Poster No: P.133

Daily regimens of prednisone, deflazacort, and vamorolone have shown to improve motor function similarly in patients with Duchenne muscular dystrophy

McDonald C,[1] Henricson E,[1,2] Leinonen M,[3] Linden A,[2] Guglieri M,[4] Clemens P,[5] Griggs R,[6] Shieh P,[7] Horrocks I,[8] Mah J,[9] Finkel R,[10] Goemans N,[11] Straub V,[4] Ryan M,[12] McMillan H,[13] Spinty S,[14] Hoffman E on behalf of the VISION-DMD,[15,16] FOR-DMD,[17] and CINRG Investigators[18]

[1]University of California Davis, Physical Medicine and Rehabilitation, Sacramento, CA, USA; [2]University of California Davis, Neuromuscular Research Center, Sacramento, CA, USA; [3]Santhera Pharmaceuticals; [4]John Walton Muscular Dystrophy Research Centre and Newcastle Hospitals NHS Foundation Trust, Newcastle-upon-Tyne, UK; [5]University of Pittsburgh School of Medicine, Pittsburgh, PA, USA; [6]University of Rochester Medical Center, New York, USA; [7]David Geffen School of Medicine, UCLA Life Sciences, Los Angeles, CA, USA; [8]Royal Hospital for Children, Glasgow, UK; [9]University of Calgary, Cumming School of Medicine, Calgary, AB, Canada; [10]St Jude Children's Research Hospital, Memphis, TN, USA; [11]University Hospitals Leuven, Leuven, Belgium; [12]Royal Children's Hospital, Melbourne, Victoria, Australia; [13]Children's Hospital of Eastern Ontario, Pediatric Neurology, Ottawa, ON, Canada; [14]Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [15]ReveraGen BioPharma, Rockville, MD, USA; [16]Binghamton University, Binghamton, NY, USA; [17]University of Rochester, New York, NY, USA; [18]The Cooperative International Neuromuscular Research Group

Introduction

- Glucocorticoids (GC) are recommended as a standard-of-care treatment in Duchenne muscular dystrophy (DMD). Daily regimens of GCs such as prednisone or deflazacort are efficacious in the treatment of DMD by improving muscle function.
- The efficacy and safety of prednisone and deflazacort were compared in the randomized, double-blind FOR-DMD study.[1]
  - Daily treatment with prednisone or deflazacort, compared with intermittent prednisone alternating 10 days on and 10 days off in boys with DMD aged 4 to 8 years of age, resulted in significant improvement over 3 years in the efficacy outcomes. There was no significant difference between the two daily GC regimens, which outperformed the intermittent regimen.
- Vamorolone is a dissociative steroidal anti-inflammatory drug that seeks to retain efficacy and potentially reduce select safety concerns in patients with DMD compared to GCs via changes to structure/activity relationships with the GC receptor.[2]
- The efficacy and safety of vamorolone were investigated during the first 24 weeks (Period 1) of the randomized, double-blind VISION-DMD (VBP15-004, NCT03439670) study in boys with DMD aged 4 to <7 years of age:
  - The results of the primary analysis at 24 weeks have been reported previously.[3]
  - The study met its primary endpoint; both doses of vamorolone (6 mg/kg/day and 2 mg/kg/day) showed statistically significant and clinically meaningful improvement in functional outcomes vs. placebo after 24 weeks of treatment.
  - Since the long-term efficacy of vamorolone 6 mg/kg/day was more persistent than vamorolone 2 mg/kg/day at 48 weeks, the vamorolone dose level of 6 mg/kg/day was selected for the present comparison.

Objective

- This analysis aims to compare the effect of prednisone (PDN), deflazacort (DFZ), and vamorolone (VAM) on muscle function after 1 year of treatment in steroid-naïve patients with DMD who were 4 to <7 years of age at the time of treatment initiation.

Methods

- In this post-hoc, cross-study comparison, data were analyzed from the FOR-DMD and VISION-DMD studies. Visits up to 1 year (or 48 weeks) of follow-up were extracted from both studies.
- Two groups from the FOR-DMD study (daily PDN 0.75 mg/kg/day and daily DFZ 0.9 mg/kg/day) were compared to patients treated with VAM 6 mg/kg/day in the VISION-DMD study.
- A 2-stage matching approach was used to identify subjects from the FOR-DMD study to include in these analyses. In the first stage, subjects from the FOR-DMD study were matched based on the key inclusion criteria for this study, including confirmed DMD, between 4 and <7 years of age at Baseline, able to walk independently, and able to complete TTSTAND without assistance. In the second stage, propensity scores were calculated using a logistic regression model baseline age, time to stand (TTSTAND) velocity, North Star Ambulatory Assessment score, weight Z-score, and height Z-score.
- The data on TTSTAND velocity and other measures of motor function were compared for each vamorolone dose versus the matched external controls from the FOR-DMD study and analyzed using the mixed model for repeated measures (MMRM) model, observed data (i.e., without imputation as there was no control group at 48 weeks), and modified intent to treat analysis set. Within this model, pairwise comparisons (using least square mean [LSM] contrasts) were made to compare the treatment difference between vamorolone 6 mg/kg with the FOR-DMD prednisone and deflazacort group.

