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Long-Term Outcomes in Adults with MPS IVA Treated with Elosulfase Alfa: Findings from the Morquio A Registry Study

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Background

- Mucopolysaccharidosis (MPS) IVA is a rare, progressive lysosomal storage disorder with multisystemic clinical manifestations [1-3]
- The safety and efficacy of elosulfase alfa enzyme replacement therapy (ERT) for the treatment of MPS IVA were investigated in a phase 3 clinical trial that included both pediatric and adult patients [4-7]
- However, understanding the long-term benefits of initiating ERT in adults with pre-existing disease burden remains an important clinical question

Methods

- The Morquio A Registry Study (MARS) is an ongoing, multinational, observational study of patients with MPS IVA
  - All patients with a confirmed diagnosis of MPS IVA are eligible to participate; data are collected as part of routine care
- Data from ERT-treated patients enrolled in MARS who initiated treatment at ≥18 years of age are presented here
  - ***ERT-treated subjects*** are defined as those who were ever treated with elosulfase alfa, prior to and/or after enrollment in MARS
  - ***Registry Entry*** is defined as the date of signed consent in MARS
  - ***Baseline assessment*** was defined as the data point closest to the date of first exposure to elosulfase alfa, which may precede Registry Entry
- Change from pre-treatment baseline in clinical outcome variables are summarized for subjects with both a baseline measurement and at least one follow-up measurement
- Safety outcomes were assessed among ERT-treated subjects who received at least one dose of elosulfase alfa during MARS

Results

- As of Feb 2021, a total of 82 subjects who initiated ERT at ≥18 years were enrolled in MARS **(Table 1)**
- Mean total ERT exposure (from first exposure to Feb 2021) was 5.10 years (median: 5.0; range: 0.13, 9.67); mean age at first ERT was 32.6 years (median: 27.7; range: 18.9, 69.4)
  - 63 subjects (76.8%) initiated ERT prior to Registry Entry; 19 (23.2%) initiated ERT at or after Registry Entry

Table 1. Subject Demographics and Characteristics at Registry Entry

	ERT initiated ≥18 years (N = 82)
Sex, n (%)	
Female	52 (63.4)
Male	30 (36.6)
Race, n (%)	
Asian	11 (13.4%)
Black	2 (2.4%)
White	58 (70.7%)
Other/missing	11 (13.4%)
Age at diagnosis, years	
Mean (SD)	12.1 (14.7)
Median (range)	4.4 (0.6, 63.4)
Characteristics at Registry Entry	
Age, years	
Mean (SD)	34.4 (12.5)
Median (range)	30.7 (19.0, 73.5)
Standing height, cm	*n*=52
Mean (SD)	114.7 (20.2)
Median (range)	108.5 (88.0, 158.2)
Weight, kg	*n*=72
Mean (SD)	35.1 (12.8)
Median (range)	33.5 (19.0, 83.9)

Assessments performed at Registry Entry were defined as the closest data point within the time window from 12 months prior to Registry Entry to 90 days after Registry Entry

Safety Outcomes

- Among subjects who received ≥1 dose of elosulfase alfa during MARS (n=78), 29 subjects experienced ≥1 adverse event and 19 subjects had ≥1 serious adverse event (mean ERT exposure during MARS: 3.46 years); 11 drug-related adverse events were reported in 6 subjects **(Table 2)**
- 7 subjects died during MARS: the most frequently reported cause of death was respiratory failure **(Table 3)**; no deaths were assessed as related to ERT

Table 2. Adverse Events

Incidence, n (%)	(N = 78)
≥1 adverse event	29 (37.2)
≥1 serious adverse event	19 (24.4)
≥1 drug-related adverse event	6 (7.7)
Pyrexia	2 (2.6)
Diarrhoea	1 (1.3)
Discomfort	1 (1.3)
Gastritis	1 (1.3)
Hypertension	1 (1.3)
Infusion-related reaction	1 (1.3)
Urticaria	1 (1.3)
Adverse event leading to permanent ERT discontinuation	1 (1.3)
Deaths (see Table 3)	7 (9.0)

Table 3. Causes of Death, Age at Death, and Prior Respiratory Function Data for Subjects who Died During MARS

Primary Cause of Death	Age at Death (years)	Last Recorded Respiratory Function	
		FEV_1 (L)	FVC (L)
Respiratory failure	38.7	0.82	0.62
Respiratory insufficiency	27.8	0.37	0.33
Respiratory failure	27.2	0.92	0.40
Cardiac arrest	25.6	0.55	0.46
Cardiac arrest	26.5	0.66	0.47
Respiratory failure	65.2	0.39	0.39
Respiratory failure	31.8	not determined	not determined

