Clinical outcomes for patients enrolled in the MPS VII disease monitoring program (DMP)

Roberto Giugliani,[1] Raymond Wang,[2] Antonio Gonzalez-Meneses,[3] Barbara Burton,[4] Christina L Grant,[5] Maurizio Scarpa,[6] Monica Penon-Portmann,[7] Ans Van der Ploeg,[8] Esmeralda Martins,[9] Consuelo Durand,[10] Brigitte Chabrol,[11] Joel Hetzer,[12] Jeanne Cohen,[12] and J. Lawrence Merritt, II[12]

[1]Dep Genetics UFRGS, Med Genet Serv HCPA, IMASP, DASA and Casa dos Raros, Porto Alegre, Brazil; [2]Children's Hospital of Orange County, Orange, California and Department of Pediatrics, University of California-Irvine, Orange, California, USA; [3]Hospital Universitario Virgen del Rocio, Seville, Spain; [4]Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA; [5]Children's National Hospital, Washington, District of Columbia, USA; [6]Regional Coordinator Centre for Rare Diseases, University Hospital of Udine, Udine, Italy; [7]Seattle Children's Hospital, Seattle, Washington, USA; [8]Erasmus University Medical Center Rotterdam, Rotterdam, Netherlands; [9]Centro Hospitalar do Porto, Porto, Portugal; [10]Laboratorio Chamoles, Buenos Aires, Argentina; [11]Centre Hospitalier Universitaire La Timone, Marseille, France; [12]Ultragenyx Pharmaceutical Inc., Novato, California, USA

BACKGROUND

- Mucopolysaccharidosis VII (MPS VII) is an ultra-rare, autosomal recessive, progressively debilitating and life-threatening lysosomal storage disorder caused by beta-glucuronidase (GUS) enzyme deficiency
- GUS enzyme activity is required for degradation of glycosaminoglycans (GAGs)
- Reduction in enzyme activity results in accumulation of dermatan sulfate (DS), chondroitin-6-sulfate (CS), and heparan sulfate (HS)
- Enzyme replacement therapy with vestronidase alfa (VA), a recombinant human GUS, is approved for MPS VII treatment
- An ongoing, multicenter, observational study is collecting standardized data from patients with MPS VII treated with vestronidase alfa (VA) or any other management approach

OBJECTIVES

- Characterize MPS VII disease presentation and progression over time in patients treated and not treated with VA using performance assessments and patient/caregiver reported outcomes

METHODS

- Some patients received vestronidase alfa through clinical trials or commercial sources before enrolling in the DMP
- Data include a mix of patients treated with VA and untreated patients
- The following assessments were completed during designated visits to the DMP site:
  - Six-Minute Walk test (6MWT) was completed by ambulatory patients ≥5 years old able to follow test instructions
  - MPS Health Assessment Questionnaire (MPS HAQ) was completed by caregivers of patients ≥5 years old
  - Pediatric Quality of Life™ Multi-dimensional Fatigue Scale (PedsQL) was completed by caregivers of patients ≥2 years old
- Data cut off date: 15 Nov 2024

RESULTS

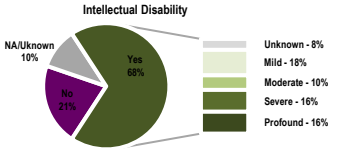
Patient Demographics and Disease Characteristics

- 38 patients have enrolled in the DMP; 7 have withdrawn, 1 due to death, 1 due to loss to follow-up, and 5 due to withdrawal of consent

Patient Demographics and Disease Characteristics at DMP Baseline

Patient Demographics and Characteristics	DMP Patients N=38
Sex, n (%)	
Female	18 (47)
Male	20 (53)
Age at MPS VII diagnosis, mean (SD)	**4.3 (3.9)**
Age at initiation of VA, mean (SD)	**N=32 8.3 (6.6)**
Age at DMP entry, mean (SD)	**13.4 (10.8)**
First Treatment with VA, n (%)	
Prior to DMP enrollment	26 (68)
After DMP enrollment	6 (16)
Untreated	6 (16)
NIHF*, n (%)	**17 (45%)**

*NIHF was identified based on clinical guidance and prenatal medical history including the following terms: hydrops fetalis, edema, dysmorphic phenotype, possible hydrops, anasarca and jaundice, and/or globus abdomen



