Poster #187

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Association of Edaravone With Improved Progression-Free Survival in Patients With Amyotrophic Lateral Sclerosis: A Propensity Score–Matched Analysis of the Optum Claims Database

Malgorzata Ciepielewska, MS[1]; Jeffrey Zhang, PhD[2]; Ying Liu, PhD[2]; Stephen Apple, MD[1]

[1]Shionogi Inc., Florham Park, NJ; [2]Princeton Pharmatech, LLC, Princeton, NJ

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Background

- Riluzole and edaravone are United States (US) Food and Drug Administration (FDA)-approved treatments for all patients with amyotrophic lateral sclerosis (PALS)[1,2]
- Edaravone was initially FDA approved as an intravenous (IV) formulation (Radicava® IV) in May 2017, followed by approval of the oral suspension formulation (Radicava ORS®) in May 2022[2]
  - In a phase 3 trial, IV edaravone was shown to slow down the rate of physical functional decline by 33% (p=0.0013) in PALS, as measured by the ALS Functional Rating Scale-Revised, compared with placebo at 24 weeks[3]
- Progression to more advanced stages of ALS is typically associated with increasing healthcare needs, and delays in diagnosis can result in greater healthcare resource utilization[4]

Objective

- Obtain real-world evidence on progression-free survival of edaravone-treated, US-based PALS in the Optum claims database

Methods/Implementation

- PALS (≥18 years old) identified in the Optum claims database from January 1, 2007, to December 31, 2025, were included
  - PALS were defined as having ≥2 claims at least 30 days apart with an ALS International Classification of Disease (ICD)-9/-10 (335.20/G12.21), or ≥1 ALS diagnosis code and prescription filled for approved drugs to treat ALS
  - For the edaravone-treated group, PALS had ≥2 claims for an edaravone prescription, and did not switch to other ALS medications
- For edaravone-treated PALS, the index date was defined as the date of first edaravone administration, and for non–edaravone-treated PALS, index dates were randomly assigned between the ALS diagnosis date and last claim date; this process was repeated 1000 times
- Disease progression was defined as transition from early to middle or late stage based on Stenson's algorithm[4] (**Table 1**)
  - Stenson's ALS severity-based staging algorithm was developed using ALS symptom and staging survey data from 142 neurologists reporting on 880 PALS[4]

Table 1. ALS Symptoms by Stenson's ALS Severity Stage[4]

Early Stage	Middle Stage	Late Stage
Fasciculations	Sialorrhea	Respiratory failure
Dysarthria	Dysphagia	Lack of voluntary muscle control
Difficulty walking/maintaining gait	Orthopnea	Difficulty communicating
Muscle weakness/impaired strength	Dyspnea	Gastrostomy
Muscle spasticity		Complete care dependence
Loss of balance/falling		
Slow movement/reflexes		
Reduced coordination		
Muscle cramping		
Physical fatigue/low energy		

ALS, amyotrophic lateral sclerosis.

- Edaravone-treated PALS were matched 1:1 to edaravone-untreated PALS using propensity scores derived from baseline covariates, including sex, age, race, pre-index disease duration, baseline riluzole use, baseline cardiovascular disease, baseline Stenson's stage of ALS disease severity; and baseline use of assistive devices (cane, walker, wheelchair), noninvasive ventilation, saliva-control medications, and artificial nutrition
- Progression-free survival was evaluated using restricted mean survival time (RMST) estimated with a doubly robust approach
- Differences in RMST between edaravone-treated PALS and matched edaravone-untreated PALS were calculated for each iteration and averaged across 1000 repetitions

Results

- PALS treated with edaravone oral suspension (n=266) were matched to PALS not treated with edaravone oral suspension (n=266) (**Table 2**)
  - In both matched cohorts, PALS were 50% male, predominantly White (74%), and the mean age was 65 years