Cause of death was assessed by the investigator and an autopsy may have not been performed/reported

Clinical Outcomes

- uKS levels declined from pre-ERT baseline to last follow-up on treatment by a mean of -51.0%, over a mean follow-up time of 5.3 years **(Figure 1)**
- 6MWT distance remained stable, with a mean change from baseline to last follow-up on treatment of +11.1 m, over a mean follow-up time of 4.9 years **(Figure 2)**
- FEV_1 and FVC were stable throughout follow-up **(Figure 3)**

Figure 1. Normalized uKS

Pre-treatment baseline and last follow-up (A); change from baseline by treatment duration (B)

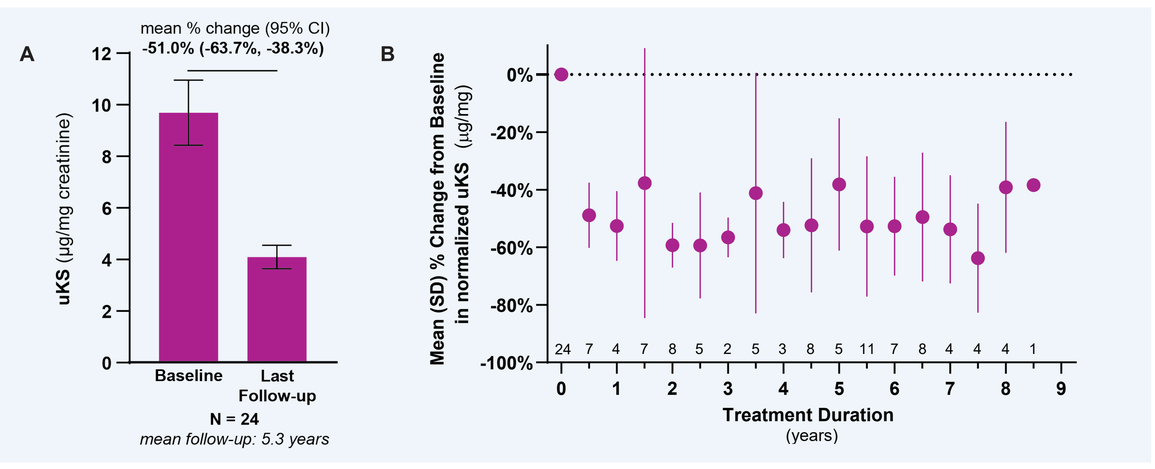


Figure 2. 6-Minute Walk Test

Pre-treatment baseline and last follow-up (A); change from baseline by treatment duration (B)

