REAL-WORLD EVIDENCE OF ETEPLIRSEN TREATMENT EFFECTS ON DUCHENNE MUSCULAR DYSTROPHY RELATED HEALTH OUTCOMES USING CLAIMS DATA IN THE UNITED STATES

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INTRODUCTION

Duchenne muscular dystrophy (DMD) is a rare, X-linked, severely debilitating, and ultimately fatal neuromuscular disease characterised by progressive muscle weakness.[1]

Eteplirsen is approved in the US to treat patients with DMD who have a confirmed mutation of the DMD gene amenable to exon 51 skipping. The rarity of DMD makes it difficult to assess real-world outcomes in these patients. This study uses a data set with claims covering a majority of the US population and linked electronic medical records (EMR) to assess DMD-related health and resource utilization outcomes in treated and untreated DMD patients.

OBJECTIVE

The objective of this study was to provide real-world perspective on healthcare resource utilization and significant disease progression events in patients with DMD treated with eteplirsen and those treated with standard of care alone.

METHODS

DATA AND MATCHING

- Linked administrative claims and EMR data (2011-2020) from Decision Resources Group data repository were used
- Patients with both administrative claims and EMR data in whom SNOMED-CT codes could positively identify DMD were selected
- Eteplirsen-treated patients were identified based on eteplirsen-related National Drug Code (NDC) and Healthcare Common Procedure Coding System (HCPCS) codes
- Stages of progression were identified based on observation of administrative claims and EMR data associated with signal markers of disease stage, with expert clinical input
- Eteplirsen-treated and standard of care patients were matched on age, disease stage, and key health events using a two-stage matching algorithm
  - Stage 1 (exact matching): each treated patient was matched exactly with the full set of untreated patients on: age at index and disease stage at index
  - Stage 2 (propensity score matching): within the existing matched sets of treated and untreated patients, patients were further matched based on DMD-related health events† in the baseline§ period using propensity score

REGRESSION ANALYSIS

- Eteplirsen-treated and standard of care cohorts were compared for post-baseline outcomes using Poisson regression methods, adjusted for length of observation in baseline and follow-up¥ period, and controlling for age, health stage, and baseline level of each health event measure
  - Hospitalization days and intensity-adjusted hospital encounters*
  - Emergency room (ER) visits and intensity-adjusted emergency room visits*
  - Intensive care unit (ICU) days and intensity-adjusted ICU*
  - Pulmonary management
  - Scoliosis
  - Cardiac management
  - Tracheostomy
  - Assisted ventilation

†The matching process and Poisson regression also include baseline rates of motorized wheelchair and cough assist device as well as ever have had a motorized wheelchair claim from start of observation to index time. However, motorized wheelchair rates and cough assist device rates are not included as outcome variables because motorized wheelchair rates are more likely to reflect health insurance coverage instead of loss of ambulation with claims for different chair accessory components and cough assist device is a standard care once a patient starts on it. Motorized wheelchair and cough assist device are included in the matching and regression analysis because they serve as good controls for unobserved patient characteristics such as health insurance coverage, socioeconomic status, and medical care consumption behavior that may be confounding factors to patients healthcare consumption behaviors in follow-up periods. The matching process excludes tracheostomy and ICU events due to rare events;

RESULTS

SAMPLE SELECTIONΦ

	Eteplirsen-treated	Untreated
Total number of patients	480	997
With at least 1 medical claim	480	955
With available health stage	428	900
After one-to-one matching (>1 month†)	333	333
After one-to-one matching (>3 months‡)	324	324
After one-to-one matching (>6 months‡)	301	301

PATIENT CHARACTERISTICS

	MATCHED SAMPLE (>6 months follow-up)		MATCHED SAMPLE (>3 months follow-up)	
	Treated	Untreated	Treated	Untreated
Age at index (Mean, SD)	**13.44** (6.06)	**13.44** (6.06)	**13.47** (6.21)	**13.47** (6.21)
Health Stage at index (N, %)				
Early ambulatory	**55** (18.27%)	**55** (18.27%)	**60** (18.52%)	**60** (18.52%)
Late ambulatory	**48** (15.95%)	**48** (15.95%)	**51** (15.74%)	**51** (15.74%)
Early non-ambulatory	**140** (46.51%)	**140** (46.51%)	**149** (45.99%)	**149** (45.99%)
Late non-ambulatory	**58** (19.87%)	**58** (19.87%)	**64** (19.75%)	**64** (19.75%)
Total Number of Patients	**301**	**301**	**324**	**324**

