# Supplementary Online Content

Guglieri M, Clemens PR, Perlman SJ, et al. Efficacy and safety of vamorolone vs placebo and prednisone among boys with Duchenne muscular dystrophy: a randomized clinical trial. *JAMA Neurol*. Published online August 29, 2022. doi:10.1001/jamaneurol.2022.2480



This supplementary material has been provided by the authors to give readers additional information about their work.

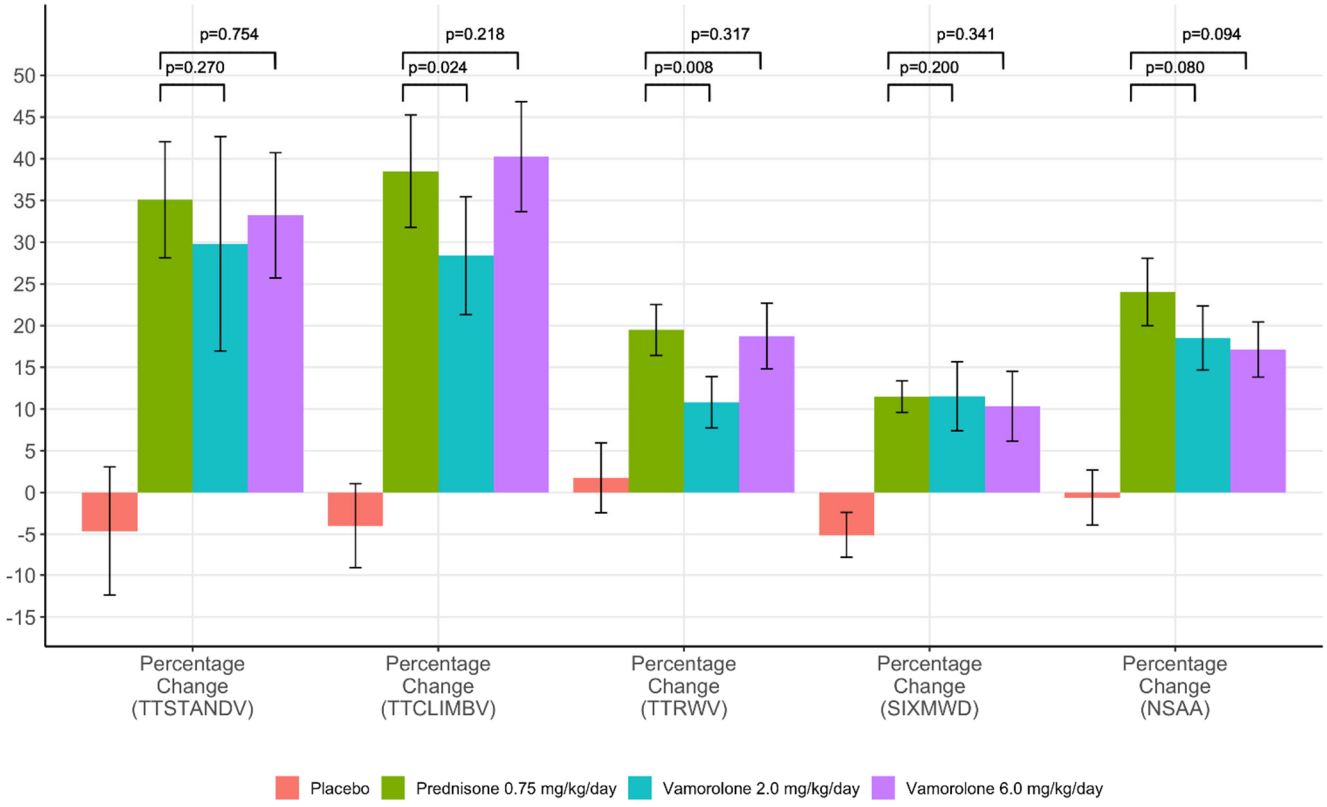
**eTable 1.** Study Populations

| | | | Treatments | | |
|---|---|---|---|---|---|
| | Placebo n (%) | Prednisone 0.75 mg/kg/day n (%) | Vamorolone 2 mg/kg/day n (%) | Vamorolone 6 mg/kg/day n (%) | Total n (%) |
| Study Populations | | | | | |
| Safety Population [1] | 29 (96.7) | 31 (100) | 30 (100) | 28 (93.3) | 118 (97.5) |
| mITT Population [1] | 28 (93.3) | 31 (100) | 30 (100) | 28 (93.3) | 117 (96.7) |
| PP Population [1] | 28 (93.3) | 30 (96.8) | 28 (93.3) | 27 (90.0) | 113 (93.4) |

