Improvements in quality of life outcomes among individuals with MPS IVA treated with elosulfase alfa: results from the Morquio A Registry Study (MARS)

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Background

- Mucopolysaccharidosis (MPS) IVA, also known as Morquio A syndrome, is an ultra-rare lysosomal storage disorder characterized by progressive multisystemic clinical manifestations[1]
- Individuals with MPS IVA experience a profound and progressive decline in quality of life (QoL); however, the impact of ERT on QoL has not previously been evaluated using a large, international, real-world dataset[2]
- The Morquio A Registry Study (MARS) was a multinational, observational study including 419 participants with MPS IVA[3]
  - The primary objectives of MARS were to characterize the heterogeneity and natural history of disease and to evaluate the long-term effectiveness and safety of elosulfase alfa enzyme replacement therapy (ERT)[3]
- The objective of this analysis was to assess the change in QoL among ERT-treated MARS participants

Methods

- The MARS study was conducted across 65 clinical sites in 16 countries and ran for 10 years (September 2014 to May 2024); data were collected as part of routine clinical care[2]
- QoL was evaluated using the EQ-5D-5L tool, a standardized instrument comprising five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression[4]
  - Each domain was rated on a 5-level scale (no problems, slight problems, moderate problems, severe problems, and extreme problems/unable)
  - To assess overall EQ-5D-5L index scores, responses were converted to a single summary value ranging from 1 (best health state) to 0 (worst health state)
- Changes in overall EQ-5D-5L index score and outcomes on individual domains were assessed among ERT-treated participants with assessments both at pre-treatment baseline and follow-up timepoints up to 3 years

Results

EQ-5D-5L at baseline

- Among 365 ERT-treated participants in MARS (≥1 ERT infusion prior to or during MARS), 48 participants had available pre-treatment baseline EQ-5D-5L data **(Table 1)**
- Median EQ-5D-5L index scores at baseline ranged from 0.25 to 0.81 across age subgroups with an overall median index score of 0.51 (n=48, **Table 2**)
- Moderate to extreme problems were commonly reported in the domains of usual activities, mobility, self-care, and pain/discomfort, with the frequency of problems in usual activities, mobility, and pain/discomfort increasing with age

Table 1. Demographics and characteristics at registry entry

	ERT-treated participants with pre-treatment EQ-5D-5L data (N=48)
Sex, n (%)	
Female	26 (54.2%)
Male	22 (45.8%)
Race, n (%)	
Asian	24 (50.0%)
White	16 (33.3%)
Black	2 (4.2%)
Other/missing	6 (12.5%)
Age at registry entry, years	
Mean (SD)	14.9 (13.64)
Median (min, max)	10.2 (0, 57)
Age at treatment initiation, years	
Mean (SD)	15.1 (13.69)
Median (min, max)	10.2 (0, 57)

