2025 Interim Analysis of EVOLVE: A Long-term Observational Study Evaluating Eteplirsen, Golodirsen, or Casimersen in Routine Clinical Practice

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Background

- Eteplirsen, golodirsen, and casimersen are phosphorodiamidate morpholino oligonucleotides (PMOs) approved for the treatment of Duchenne muscular dystrophy (DMD) in patients with pathogenic variants amenable to exon 51, 53, and 45 skipping, respectively[1-3]
- EVOLVE (NCT06606340) is a phase 4, multicenter, observational study prospectively assessing long-term functional and clinical outcomes of patients with DMD treated with PMOs
  - Eteplirsen, golodirsen, and casimersen received accelerated Food and Drug Administration (FDA) approval in 2016, 2019, and 2021, respectively[1-3]
- Real-world data from the earlier EVOLVE interim analysis of patients with DMD receiving PMOs in routine clinical practice showed a median age at loss of ambulation (LOA) of 15.36 years in eteplirsen-treated patients[4]

Objective

To present safety and LOA data as of the latest interim analysis (February 2025) in the ongoing EVOLVE study

Methods

Study population

- Male patients with an established clinical diagnosis of DMD with pathogenic variants amenable to exon 51, 53, and 45 skipping and receiving or initiating treatment with eteplirsen, golodirsen, or casimersen

Safety and functional endpoints

- Treatment-emergent serious adverse events (TESAEs) were collected by the investigator, and severity was assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events scale
- Age at LOA and time to LOA since treatment initiation were collected by the investigator
  - LOA was defined as either 1) participant (or caregiver)–reported age at continuous wheelchair use, approximated to the nearest month, and verified by an attending physician; or 2) a North Star Ambulatory Assessment (NSAA) walk score of 0 and/or inability to perform the 10-meter walk/run test (10MWR)

Statistical analysis

- Adverse events and patients' ambulatory status were summarized descriptively
- Kaplan-Meier (KM) curves were used to assess age and time to LOA from treatment initiation

Results

Patients

- As of February 2025, a total of 173 patients were enrolled in EVOLVE with 126 patients receiving eteplirsen, 25 receiving golodirsen, and 22 receiving casimersen (**Table 1**)
- At the time of the interim analysis, the mean (standard deviation [SD]) duration of treatment was 7.1 (2.2) years for eteplirsen, 3.2 (1.5) years for golodirsen, and 2.9 (0.9) years for casimersen
  - Due to different FDA approval dates, the duration of follow-up differed between eteplirsen, golodirsen, and casimersen
- The percentage of patients remaining on treatment was high across all groups, regardless of ambulatory status at treatment initiation (eteplirsen: total, 94% [118/126], ambulatory, 94% [43/46], non-ambulatory, 95% [39/41]; golodirsen: total, 72% [18/25], ambulatory, 71% [5/7], non-ambulatory, 83% [10/12]; casimersen: total, ambulatory, non-ambulatory, 100% each)
  - In the eteplirsen group, 36 of the 39 patients (92%) who lost ambulation after treatment initiation remained on treatment
  - In the golodirsen group, 3 of the 6 patients (50%) who lost ambulation after treatment initiation remained on treatment