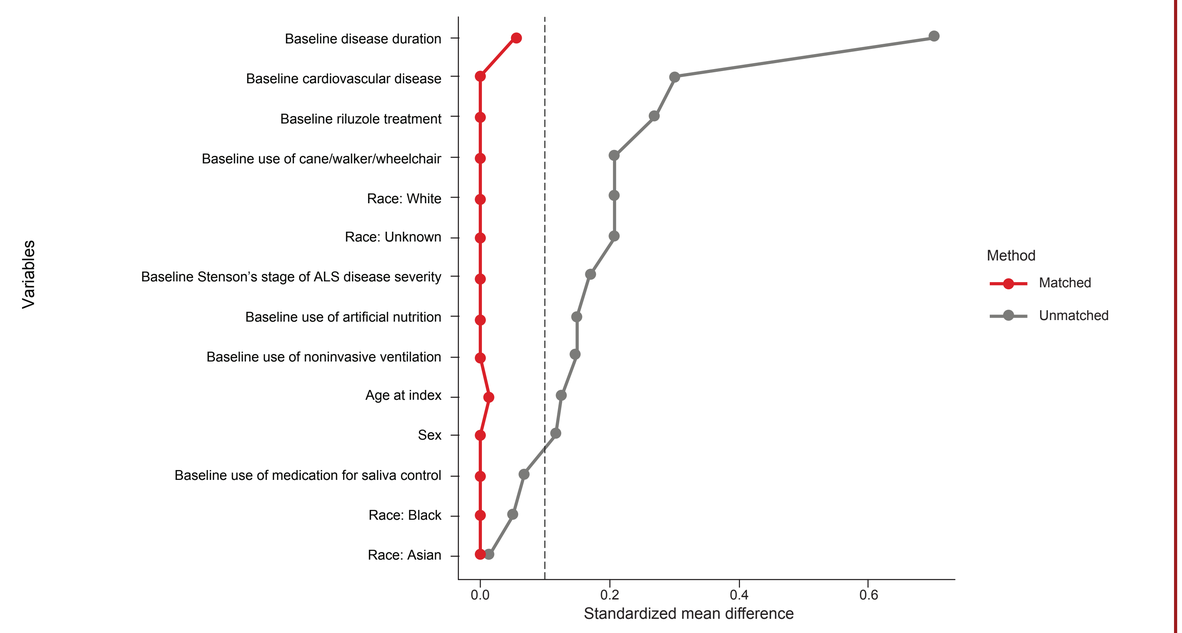
Table 2. Baseline Demographics and Clinical Characteristics of Propensity Score–Matched PALS Either Treated or Untreated With Edaravone Oral Suspension

Baseline Demographics and Clinical Characteristics	Treated With Edaravone Oral Suspension (N=266)	Not Treated With Edaravone Oral Suspension (N=266)
Sex, n (%)		
Male	133 (50%)	133 (50%)
Female	133 (50%)	133 (50%)
Age, years		
Mean (SD)	65.0 (10.4)	65.2 (10.1)
Median (Q1, Q3)	66.5 (59.0, 73.0)	67.0 (59.0, 72.0)
Min, Max	32.0, 85.0	31.0, 86.0
Race, n (%)		
White	198 (74%)	198 (74%)
Black	17 (6.4%)	17 (6.4%)
Asian	6 (2.3%)	6 (2.3%)
Unknown	45 (17%)	45 (17%)
Use of cane/walker/wheelchair, n (%)	49 (18%)	49 (18%)
Use of noninvasive ventilation, n (%)	49 (18%)	49 (18%)
Use of artificial nutrition/gastrostomy tube, n (%)	47 (18%)	47 (18%)
Use of medication for saliva control, n (%)	51 (19%)	51 (19%)
Cardiovascular disease, n (%)	36 (14%)	36 (14%)
Stenson's stage of ALS disease severity, n (%)		
Early	64 (24%)	64 (24%)
Middle	109 (41%)	109 (41%)
Late	93 (35%)	93 (35%)
Disease duration, years		
Mean (SD)	0.5 (0.7)	0.4 (0.6)
Median (Q1, Q3)	0.2 (0.1, 0.5)	0.3 (0.1, 0.5)
Min, Max	0.0, 6.0	0.0, 5.0
Treatment with riluzole, n (%)	129 (48%)	129 (48%)

ALS, amyotrophic lateral sclerosis; PALS, patients with ALS; Q, quartile; SD, standard deviation.

