Deflazacort and Prednisone Treatment for Duchenne Muscular Dystrophy (DMD): Real-world Outcomes at Cincinnati Children's Hospital Medical Center (CCHMC)

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1. Introduction

- Corticosteroids are the standard of care for the treatment of Duchenne muscular dystrophy (DMD), and have modified the natural history of the disease by slowing the progression of motor and pulmonary functional decline and extending survival[1]
- Deflazacort and prednisone/prednisolone are glucocorticoids that are used in the treatment of DMD
- Prolonged glucocorticoid steroid treatment is associated with linear growth failure, excessive weight gain, and heightened risk of osteoporosis[2]

2. Objectives

- To assess real-world ambulatory, pulmonary, cardiac, growth, and bone-health outcomes among patients with DMD who received deflazacort or prednisone as part of coordinated, interdisciplinary care at CCHMC

3. Patients

- Retrospective, de-identified clinical data from routine care at CCHMC (2004-2017)
- Genetically confirmed diagnosis of DMD

4. Methods

- **Data source:** Retrospective clinical data from 435 boys with genetically confirmed DMD (2004-2017)

Ages at loss of ambulation and scoliosis

- Patients were categorized into prednisone- and deflazacort-initiated groups based on their first recorded steroid type
- Loss of ambulation (LoA) was identified as Functional Mobility Scale (FMS) score >4, indicative of patients' primary use of a wheelchair for mobility; patients were required to have an FMS score of ≤4 at their first clinic visit
- Age at onset of scoliosis was defined as the first recorded clinical diagnosis of scoliosis in a patient's medical record; patients were required to be free of scoliosis at their first clinic visit
- Kaplan-Meier curves and adjusted Cox proportional hazards analyses were used to assess outcomes by steroid type; sensitivity analyses were conducted for patients who switched steroid type

Cross-sectional associations between steroid type and clinical measures

- Associations between steroid type and clinical measures (listed in **Table 2**) were studied across all clinic visits at which patients were aged ≥4 years using multivariable regression adjusting for age, visit year, steroid duration at the time of the clinic visit, and the interaction between age and steroid duration; generalized estimating equations accounted for multiple clinic visits per patient
- Patients who switched steroid types were excluded from this analysis

5. Results

Ages at loss of ambulation and scoliosis

- N=414 patients were included in the analysis of age at LoA; n=412 were included for age at scoliosis onset
- Approximately 75% of patients received deflazacort (~95% of whom were on a daily regimen), 13% received prednisone (~75% of whom were on a daily regimen), and 12% switched from prednisone to deflazacort
- At first clinic visit at CCHMC, patients who received prednisone tended to have poorer motor and pulmonary function, and to be older, taller and heavier, than those who received deflazacort
- Based on Kaplan-Meier analyses, initiation with deflazacort was associated with delayed onset of LoA by a median of 2 years **(Figure 1)** and delayed scoliosis (median of 18.6 years for prednisone, median not reached for deflazacort) **(Figure 2)** compared with prednisone

Figure 1: Ages at loss of ambulation by steroid type (Kaplan-Meier Analysis) (FMS >4)

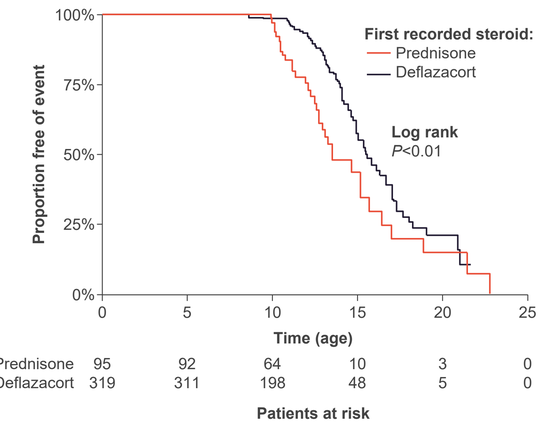
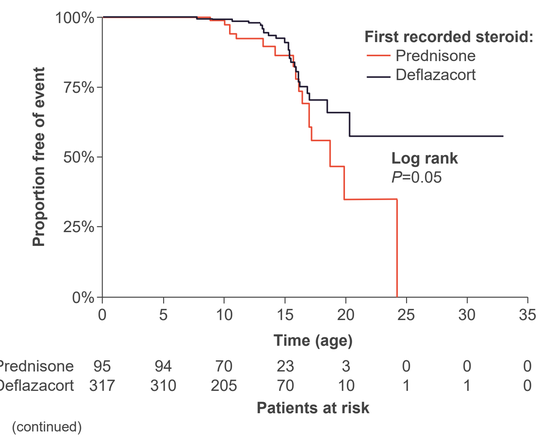


