Supplementary Material

A Real-World Target Trial Emulation of Eteplirsen, Casimersen, and Golodirsen to Evaluate Survival Among Patients with Duchenne Muscular Dystrophy

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Figure S1. Process of generating de-identified linked dataset

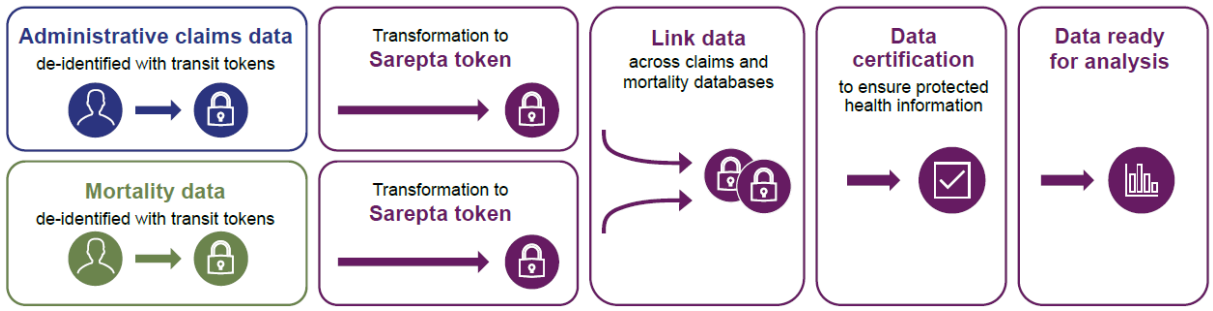


Figure S1. Process of generating de-identified linked dataset. This study used tokenization to merge data across an administrative claims database and a mortality database while protecting patient identity and protected health information.

Figure S2. Definition of validated claims-based DMD identification algorithm [28]

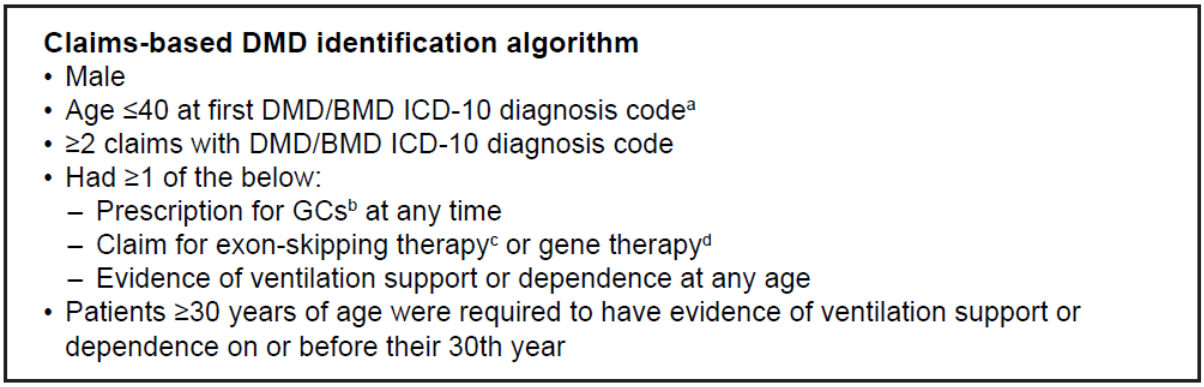


Figure S2. Definition of validated claims-based DMD identification algorithm [28]. List of criteria required by claims-based DMD identification algorithm to classify a patient as having DMD.

[a]ICD-10 diagnosis code for BMD and DMD is G71.01.

[b]GCs included betamethasone, budesonide, cortisone, deflazacort, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, or triamcinolone.

[c]Exon-skipping therapy included casimersen, eteplirsen, golodirsen, or viltolarsen.