HEALTH EVENTS OBSERVED IN MATCHED SAMPLE AT BASELINE

Baseline yearly average rates

DMD-related Medical Events (Mean, SD)	Primary Scenario (>6 months follow-up) Treated	Untreated	T-test (P-value)	Sensitivity Scenario (>3 months follow-up) Treated	Untreated	T-test (P-value)
Adjusted Emergency Room	**0.53** (1.72)	**0.53** (1.85)	0.979	**0.52** (1.67)	**0.42** (1.48)	0.430
Emergency Room Days	**0.34** (0.99)	**0.32** (1.27)	0.817	**0.34** (0.97)	**0.24** (0.72)	0.113
Adjusted Hospital Encounter	**3.43** (7.42)	**3.12** (10.44)	0.677	**3.39** (7.25)	**3.56** (10.36)	0.807
Hospital Days	**1.89** (3.94)	**1.79** (5.81)	0.797	**1.89** (3.88)	**1.88** (5.66)	0.989
Adjusted ICU	**0.15** (1.26)	**0.07** (0.73)	0.342	**0.14** (1.21)	**0.09** (0.72)	0.498
ICU Days	**0.14** (1.18)	**0.06** (0.64)	0.312	**0.13** (1.14)	**0.07** (0.62)	0.420
Pulmonary Management	**0.94** (3.47)	**0.76** (2.70)	0.481	**1.05** (3.72)	**0.97** (4.04)	0.785
Motorized Wheelchair	**0.82** (2.36)	**0.83** (2.33)	0.965	**0.80** (2.30)	**0.63** (1.92)	0.310
Scoliosis	**1.04** (6.79)	**0.85** (5.35)	0.703	**1.06** (6.61)	**0.84** (4.65)	0.703
Cardiac Management	**1.56** (3.13)	**1.38** (2.89)	0.459	**1.54** (3.05)	**1.44** (2.78)	0.671
Tracheostomy	**0.76** (9.07)	**0.60** (6.42)	0.804	**0.70** (8.74)	**0.70** (5.54)	0.999
Cough Assist Device	**0.44** (1.78)	**0.28** (1.47)	0.234	**0.41** (1.72)	**0.23** (1.25)	0.127
Assisted Ventilation	**0.78** (4.86)	**0.58** (4.37)	0.596	**1.09** (7.35)	**0.63** (3.90)	0.323
Baseline length in Months (Mean, SD)	**10.69** (1.58)	**10.51** (1.71)	--	**10.65** (1.61)	**10.60** (1.59)	--
Follow-up length in Months (Mean, SD)	**30.29** (18.22)	**45.29** (24.62)	--	**28.49** (11.83)	**43.83** (24.56)	--
Total Number of Patients	**301**	**301**	--	**324**	**324**	--

*Intensity adjusted hospital, ER, and ICU encounters account for both length of stay (days) and number of distinct claims during the visit to account for complexity of care required; §Baseline is defined as the shorter of 1 year before index time or the period from the earliest observation to index time; ¥Follow-up period is defined as the period from index time to the last observation.

ADJUSTED HEALTH EVENTS IN FOLLOW-UP PERIODS

Yearly average rates based on Poisson model estimates

DMD-related Medical Events (Mean, SE)	Primary Scenario (>6 months follow-up) Treated	Untreated	T-test (P-value)	Sensitivity Scenario (>3 months follow-up) Treated	Untreated	T-test (P-value)
Adjusted Emergency Room	**0.060** (0.009)	**0.101** (0.012)	**0.004**	**0.061** (0.009)	**0.098** (0.019)	**0.035**
Emergency Room Days	**0.038** (0.006)	**0.057** (0.007)	**0.024**	**0.035** (0.006)	**0.065** (0.016)	**0.027**
Adjusted Hospital Encounter	**0.361** (0.045)	**0.597** (0.106)	**0.027**	**0.376** (0.048)	**0.599** (0.105)	**0.043**
Hospital Days	**0.168** (0.019)	**0.255** (0.025)	**0.005**	**0.178** (0.020)	**0.260** (0.030)	**0.015**
Adjusted ICU	**0.023** (0.005)	**0.054** (0.017)	**0.038**	**0.023** (0.005)	**0.039** (0.014)	0.251
ICU Days	**0.021** (0.004)	**0.047** (0.014)	**0.038**	**0.021** (0.004)	**0.034** (0.011)	0.278
Pulmonary Management	**0.089** (0.011)	**0.173** (0.034)	**0.004**	**0.100** (0.013)	**0.206** (0.033)	**<0.001**
Scoliosis	**0.092** (0.021)	**0.110** (0.018)	0.552	**0.086** (0.020)	**0.141** (0.027)	0.119
Cardiac Management	**0.127** (0.010)	**0.187** (0.016)	**0.001**	**0.128** (0.010)	**0.159** (0.013)	0.070
Tracheostomy	**0.072** (0.015)	**0.351** (0.116)	**0.001**	**0.064** (0.015)	**0.358** (0.168)	**0.004**
Assisted Ventilation	**0.124** (0.016)	**0.210** (0.032)	**0.011**	**0.145** (0.017)	**0.261** (0.040)	**0.004**
Total Number of Patients	**602**			**648**		

The primary analysis (>6 months follow-up) demonstrated that **Eteplirsen treatment is associated with significantly lower rates of**:

- Adjusted hospital encounter (P=0.027) and hospital days (p=0.005)
- Adjusted ER (P=0.004) and ER days (p=0.024)
- Adjusted ICU rates (P=0.038) and days (p=0.038)
- Pulmonary management (p=0.004)
- Cardiac management (p=0.001)
- Tracheostomy (p=0.001)
- Assisted ventilation (p=0.011)

The results are robust in sensitivity analyses

CONCLUSION

This study provides the first real-world evidence of eteplirsen treatment effects on key health outcomes in DMD patients.

ΦPatients with first DMD diagnosis or eteplirsen treatment initiation older than 40 years and patients with less than 6 months baseline observation are excluded; ‡The cut-off time length is for observed follow-up period.

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