Table 1 *Baseline patient characteristics*

Parameter	Eteplirsen (n=126)	Golodirsen (n=25)	Casimersen (n=22)
Age at PMO initiation, years			
Mean (SD)	10.7 (5.1)	12.3 (4.2)	15.1 (6.0)
Median (range)	9.9 (1.7-24.4)	12.0 (4.7-19.3)	13.7 (6.2-33.6)
Age at study enrollment, years			
Mean (SD)	14.0 (5.5)	13.4 (4.2)	16.4 (5.9)
Median (range)	13.8 (1.7-28.6)	14.3 (6.6-20.1)	15.3 (6.7-33.6)
Age at treatment initiation by ambulatory status, mean (SD), years			
n (ambulatory; non-ambulatory)	46; 41	7; 12	8; 14
Ambulatory	7.0 (3.9)	10.0 (3.2)	11.3 (3.5)
Non-ambulatory	15.4 (4.1)	15.7 (2.6)	17.2 (6.2)
Non-ambulatory, n (%)			
At PMO initiation	41 (32.5)	12 (48.0)	14 (63.6)
At last available visit	78 (61.9)	18 (72.0)	14 (63.6)
PMO treatment, mean (SD), years			
Total duration	7.1 (2.2)	3.2 (1.5)	2.9 (0.9)
At study enrollment	3.4 (1.9)	1.1 (1.4)	1.4 (1.3)
Treatment status as of last available visit, n (%)			
Continuing therapy	118 (93.7)	18 (72.0)	22 (100)
Discontinued	8 (6.3)	7 (28.0)	0
Corticosteroid use, n (%)			
Prior to PMO initiation	76 (60.3)	22 (88.0)	17 (77.3)
At or after PMO initiation	114 (90.5)	24 (96.0)	21 (95.5)
Within 12 months prior to study enrollment	112 (88.9)	24 (96.0)	20 (90.9)
Age at documented first use of corticosteroid treatment, years			
n	116	24	21
Mean (SD)	8.9 (4.3)	8.3 (3.5)	11.3 (6.0)
Median (range)	8.0 (1.7-22.9)	7.3 (3.0-16.4)	9.6 (4.7-29.7)

Data are not final until study completion and database lock occur.
PMO, phosphorodiamidate morpholino oligomer; SD, standard deviation.

Safety

- All PMOs showed favorable safety profiles and were well tolerated; no TESAEs were deemed related to treatment (**Table 2**)
- Across all TESAEs, exposure-adjusted incidence rate per 100 patient-years (PY) remained flat over time across all PMOs and was 10.5 PY for eteplirsen, 4.0 PY for golodirsen, and 23.0 PY for casimersen

Loss of ambulation

- Of the 126 eteplirsen patients, 85 (67%) were ambulatory at treatment initiation; of these 85 patients, 39 (46%) lost ambulation after starting treatment[a]
- Among the 85 patients who were ambulatory at treatment initiation and included in the KM analysis for the eteplirsen group, the median age (95% CI) at LOA was 15.8 (14.9-19.6) years (**Figure 1**) and median time to LOA was 9.1 years from treatment initiation (**Figure 2**)
- In the golodirsen group, 13 of 25 patients (52%) were ambulatory at treatment initiation; of these 13 patients, 6 (46%) lost ambulation after treatment initiation
- Of the 22 casimersen patients, 8 (36%) were ambulatory at treatment initiation, none of whom lost ambulation in the average 2.9 years of follow-up
- KM analyses for golodirsen and casimersen were not reported due to limited follow-up and ongoing enrollment

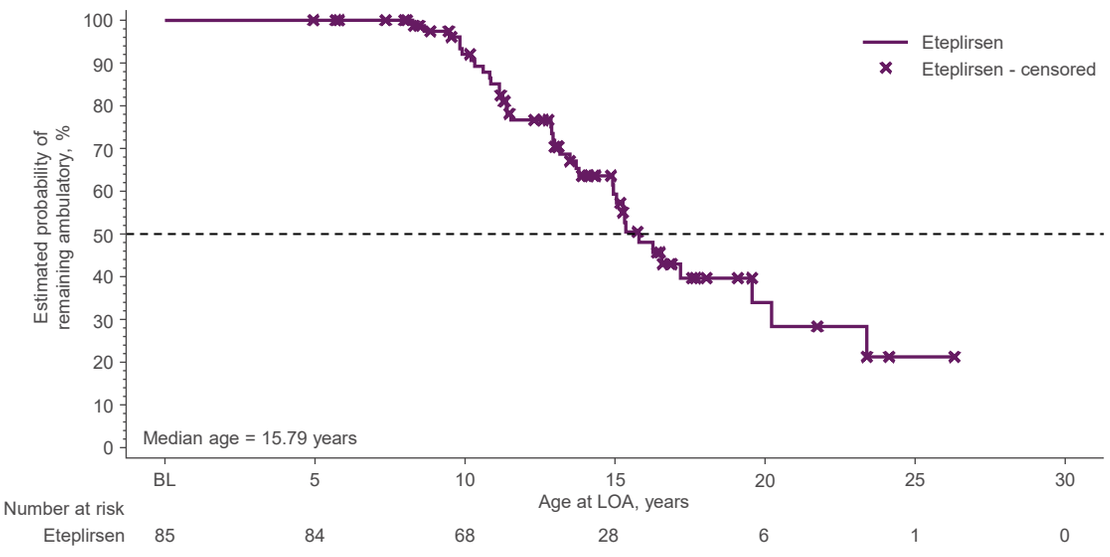
[a]Based on the wheelchair definition of LOA; 38 participants lost ambulation based on the 10MWR definition of LOA.