Figure 2: Ages at scoliosis onset by steroid type (Kaplan-Meier Analysis)



(continued)

5. Results (continued)

- These differences persisted in Cox proportional hazards models adjusting for age at steroid initiation and year of steroid initiation (both *P*<0.05) **(Table 1)**

Table 1: Hazard ratios for ages at loss of ambulation and scoliosis onset

Outcome	Unadjusted HR for deflazacort vs. prednisone (95% CI)	*P*-value	Adjusted[†] HR for deflazacort vs. prednisone (95% CI)	*P*-value
Loss of ambulation	0.55 (0.36, 0.83)	<0.01*	0.45 (0.29, 0.69)	<0.001*
Scoliosis onset	0.54 (0.29, 1.01)	0.05	0.52 (0.28, 0.97)	<0.05*

Abbreviations: HR: hazard ratio; CI: confidence interval; FMS: Functional Mobility Scale.
*Denotes statistical significance.
[†] Adjusted for age at steroid initiation and year of steroid initiation.

- In the sensitivity analyses, ages at LoA and scoliosis onset among prednisone-to-deflazacort switchers were older compared to those consistently receiving prednisone patients, but younger compared to those consistently receiving deflazacort

Cross-sectional associations between steroid type and clinical measures

- Sample sizes, which were based on assessment frequency of each outcome across clinic visits, ranged from 687 observations from 225 patients to 2237 observations from 326 patients
- Across all visits used in the cross-sectional analyses, patients had a median age of 9.9 years; median age was higher in the prednisone group (11.3 years) compared to the deflazacort group (9.6 years)
- Across all clinic assessments, and after adjusting for age at assessment and steroid duration, deflazacort-treated patients exhibited, on average, better ambulatory and pulmonary function, greater % lean body mass, shorter stature and lower weight; no differences were observed in left ventricular ejection fraction or whole body bone mineral density **(Table 2)**

Table 2: Cross-sectional associations between steroid type and clinical measures

Outcome	Adjusted[†] difference between deflazacort and prednisone (95% CI)	*P*-value
4-stair climb (velocity) (stairs/seconds)	0.59 (0.34; 0.84)	<0.001*
North Star Ambulatory Assessment	4.58 (2.60; 6.56)	<0.001*
Forced vital capacity %-predicted (%)	9.90 (3.77; 16.03)	<0.01*
Left ventricular ejection fraction (%)	0.92 (-1.49; 3.32)	0.45
Height (cm)	-6.16 (-8.65; -3.67)	<0.001*
Total body mass (kg)	-6.93 (-10.47; -3.40)	<0.001*
% Lean body mass	4.39 (2.27; 6.50)	<0.001*
% Body fat	-4.60 (-6.84; -2.37)	<0.001*
Whole body bone mineral density (g/cm²)	-0.00 (-0.02; 0.01)	0.67

Abbreviations: CI: confidence interval; cm: centimeters; g: grams; kg: kilograms
*Denotes statistical significance.
[†] Adjusted for age, visit year, steroid duration, and the interaction between age and steroid duration.

6. Limitations

- As a non-randomized comparisons of real-world treatment groups, differences in outcomes could be confounded by factors that differ between these groups, such as socio-economic status or care plan adherence
- Dosing data were not available to characterize steroid exposure beyond daily vs. non-daily

7. CONCLUSIONS

This real-world, non-randomized study adds to the evidence from other observational studies[3] associating use of deflazacort with greater preservation of motor and pulmonary function relative to the use of prednisone in DMD, and suggests concurrent preservation of lean body mass and delay of scoliosis.

References

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Disclosures

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