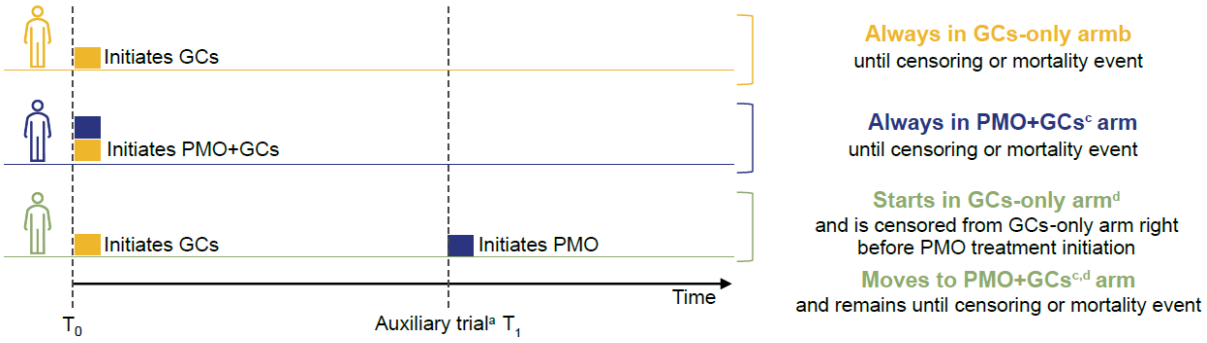
[d]Gene therapy included delandistrogene moxeparvovec-rokl.

BMD, Becker muscular dystrophy; DMD, Duchenne muscular dystrophy; GC, glucocorticoid; ICD-10, International Classification of Diseases, Tenth Revision.

Figure S3. Sequential target trial design

A. Emulated trial design

B. Example time progression for 3 patients in sequential trial design



C. Patient populations in sequential trial study

	Always in the GCs-only arm	Always in the PMO+GCs arm[c]	Start in the GCs-only arm, move to the PMO+GCs arm[d]
N	2,656	112	260
T_0	First observed date of ≥30 days of GCs use	First observed date of PMO use	First observed date of ≥30 days of GCs use[c]
Initiates PMO treatment	Not observed	At T_0	On auxiliary trial T_X, which occurs after T_0

Figure S3. Sequential target trial design. (A) Timeline of observation period for the 2 study groups in the emulated trial. (B) Example time progression for 3 patients in the sequential TTE study. (C) Information about patient populations in the sequential TTE design.

[a]A new auxiliary trial started each month that new patients began PMO treatment.

[b]Patients in the GCs-only arm could enroll in auxiliary trials in the GCs-only arm.

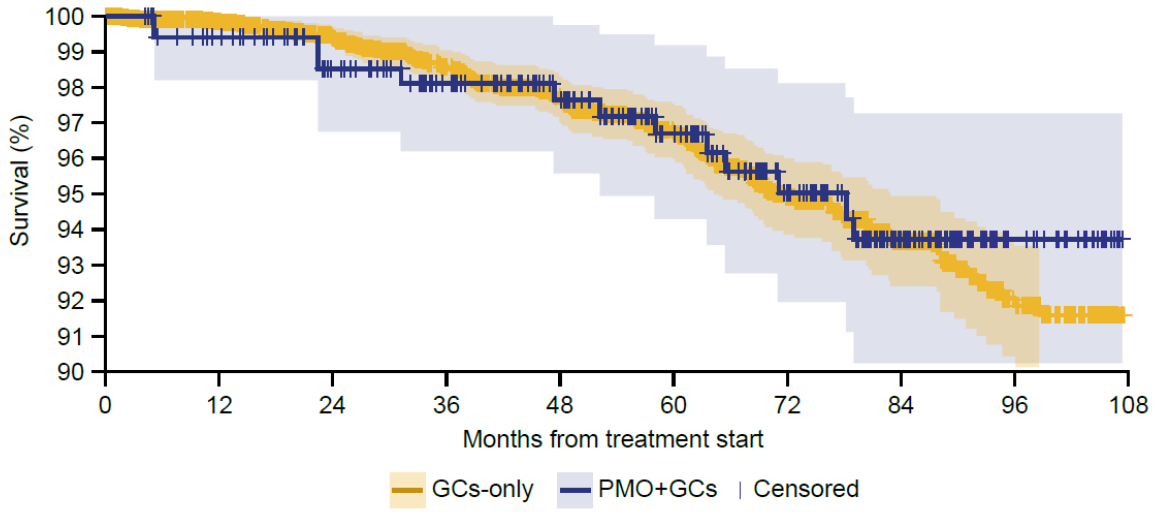
[c]In the PMO + GCs arm, patients were not required to be taking PMOs and GCs concurrently.