Table 2 *Summary of TESAEs*

Parameter	Eteplirsen (n=126)	Golodirsen (n=25)	Casimersen (n=22)
Any TESAE, n/N (%)			
Year 1	14/126 (11.1)	0/25 (0)	3/22 (13.6)
Year 2	13/122 (10.7)	1/19 (5.3)	2/12 (16.7)
Year 3	15/122 (12.3)	1/16 (6.3)	4/11 (36.4)
Year 4	12/119 (10.1)	0/15 (0)	-
Year 5	6/86 (7.0)	-	-
Year 6	2/40 (5.0)	-	-
Overall follow-up	40/126 (31.7)	2/25 (8.0)	6/22 (27.3)
TESAEs by system organ class in ≥5% of patients across groups, n (%)			
Infections and infestations	16 (12.7)	1 (4.0)	3 (13.6)
Injury, poisoning, and procedural complications	12 (9.5)	0	0
Cardiac disorders	11 (8.7)	0	2 (9.1)
Respiratory, thoracic, and mediastinal disorders	8 (6.3)	0	2 (9.1)
Psychiatric disorders	2 (1.6)	0	2 (9.1)

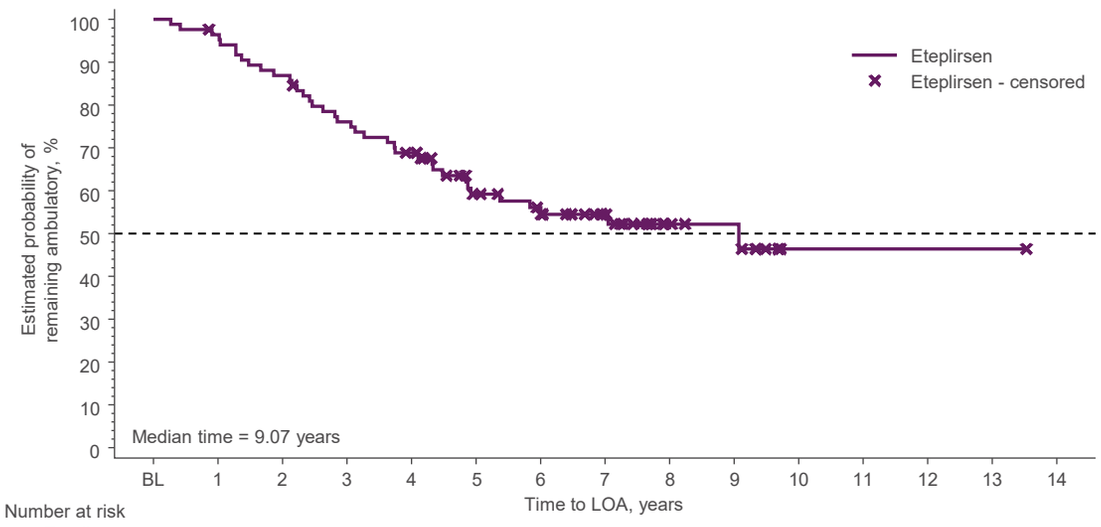
TESAE, treatment-emergent serious adverse event.

Figure 1 *Age at LOA in eteplirsen-treated patients ambulatory at treatment initiation*



BL, baseline; LOA, loss of ambulation.

Figure 2 *Time to LOA since treatment initiation in eteplirsen-treated patients*



BL, baseline; LOA, loss of ambulation.

Conclusions

- The overall safety profile in EVOLVE has been consistent with no increase in adverse event rates over time, supporting the observed real-world safety of PMOs
- Median age at LOA was consistent with previously published findings across clinical trials, post hoc analyses, and prior EVOLVE interim analyses
- This interim analysis shows treatment continuation remained high over time
- EVOLVE continues to support the long-term impact of eteplirsen, golodirsen, and casimersen on meaningful clinical outcomes, such as LOA

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