LB-11

Enzyme replacement therapy is associated with improved endurance in MPS IVA patients at different ages

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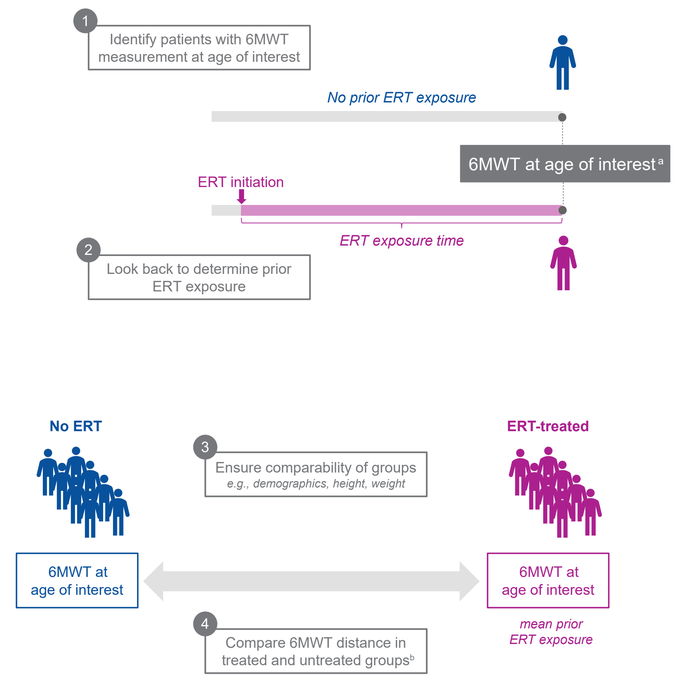
Background

- Assessments of the real-world impact of elosulfase alfa enzyme replacement therapy (ERT) in the MPS IVA population are challenging due to limited longitudinal natural history data
- We conducted a cross-sectional analysis comparing 6-minute walk test distance (6MWT; a measure of endurance) in ERT-treated and untreated patients at different ages using data from the Morquio A Registry Study (MARS) and the Morquio A Clinical Assessment Program (MorCAP) natural history study
  - MARS is an ongoing multinational, observational study of patients with MPS IVA: patients with a confirmed diagnosis of MPS IVA are eligible to participate and data are collected as part of routine care; the study includes both ERT-treated and untreated patients [1]
  - The MorCAP natural history study was a multinational, observational study of patients with MPS IVA: patients were assessed at study entry and over time thereafter [2,3]

Methods

- Separate analyses were conducted including patients with a 6MWT measurement (in either dataset) at age 5-<7 (n = 120), 9-<11 (n = 127), 14-<16 (n = 102), or 20-<30 years (n = 122)
- For each age group, patients were stratified by ERT exposure prior to the 6MWT measurement (≥ 180 days ERT treatment vs no prior ERT exposure); characteristics of ERT-treated and ERT-naïve patients were described and 6MWT distance compared (**Figure 1**)
- Univariate and multivariate quantile regression analyses including ERT treatment, age at measurement, sex, race, region, height, and weight as covariates were performed to assess associations between ERT exposure and 6MWT distance

Figure 1. Analytic approach



[a]Assessment closest to the age of interest was utilized for analysis
[b]Groups were mutually exclusive: individual subjects identified in both datasets were included in the no ERT exposure group only