[d]Patients had a first date of PMO use after the first observed date of ≥ 30 days of GCs use that qualified as T_0. T_1 indicates a new sequential trial (defined in month since T_0) where new PMO initiators from that month are compared with all patients still in the GCs-only arm. Note that patients in the GCs-only arm can be included in multiple trials up until they are censored or have an event.

GC, glucocorticosteroid; PMO, phosphorodiamidate morpholino oligomer; TTE, target trial emulation.

Figure S4. Unadjusted time to death

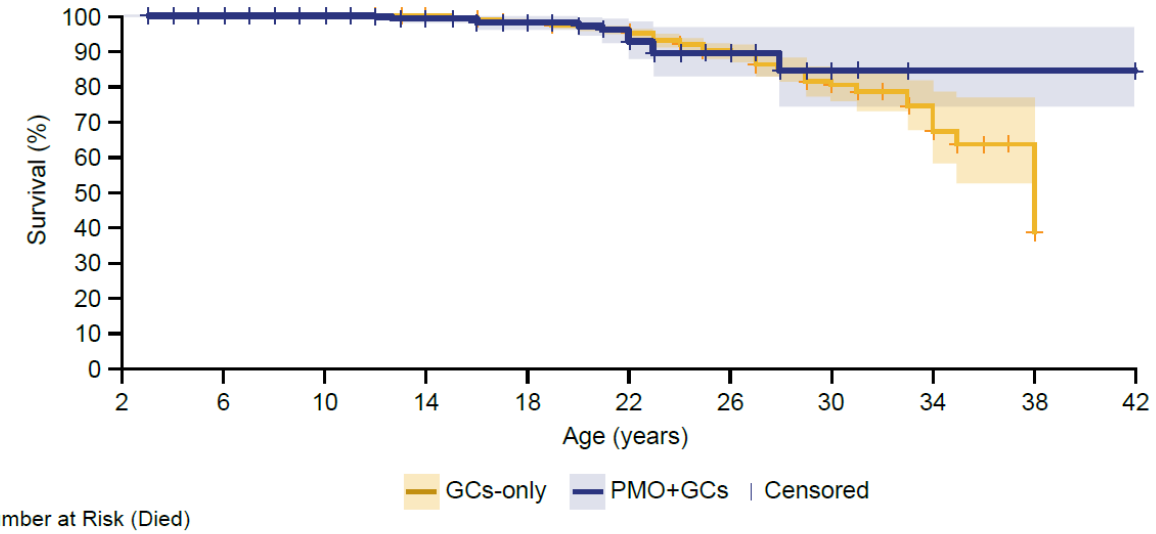
A. Time from treatment start to death



Number at Risk (Died)

GCs-only	2916 (0)	2525 (5)	2352 (11)	2076 (19)	1764 (18)	1430 (15)	1010 (24)	728 (11)	388 (9)	0 (2)
PMO+GCs	112 (0)	184 (1)	217 (2)	232 (1)	219 (1)	189 (2)	155 (3)	116 (2)	65 (0)	0 (0)

B. Time from birth to death



Number at Risk (Died)

GCs-only	2916 (0)	2848 (0)	2492 (0)	1862 (5)	1217 (24)	677 (30)	307 (27)	102 (19)	31 (7)	2 (2)	0 (0)
PMO+GCs	372 (0)	361 (0)	322 (0)	235 (3)	138 (2)	64 (4)	30 (2)	5 (1)	1 (0)	1 (0)	0 (0)

Figure S4. Unadjusted time to death. Kaplan–Meier curves of unadjusted data; shadings represent 95% confidence intervals. (A) Time from treatment initiation to death and (B) time from birth to death for patients who were treated with PMO + GCs or with GCs only. Patients who initially were in the GCs-only group but subsequently started treatment with PMOs were included in both GCs-only and PMO + GCs groups.