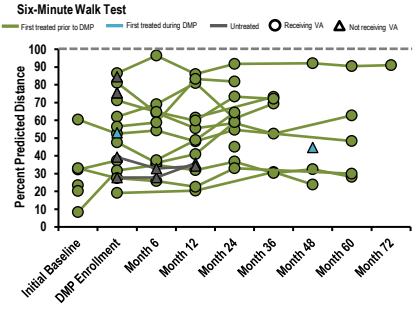
Dermatan Sulfate Urinary GAG Excretion

- Among patients treated prior to DMP enrollment, dermatan sulfate was reduced >60% since pre-treatment baseline levels
- Reductions have been maintained through at least month 60

RESULTS

Six-Minute Walk Test Over Time

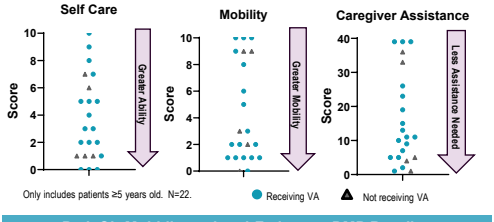
- A wide range in walking capacity across groups was observed, ranging from below 25% predicted to approaching 100% predicted
- All participants showed a deficit on the 6MWT



Only includes ambulatory patients ≥5 years old. N=23.

MPS HAQ at DMP Baseline

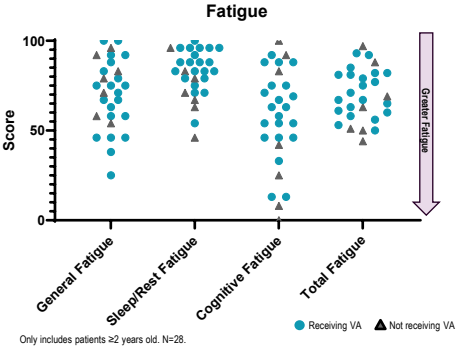
- Wide variability was seen, with some patients requiring little to no assistance and some patient requiring complete assistance



Only includes patients ≥5 years old. N=22.

PedsQL Multidimensional Fatigue at DMP Baseline

- Wide variability was seen with some caregivers reporting the patient had profound fatigue and others reporting the patient had no fatigue



Only includes patients ≥2 years old. N=28.

CONCLUSIONS

- These preliminary results confirm the heterogeneity of patients with MPS VII
- This heterogeneity creates issues with grouping all patients together when reviewing results
- Additional data over the next few years will help determine trends among participants treated with VA

DISCLOSURES AND ACKNOWLEDGMENTS

- **Jeanne Cohen, Joel Hetzer,** and **J. Lawrence Merritt II** are employees and shareholders of Ultragenyx Pharmaceutical Inc.
- All other authors are PIs in the MPS VII DMP.
- **Roberto Giugliani** served on an advisory board for Amicus, BioMarin, Inventiva, JCR, RegenCBio, Sanofi, Sigilon, Sobi, Takeda, and Ultragenyx Pharmaceutical Inc.; received travel support from Amicus, BioMarin, JCR, Sanofi, Takeda, and Ultragenyx Pharmaceutical Inc.; served as an investigator for Allevex, JCR, Lysogene, RegenxBio, Sanofi, Takeda, Ultragenyx Pharmaceutical Inc.; received honoraria from Amicus, BioMarin, Denali, JCR, Novartis, PTC, RegenxBio, Sanofi, Takeda, and Ultragenyx Pharmaceutical Inc.
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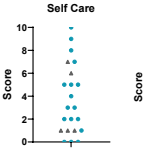
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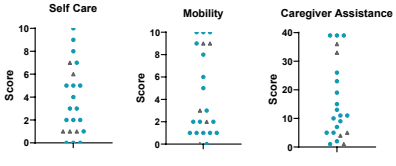
Score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Mobility
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Caregiver Assistance
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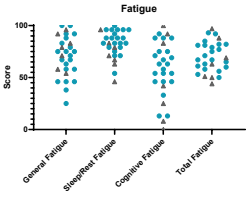
Fatigue
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Sleep/Rest Fatigue
Cognitive Fatigue
Total Fatigue