Results

Patient characteristics and descriptive analyses

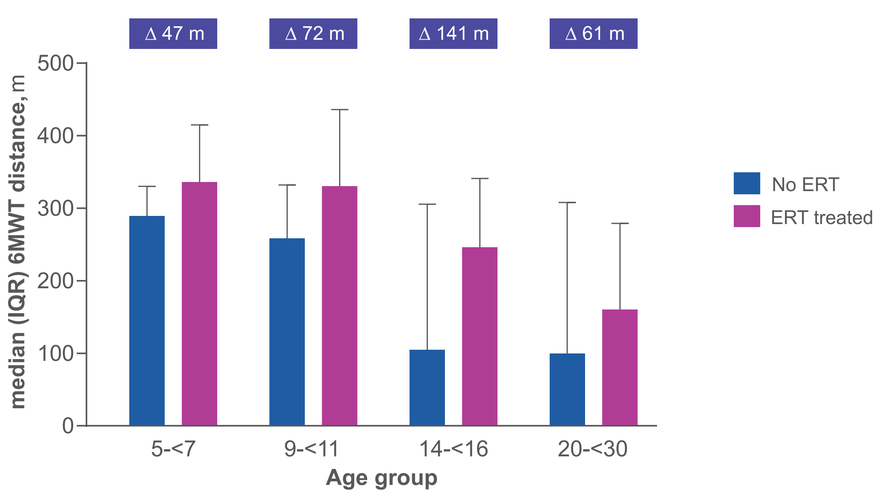
- Mean (SD) ERT exposure time for ERT-treated patients was 2.7 (1.2) years for the 5-<7 year age group, 4.5 (2.0) years for the 9-<11 year age group, 5.3 (2.8) years for the 14-<16 year age group and 5.2 (3.3) for the 20-<30 year age group (**Table 1**)
- Sex, age at assessment, mean standing height, and weight were similar for ERT-treated and untreated patients within each age group (**Table 1**)
- Median 6MWT distance was greater for ERT-treated patients than untreated patients in all age groups, with differences between treated and untreated patients ranging from 47 m to 141 m (**Table 1** and **Figure 2**)

Table 1. Patient characteristics

		Age 5-<7		Age 9-<11	
		No ERT n = 85	ERT Treated n = 35	No ERT n = 69	ERT Treated n = 58
Age at assessment, y	mean (SD)	5.6 (0.5)	5.7 (0.4)	9.6 (0.5)	9.7 (0.5)
ERT exposure, y	mean (SD) range	N/A	2.7 (1.2) 0.9–5.3	N/A	4.5 (2.0) 0.5–9.5
Female	n (%)	42 (49.4)	16 (45.7)	32 (46.4)	20 (34.5)
Race White Non-white Not reported	n (%)	 58 (68.2) 23 (27.1) 4 (4.7)	 10 (28.6) 18 (51.4) 6 (17.1)	 51 (73.9) 11 (15.9) 7 (10.1)	 29 (50.0) 24 (41.4) 5 (8.6)
Region Europe N America Other Not reported	n (%)	 28 (32.9) 23 (27.1) 32 (37.6) 2 (2.4)	 15 (42.9) 6 (17.1) 14 (40.0) 0	 28 (40.6) 18 (26.1) 2 (2.9) 21 (30.4)	 22 (37.9) 12 (20.7) 0 24 (41.4)
6MWT distance, m	mean (SD) median	275.7 (87.4) 289.3	322.6 (132.8) 336.0	242.6 (116.8) 258.3	308.0 (153.8) 330.5
Height, cm[a]	 mean (SD) median	*n=81* 94.4 (6.4) 93.0	*n=30* 97.4 (7.4) 96.8	*n=61* 105.7 (12.8) 100.9	*n=52* 107.6 (11.8) 104.3
Weight, kg[a]	 mean (SD) median	*n=82* 15.7 (2.5) 15.3	*n=34* 16.5 (2.9) 16.4	*n=66* 22.3 (6.5) 21.0	*n=55* 21.9 (6.0) 20.0
FEV_1, L[b]	 mean (SD)	*n=31* 0.71 (0.19)	*n=15* 0.80 (0.25)	*n=35* 0.95 (0.45)	*n=33* 1.04 (0.48)
FVC, L[b]	 mean (SD)	*n=31* 0.75 (0.21)	*n=15* 0.94 (0.39)	*n=35* 1.11 (0.58)	*n=33* 1.18 (0.52)
		Age 14-<16		**Age 20-<30**	
		No ERT n = 65	**ERT Treated n = 37**	**No ERT n = 76**	**ERT Treated n = 46**
Age at assessment, y	mean (SD)	14.6 (0.5)	14.6 (0.5)	24.3 (2.9)	24.0 (2.7)
ERT exposure, y	mean (SD) range	N/A	5.3 (2.8) 0.5–10.4	N/A	5.2 (3.3) 0.9–14.1
Female	n (%)	33 (50.8)	18 (48.6)	37 (48.7)	26 (56.5)
Race White Non-white Not reported	n (%)	 41 (63.1) 22 (33.8) 1 (3.1)	 17 (45.9) 17 (45.9) 3 (8.1)	 52 (68.4) 17 (22.4) 7 (9.2)	 24 (52.2) 20 (43.5) 2 (4.3)
Region Europe N America Other Not reported	n (%)	 26 (40.0) 21 (32.3) 17 (26.2) 1 (1.5)	 13 (35.1) 11 (29.7) 13 (35.1) 0	 35 (46.1) 14 (18.4) 24 (31.6) 3 (3.9)	 6 (13.0) 20 (43.5) 20 (43.5) 0
6MWT distance, m	mean (SD) median	167.2 (168.7) 105.0	244.5 (200.8) 246.0	157.4 (158.1) 99.5	166.3 (163.5) 160.4
Height, cm[a]	 mean (SD) median	*n=48* 117.5 (21.2) 113.3	*n=31* 116.0 (23.6) 103.5	*n=59* 109.9 (20.9) 101.3	*n=31* 111.6 (20.7) 105.0
Weight, kg[a]	 mean (SD) median	*n=63* 30.4 (12.2) 28.0	*n=31* 33.4 (14.6) 26.9	*n=74* 33.4 (14.5) 27.8	*n=42* 34.0 (12.9) 30.0
FEV_1, L[b]	 mean (SD)	*n=32* 1.26 (0.92)	*n=23* 1.36 (1.12)	*n=37* 1.26 (1.03)	*n=24* 1.28 (1.11)
FVC, L[b]	 mean (SD)	*n=32* 1.48 (1.09)	*n=23* 1.60 (1.24)	*n=37* 1.49 (1.27)	*n=24* 1.58 (1.48)