GC, glucocorticosteroid; PMO, phosphorodiamidate morpholino oligomer.

Figure S5. Covariate balance (SMD) pre- and post-weighting

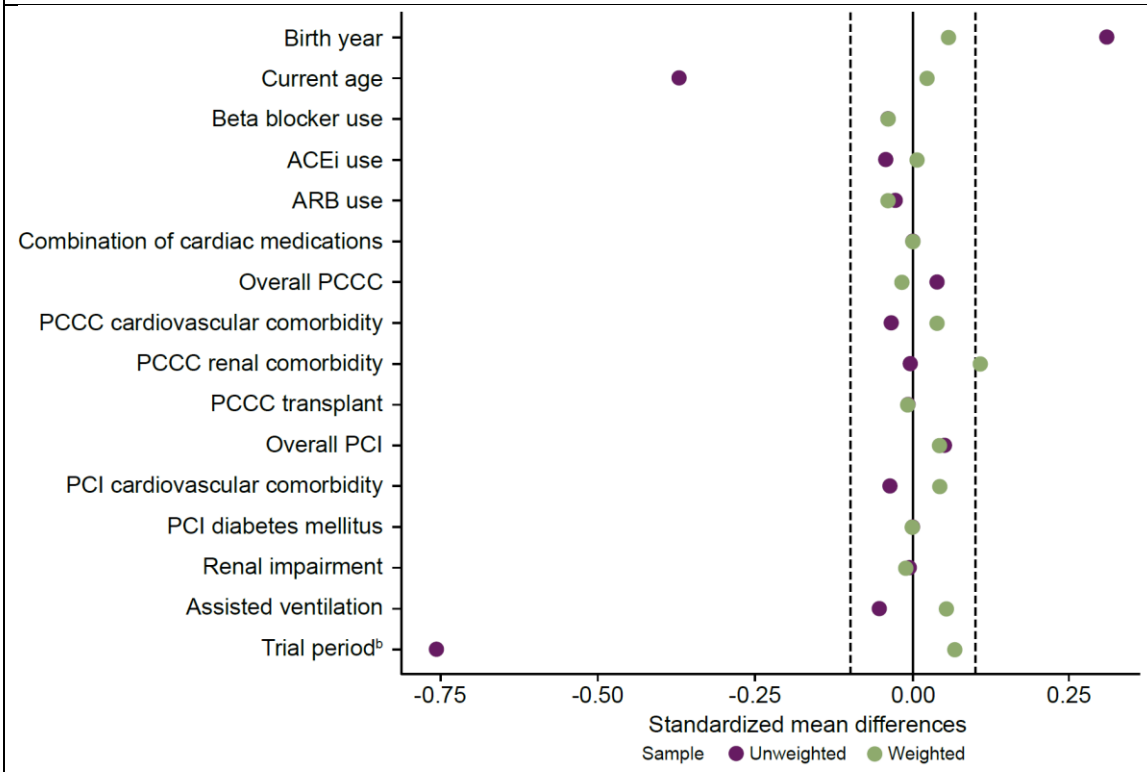


Figure S5. Covariate balance (SMD) pre- and post-weighting. In addition to sequential TTE, inverse probability of treatment weighing was used to ensure covariate balance in both treatment arms. All variables were measured in the preceding 12 months, except for birth year, current age, and trial period.

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; PCCC, Pediatric Complex Chronic Conditions; PCI, Pediatric Comorbidity Index; SMD, standardized mean difference; TTE, target trial emulation.