Table 2. Baseline EQ-5D-5L across age subgroups in ERT-treated participants

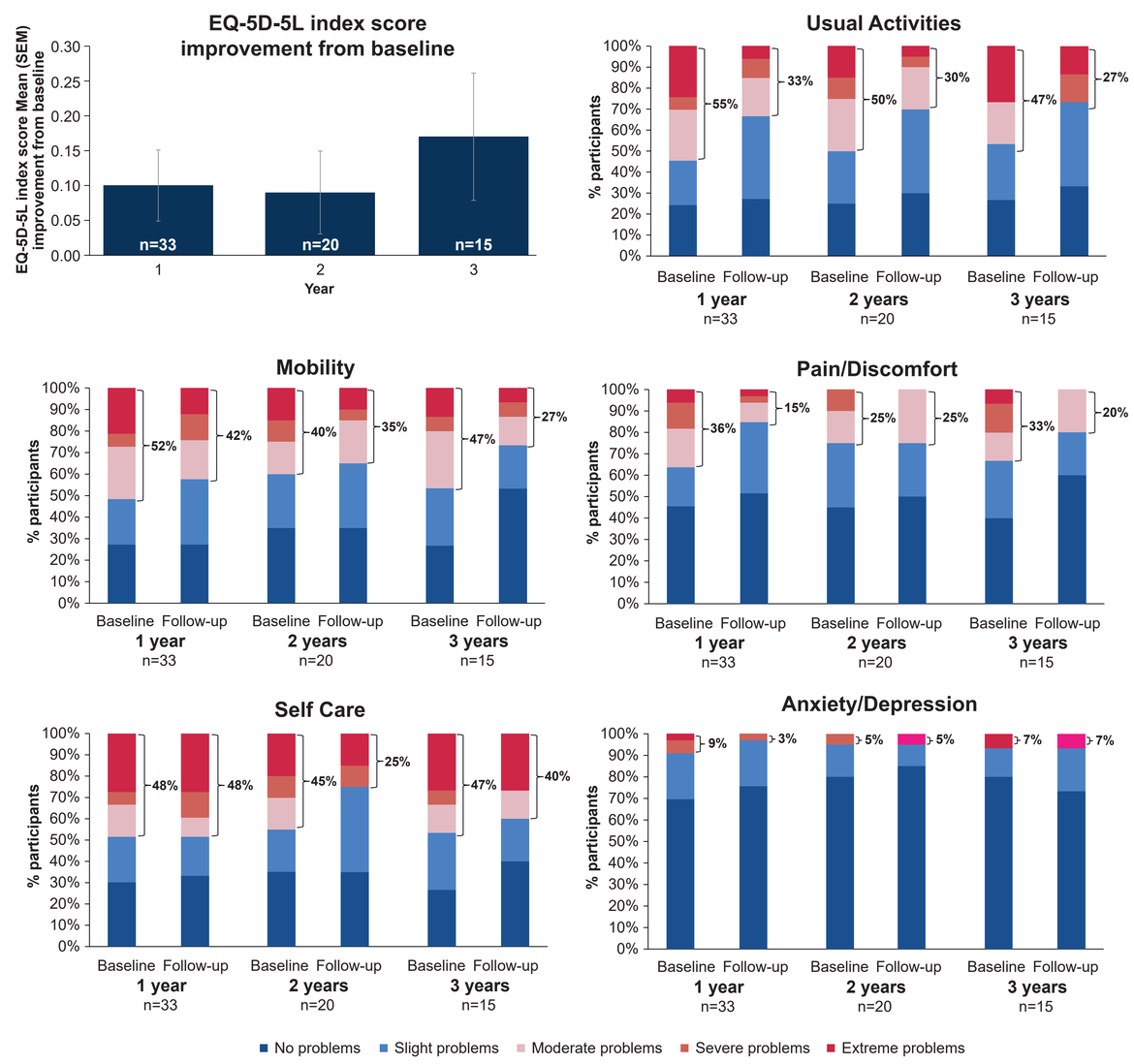
	Age at treatment initation (Baseline)				
	<5 years (n=14)	5–11 (n=12)	12–18 (n=6)	>18 (n=16)	Overall (n=48)
EQ-5D-5L index score					
Mean (SD)	0.37 (0.48)	0.76 (0.20)	0.32 (0.48)	0.53 (0.39)	0.51 (0.42)
Median (min, max)	0.47 (–0.64, 0.88)	0.81 (0.38, 1.00)	0.25 (–0.15, 0.88)	0.59 (–0.41, 1.00)	0.66 (–0.64, 1.00)
Participants reporting moderate to extreme problems, n (%)					
Usual activities	7 (50%)	2 (17%)	4 (67%)	11 (69%)	24 (50%)
Mobility	5 (36%)	3 (25%)	5 (83%)	10 (63%)	23 (48%)
Self-care	9 (64%)	4 (33%)	5 (83%)	4 (25%)	22 (46%)
Pain/discomfort	1 (7%)	3 (25%)	2 (33%)	11 (69%)	17 (35%)
Anxiety/depression	1 (7%)	0	1 (17%)	3 (19%)	5 (10%)

SD: standard deviation

Change in EQ-5D-5L over time

- Among participants with both baseline and follow-up assessments, the mean (SD) change in EQ-5D-5L index score from baseline was +0.10 (0.29) at 1 year (n=33), +0.09 (0.27) at 2 years (n=20), and +0.17 (0.35) at 3 years (n=15) following initiation of ERT **(Figure 1)**
- Domain-level outcomes at 1 year (n=33) showed reductions in the proportion of participants reporting moderate to extreme problems in usual activities (baseline: 55%, vs. 1 year: 33%), mobility (baseline: 52%, vs. 1 year: 42%), and pain/discomfort (baseline: 36%, vs. 1 year: 15%) **(Figure 1)**
- Self-care and anxiety/depression domains remained relatively stable from baseline to 1 year (n=33), with no increase in reported moderate to extreme problems (baseline: 48%, vs. 1 year: 48%; baseline: 9%, vs. 1 year: 3%, respectively)
- The domain score trends seen at the 1-year assessment remained consistent through 3 years of treatment
  - After 3 years of treatment, the greatest reductions in participants reporting moderate to extreme problems were observed in usual activities (baseline: 47%, vs. 3 years: 27%, n=15) and mobility (baseline: 47%, vs. 3 years: 27%, n=15)

Figure 1. EQ-5D-L index score and domain scores in participants with baseline and follow-up data at 1, 2 and 3 years of treatment



SEM: standard error of the means

Conclusions

- Consistent with published literature, MPS IVA participants in MARS showed impairments in QoL as assessed by EQ-5D-5L, with baseline data suggesting that QoL declines with age in untreated individuals[2]
- Participants treated with elosulfase alfa demonstrated sustained improvements in QoL over 3 years, particularly in the domains of usual activities, mobility, and pain/discomfort
  - No increase in proportion of participants experiencing moderate-to-extreme problems was observed in any domain throughout the 3-year follow-up
- This analysis of QoL in individuals with MPS IVA treated with elosulfase alfa ERT, using a large international real-world dataset collected over 10 years of routine care, suggests that ERT may support meaningful and sustained improvments in QoL

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