[a]within ± 365 days of 6MWT assessment of interest
[b]within ± 180 days of 6MWT assessment of interest
FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation

Figure 2. Median 6MWT distance



Regression analyses

- In each age group, separate multivariate quantile regression analyses were conducted including either *(a)* variables that were significantly associated ($P < 0.1$) with 6MWT distance in univariate analyses or *(b)* all base case variables (ERT exposure, sex, age at 6MWT assessment, standing height, weight, region and race)
  - Endurance impacts of ERT were maintained after adjusting for other covariates (coefficient range: 33.1-101.8 m; **Table 2**)

Table 2. Associations with 6MWT distance: regression analysis

	Variables significant ($P < 0.1$) in univariate				All base case variables			
	5-<7 y	9-<11 y	14-<16 y	20-<30 y	5-<7 y	9-<11 y	14-<16 y	20-<30 y
ERT: treated	**46.7**	**66.2**	**68.5**	**62.5**	**83.0**	**101.8**	**87.6**	**33.1**
Sex: female					-30.5	-40.2	-24.9	-55.2
Age					18.9	-63.8	-39.7	-4.1
Height		3.5[†]	4.8	7.0	2.7	5.6	4.7	5.6
Weight			0.5	-3.2	-5.1	-8.0	1.6	-1.9
Region: N America					-4.6	39.2	-15.6	31.1
Region: Other					-2.1	22.6	-3.6	65.3
Race: Non-white					-64.2	-111.5	28.5	-32.5

Numbers in cells show coefficients
Colors indicate significance of association with 6MWT distance $P < 0.05$ $P = 0.05$-< 0.1 $P \geq 0.1$
Referent groups: ERT (untreated), sex (male), region (EU), race (white); coefficients represent difference in 6MWT in m per cm for height, per kg for weight, and per year for age

Conclusions

- Patients treated with ERT demonstrated greater endurance (as determined by 6MWT distance) than age-matched untreated patients
- These results demonstrate a consistent impact of ERT on endurance in MPS IVA patients, with improved 6MWT distance across all age groups assessed

References

1. Mitchell JJ, Burton BK, Bober MB, et al. *Mol Genet Metab* 2022;137:164-72. **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.

Disclosures

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