**eTable 2.** Parent-Reported PARS III Outcome of Anxiety and Depression

| **Visit** | **Comparison** | **n** | **LSM (SE)** | **LSM Difference (SE)** | **LSM Difference 95% CI** | **p-Value** |
|---|---|---|---|---|---|---|
| **Week 12** | Vamorolone 2 | | | | | |
| **Change** | mg/kg/day vs. | 23 vs. 25 | 0.68 (0.44) vs. 0.03 (0.42) | 0.65 (0.59) | -0.53, 1.83 | >.05 |
| **from** | Placebo | | | | | |
| **Baseline** | Vamorolone 6 | | | | | |
| | mg/kg/day vs. | 24 vs. 25 | -0.81 (0.43) vs. 0.03 (0.42) | -0.84 (0.59) | -2.00, 0.33 | >.05 |
| | Placebo | | | | | |
| | Vamorolone 2 | | | | | |
| | mg/kg/day vs. | 23 vs. 29 | 0.68 (0.44) vs. -1.06 (0.41) | 1.74 (0.59) | 0.57, 2.92 | .004 |
| | Prednisone | | | | | |
| | Vamorolone 6 | | | | | |
| | mg/kg/day vs. | 24 vs. 29 | -0.81 (0.43) vs. -1.06 (0.41) | 0.25 (0.60) | -0.93, 1.43 | >.05 |
| | Prednisone | | | | | |
| **Week 24** | Vamorolone 2 | | | | | |
| **Change** | mg/kg/day vs. | 26 vs. 26 | 0.79 (0.39) vs. 0.27 (0.40) | 0.52 (0.55) | -0.57, 1.61 | >.05 |
| **from** | Placebo | | | | | |
| **Baseline** | Vamorolone 6 | | | | | |
| | mg/kg/day vs. | 28 vs. 26 | -1.32 (0.39) vs. 0.27 (0.40) | -1.59 (0.53) | -2.65, -0.53 | .004 |
| | Placebo | | | | | |
| | Vamorolone 2 | | | | | |
| | mg/kg/day vs. | 26 vs. 29 | 0.79 (0.39) vs. -0.49 (0.39) | 1.28 (0.54) | 0.21, 2.35 | .02 |
| | Prednisone | | | | | |
| | Vamorolone 6 | | | | | |
| | mg/kg/day vs. | 28 vs. 29 | -1.32 (0.39) vs. -0.49 (0.39) | -0.83 (0.54) | -1.90, 0.25 | >.05 |
| | Prednisone | | | | | |

**eFigure.** Post hoc Analysis of Percentage Change in Motor End Points at 24 Weeks vs Baseline




The unadjusted mean relative percentage change at 24 weeks is plotted for time to stand from supine velocity, time to climb 4 steps velocity, time to run/walk 10m velocity, six-minute walk distance, and NorthStar Ambulatory Assessment. The p-values are from a restricted maximum likelihood (REML)-based MMRM of percentage change over time run with treatment (vamorolone 2 mg/kg/day,vamorolone 6 mg/kg/day, prednisone 0.75 mg/kg/day, and placebo), enrollment stratification age group (4-5 years; 6-<7 years), week (as a categorical variable), baseline response, and the treatment-by-week interaction. The Kenward-Roger approximation was used to estimate denominator degrees of freedom as recommended for SAS Proc Mixed when

used for repeated measures (MMRM) (SAS for Mixed Models, second edition, by Littell, Milliken, Stroup, Wolfinger, and Schabenberger 2006; SBN 978-1-59047-500-3). Error bars are ±SE.