Results

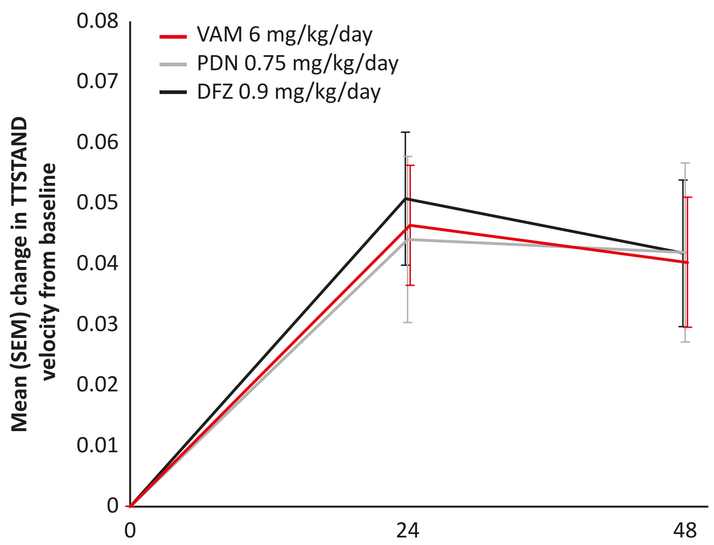
- Based on the propensity scores, 39 PDN- and 47 DFZ-treated patients were extracted from the FOR-DMD study and 27 VAM-treated patients from the VISION-DMD study.
- The demographic characteristics of the matched population are summarized in Table 1. Baseline age, height, and weight were well matched, while the patients in the VAM group had more advanced disease based on the baseline disease characteristics.
- After 48 to 52 weeks of treatment, TTSTAND velocity increased in all treatment groups by 0.04 rises/sec, with no significant least squares mean (LSM) difference between PDN vs VAM (0.002 rises/sec; 95% confidence interval [CI] –0.033 to 0.037 rises/sec; p=0.929) or DFZ vs VAM (0.002 rises/sec; 95% CI –0.029 to 0.032 rises/sec; p=0.923) (**Figure 1**).
- Similarly, after 48 to 52 weeks of treatment, the LSM 6-minute walk test distance increased in all treatment groups, with no significant LSM difference between PDN vs VAM (–9 m; 95% CI –37 to 18 m; p=0.510) or DFZ vs VAM (6 m; 95% CI –19 to 30 m; p=0.652) (**Figure 2**).

Table 1. Demographic and baseline characteristics of the matched population (FOR-DMD and VISION-DMD studies)

Baseline characteristic	PDN 0.75 mg/kg/day (N=39)	DFZ 0.9 mg/kg/day (N=47)	VAM 6 mg/kg/day (N=27)
Age (years)	5.4 (0.6)	5.4 (0.8)	5.5 (0.9)
Height (Z-score)	–1.0 (0.8)	–0.8 (1.1)	–1.0 (1.1)
Weight (Z-score)	–0.3 (0.9)	–0.2 (1.2)	–0.3 (1.0)
Baseline TTSTAND velocity (rises/sec)	0.21 (0.089)	0.20 (0.07)	0.19 (0.06)
Baseline 6MWT (m)	343 (53)	326 (63)	313 (56)
Baseline NSAA score	22.1 (5.0)	20.7 (4.9)	18.8 (4.1)

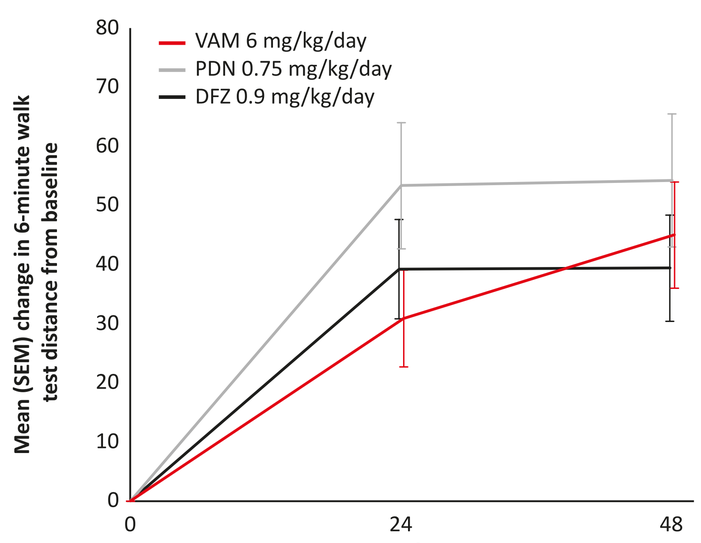
Data are shown as mean (SD).
6MWT, 6-minute walk test; DFZ, deflazacort; NSAA, North Star Ambulatory Assessment score; PDN, prednisone; TTSTAND, time to stand; VAM, vamorolone.

Figure 1. Change from baseline TTSTAND velocity (rises/sec), MMRM with propensity score weighting (FOR-DMD and VISION-DMD studies)



DFZ, deflazacort; MMRM, mixed model for repeated measures; PDN, prednisone; SEM, standard error of the mean; TTSTAND, time to stand; VAM, vamorolone.

Figure 2. Change from baseline in 6-minute walk test distance (meters), MMRM with propensity score weighting (FOR-DMD and VISION-DMD studies)



DFZ, deflazacort; MMRM, mixed model for repeated measures; PDN, prednisone; SEM, standard error of the mean; TTSTAND, time to stand; VAM, vamorolone.

Conclusion

- In this post-hoc, cross-study comparison data were matched from two randomized, double-blind studies.
- Overall, these data show that daily regimens of PDN 0.75 mg/kg, DFZ 0.9 mg/kg, and VAM 6 mg/kg improved motor function over 48 weeks in patients with DM. Any differences between groups did not reach accepted minimally clinical important differences.
- Interpretation of the results are limited by this being a post-hoc, cross-study comparison and any conclusions should be made taking this factor into account, given the studies were conducted at different times, under different circumstances and in different protocols.

References

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