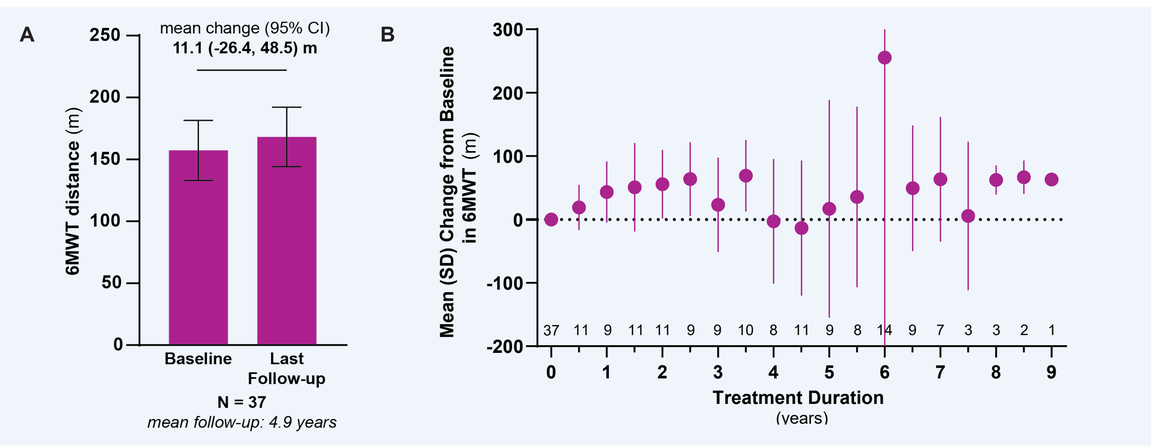
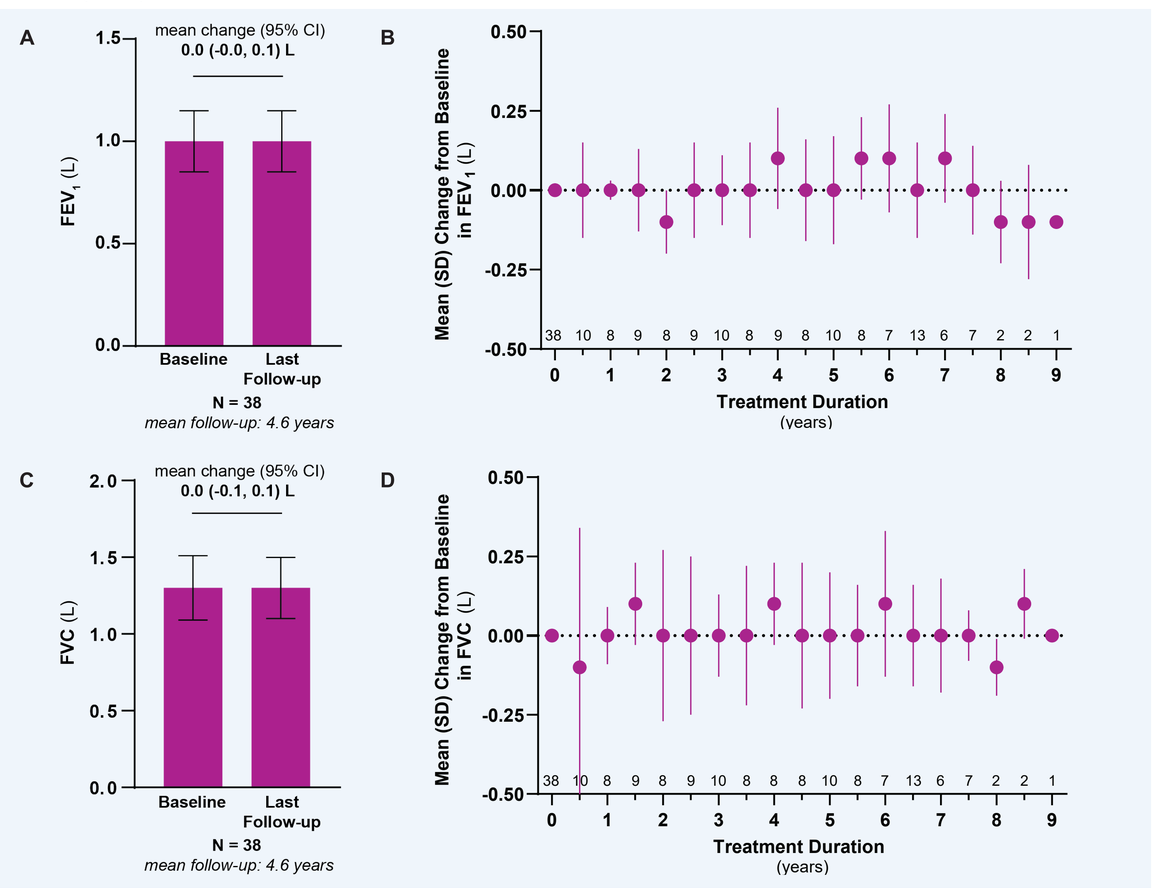


Figure 3. Respiratory Function

FEV_1 and FVC at pre-treatment baseline and last follow-up (A, C); change from baseline by treatment duration (B, D)



Conclusions

- Data from MPS IVA patients enrolled in a multinational, observational registry study who initiated ERT treatment as adults show a sustained reduction in uKS and long-term stabilization of clinical outcomes, relative to declines that would be expected due to disease progression
- No new safety concerns related to elosulfase alfa treatment were identified in this population
- Overall, these results from a real-world MPS IVA population with pre-existing disease burden support findings from clinical trials

References

1. Hendriksz CJ, Harmatz P, Beck M, et al. *Mol Genet Metab* 2013;110:54-64. **2.** Harmatz P, Mengel KE, Giugliani R, et al. *Mol Genet Metab* 2013;109:54-61. **3.** Harmatz PR, Mengel KE, Giugliani R, et al. *Mol Genet Metab* 2015;114:186-94. **4.** Hendriksz CJ, Burton B, Fleming TR, et al. *J Inherit Metab Dis* 2014;37:979-90. **5.** Hendriksz CJ, Parini R, AlSayed MD, et al. *Mol Genet Metab* 2016;119:131-43. **6.** Hendriksz CJ, Berger KI, Parini R, et al. *J Inherit Metab Dis* 2016;39:839-47. **7.** Hughes D, Giugliani R, Guffon N, et al. *Orphanet J Rare Dis* 2017;12:98.

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