**eTable 3.** Treatment-Emergent Adverse Events (TEAEs)

| **Event type** | **Placebo (N=29) n (%); F** | **Prednisone 0.75 mg/kg/day (N=31) n (%); F** | **Vamorolone 2 mg/kg/day (N=30) n (%); F** | **Vamorolone 6 mg/kg/day (N=28) n (%); F** |
|---|---|---|---|---|
| **All TEAEs** | 23 (79.3); 77 | 26 (83.9); 121 | 25 (83.3); 97 | 25 (89.3); 91 |
| **Severe TEAEs (CTCAE Grade ≥3)** | --- | 1 (3.2); 1 | --- | --- |
| **Deaths** | --- | --- | --- | --- |
| **Serious adverse events** | --- | --- | 1 (3.3); 1 | --- |
| **TEAEs leading to discontinuation** | --- | 1 (3.2); 1 | --- | --- |

**eTable 4.** Laboratory Measures of Pharmacodynamic Safety Biomarkers

| | | Placebo Group | Prednisone Group | Vamorolone 2 mg/kg/day Group | Vamorolone 6 mg/kg/day Group |
|---|---|---|---|---|---|
| Osteocalcin ng/mL (SD) | Baseline | 55 (14) | 56 (13) | 57 (18) | 60 (15) |
| | 12-weeks | 53 (14) | 43 (9)*** | 59 (16) | 58 (12) |
| | 24-weeks | 50 (17) | 41 (9)*** | 63 (15) | 60 (13) |
| P1NP ng/mL (SD) | Baseline | 483 (161) | 480 (116) | 521 (204) | 490 (145) |
| | 12-weeks | 475 (139) | 315 (68)*** | 478 (137) | 424 (92)*** |
| | 24-weeks | 452 (139) | 335 (85)*** | 512 (133) | 493 (146) |
| CTX pg/mL (SD) | Baseline | 1079 (258) | 1125 (162) | 1127 (382) | 1074 (206) |
| | 12-weeks | 1092 (220) | 859 (177)*** | 1192 (284) | 1116 (202) |
| | 24-weeks | 1066 (266) | 805 (187)*** | 1234 (299) | 1176 (224) |
| Cortisol Morning nmol/L (SD) | Baseline | 199 (62) | 212 (66) | 238 (83) | 235 (67) |
| | 12-weeks | 221 (95) | 85 (56)*** | 141 (46)*** | 43 (36)*** |
| | 24-weeks | 218 (84) | 76 (43)*** | 128 (56)*** | 36 (41)*** |
| Standard Dose ACTH Stimulation Test nmol/L (SD) | Baseline<br>30 min<br>60 min | <br>550 (104)<br>628 (112) | <br>532 (101)<br>612 (97) | <br>553 (86)<br>648 (94) | <br>547 (119)<br>659 (105) |
| | 24-weeks<br>30 min<br>60 min | <br>500 (76)<br>584 (103) | <br>250 (78)<br>274 (83) | <br>332 (102)<br>393 (119) | <br>158 (147)<br>181 (170) |

Mean (SD). ***p<0.001 Within-group paired T test vs. baseline.

**eTable 5.** Central Laboratory "LOW" Calls for Cortisol Measures in Placebo Group and at Screening in Drug-Treated Groups

Morning cortisol and ACTH challenge tests were not done on the same days.

| | | **ACTH challenge** | | |
|---|---|---|---|---|
| | **Morning cortisol** (<138 nmol/L) % (n: low/total) | Basal (<138 nmol/L) % (n: low/total) | 30 minute (<497 nmol/L) % (n: low/total) | 60 minute (<497 nmol/L) % (n: low/total) |
| **Placebo group**[1] | 11% (9/179) | 25% (12/46) | 33% (16/49) | 15% (8/52) |
| **Drug-treated at Screening** | 8% (7/88) | 14% (12/88) | 25% (22/88) | 8% (7/87) |

[1]Data from both Screening and Week 24 in placebo group.

**eTable 6.** Percentage of Participants With Peak ACTH-Stimulated Cortisol Measures <500 nmol/L at Both 30 Minutes and 60 Minutes

| | Placebo Group n (%) | Prednisone Group n (%) | Vamorolone 2 mg/kg/day Group n (%) | Vamorolone 6 mg/kg/day Group n (%) |
|---|---|---|---|---|
| Baseline | 3 (11%) | 5 (17%) | 2 (7%) | 0 (0%) |
| 24-weeks | 4 (20%) | 26 (100%) | 18 (86%) | 20 (95%) |