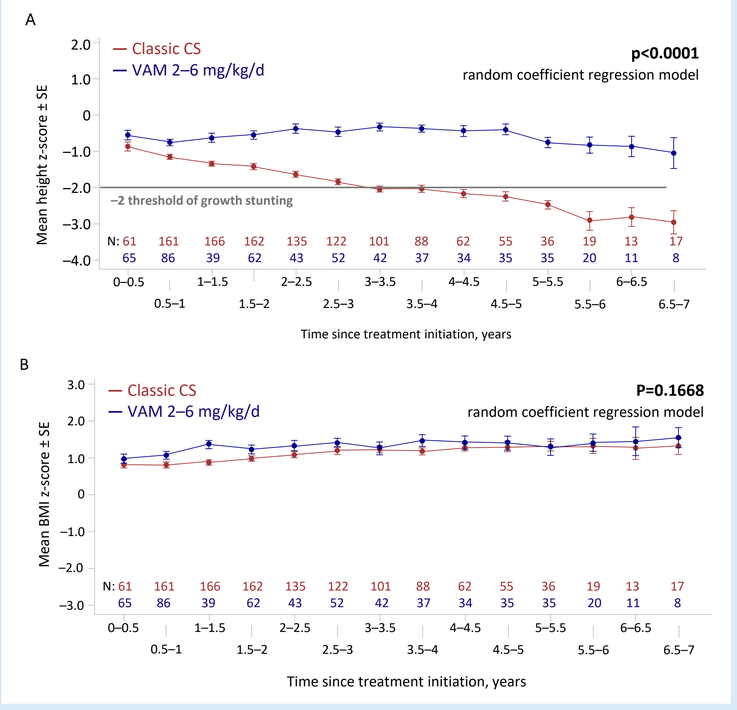
Anthropometric Results

- The mean (SD) dosage of vamorolone in the anthropometric cohort was 4.5 (1.1) mg/kg/d and the median treatment duration was 4.7 years (range: 1.6–8.1). The classic CS cohort had a median treatment duration of 4.1 years (range: 1.5–10.9).

Key Anthropometric Findings

Figure 4. Height (A) and BMI (B) z-score evolution over time since treatment initiation

- Height trajectories were maintained on vamorolone but decreased on classic CS, which showed growth stunting (Figure 4A; growth stunting: height z-score <–2.0 standard deviations).
- After 5 years, the mean height difference between vamorolone- and classic-CS-treated boys was 12.17 cm.
- BMI z-scores increased in both vamorolone and classic CS cohorts (Figure 4B).



BMI, body mass index; CS, corticosteroid; SE, standard error; VAM, vamorolone.

Cataract Results

- Significantly fewer patients had cataracts on vamorolone (5.3%) versus deflazacort (37.8%), p=0.015. Vamorolone cataract prevalence versus prednisone (12.1%) was numerically lower, at the threshold of significance, p=0.0502.

Study limitations: data are from an indirect historical comparison of classic CS that included intermittent dosing in a small number of individuals and measures for loss of ambulation varied across studies.

References: 1. AGAMREE 40 mg/ml oral suspension. US Prescribing Information version June 2024; **2.** AGAMREE 40 mg/ml oral suspension. EU Summary of product characteristics version January 2026; **3.** AGAMREE 40 mg/ml oral suspension. UK Summary of product characteristics version March 2025; **4.** Guglieri M, *et al.* JAMA Neurol. 2022;79(10):1005–14; **5.** Dang UJ, *et al.* Neurology. 2024;102:e208112; **6.** Mah JK, *et al.* JAMA Netw Open. 2022;5:e2144178; **7.** Guglieri M, *et al.* JAMA. 2022;327:1456–68; **8**. McDonald CM, *et al.* Lancet. 2018;391: 451–61; **9.** Centers for Disease Control and Prevention. CDC Growth Charts Data Files, https://www.cdc.gov/growthcharts/percentile_data_files.htm (accessed February 2026).

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[a]Vamorolone should be prescribed according to local approval and indication.

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