- After propensity score matching, variables had a standardized mean difference of <0.1, indicating variables were well balanced with minimal confounding bias (**Figure 1**)

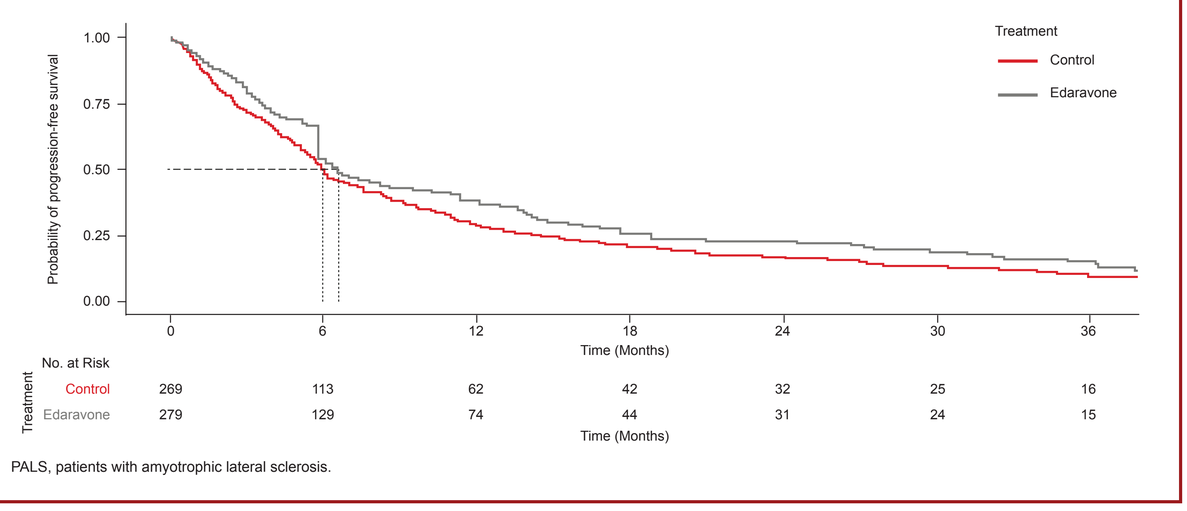
Figure 1. Standardized Mean Differences for Propensity Score–Matched Variables Before and After Matching



ALS, amyotrophic lateral sclerosis.

- **Figure 2** presents the weighted Kaplan-Meier estimates of progression-free survival for matched edaravone-treated vs edaravone-untreated PALS through 36 months
- Over 12 months, covariate-adjusted RMST was 10.89 months for PALS receiving edaravone vs 6.91 months for edaravone-untreated PALS, corresponding to a 3.98-month greater mean progression-free survival time (95% confidence interval, 0.57-7.63, p<0.05)

Figure 2. Weighted Kaplan-Meier Estimates of Progression-Free Survival in Edaravone-Treated vs Untreated Matched PALS



PALS, patients with amyotrophic lateral sclerosis.

Conclusions

- These ongoing analyses suggest that, over 12 months of follow-up, edaravone-treated PALS from the Optum claims database had 3.98 additional months of progression-free survival compared with matched edaravone-untreated PALS, based on RMST analysis
- Therefore, these findings suggest a potential association between edaravone treatment and longer time spent free from progression to more advanced, resource-intensive stages of ALS
- This retrospective analysis is subject to the inherent limitations of observational claims database research, including potential residual confounding, limited clinical detail, possible coding inaccuracies, and reliance on a claims-based algorithm to assess ALS disease progression
- These results may help inform clinical and payer discussions regarding treatment and disease progression in PALS

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Disclosures

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JZ and **YL** are employees of Princeton Pharmatech, which has received consultancy fees from Shionogi.
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