February 2024

Characterizing Disability Accumulation With Patient-Reported Outcomes and Clinical Outcomes in Patients With Multiple Sclerosis in the MS-LINK Outcomes Study Cohort

Jeffrey English,[1] Carlo Tornatore,[2] Emily Riser,[3] Gabriel Pardo,[4] Leorah Freeman,[5] Jacob Sloane,[6] Jeanie Cote,[7] Rana Zabad,[8] Tania Reyna,[9] Elizabeth Piette,[10] Christina Caon,[10] Terrie Livingston[10]

[1]Atlanta Neurological Institute, Atlanta, GA, USA; [2]Georgetown University Medical Center, Medstar Georgetown University Hospital, Medstar Health, Washington, DC, USA; [3]Alabama Neurology Associates, Birmingham, AL, USA; [4]Oklahoma Medical Research Foundation, Multiple Sclerosis Center of Excellence, Oklahoma City, OK, USA; [5]Dell Medical School, The University of Texas at Austin, Austin, TX, USA; [6]Beth Israel Deaconess Medical Center, Boston, MA, USA; [7]Memorial Healthcare Institute for Neuroscience, Owosso, MI, USA; [8]University of Nebraska Medical Center, Omaha, NE, USA; [9]University of Texas Health Science Center at San Antonio, San Antonio, TX, USA; [10]EMD Serono, Inc., Rockland, MA, USA

CONCLUSIONS

- **In this real-word observational study, disability accumulation independent of relapse was observed over a 12-month period in various patient-reported outcomes (PROs) and clinical outcomes across sex, race, ethnicity, type of multiple sclerosis (MS), and class of disease-modifiying therapy (DMT)**
- **Use of PROs in clinical practice may help identify disability accumulation independent of relapse**

INTRODUCTION

- MS is a chronic neurodegenerative condition affecting the central nervous system and is marked by inflammation and demyelination[1]
- Clinical assessments, commonly conducted annually, may not provide frequent enough insight into patient disability accumulation
- PROs, which may provide additional ways to assess and monitor disability accumulation in MS and provide a more holistic understanding of the impact of the disease on daily living, are underutilized[2]
- PROs can be a valuable tool to collect and assess the quality of life of an individual in a real-world setting
- Here we present the MS-LINK Outcomes Study findings focused on data gathered from PROs and clinical outcomes

OBJECTIVE

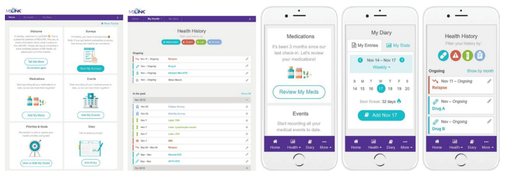
- **To characterize disability accumulation independent of relapse activity in DMT-treated patients with MS in terms of changes in PROs and clinical measures over the course of 1 year**

METHODS

- The MS-LINK Outcomes Study is a prospective longitudinal multicenter observational study focused on digital data collection of PROs in addition to clinical outcomes, medical history, and sociodemographic characteristics in patients with MS (**Figure 1**)
- This investigation outlines the changes observed in the absence of relapse activity over a period of approximately 1 year from the study baseline
- The following PROs were collected and the clinically meaningful differences were measured as described below:
  - Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue SF 8a: increase of ≥3.4 points from baseline at 13 months*
  - PROMIS Physical Function 15: decrease of ≥2.3 points from baseline at 13 months*
  - PROMIS Anxiety: increase of ≥5 points (0.5 SD) at 14 months*
  - PROMIS Cognition: decrease of ≥5 points (0.5 SD) at 12 months*
  - Patient Determined Disease Steps (PDDS): change in 1 point from baseline sustained for more than 3 months*
  - Timed 25-Foot Walk (T25W) and 9-Hole Peg Test (9HPT): change of 20% from baseline at 11-13 months†
  - Symbol Digit Modalities Test (SDMT): change of 4 points from baseline at 11-13 months†
- All patients included in the analysis were receiving treatment with a DMT

*Patient reported. †HCP reported.

Figure 1. Digital Data Collection Portal



RESULTS

Patient Demographics

- As of January 2024, 2126 patients were enrolled in the MS-LINK Outcomes study
- This analysis includes 637 patients who are treated with a DMT, relapse free for the duration of the study and enrolled for ≥12 months (**Table 1**)

Table 1. Demographics and Disease Characteristics of DMT-Treated Patients Free of Relapse Activity With at Least 1 Year of Follow-up From Baseline (n=637)[a]

Characteristics	
Age, years	
Mean (SD) [Range]	51.6 (11.2) [21-83]
Sex, n (%)	
Female	511 (80.2)
Male	121 (19.0)
Race, n (%)	
White or Caucasian	492 (77.2)
Black or African American	105 (16.5)
Two or more races	23 (3.6)
American Indian or Alaska Native	7 (1.1)
Asian	3 (0.5)
Ethnicity, n (%)	
Not Hispanic	507 (79.6)
Hispanic	25 (3.9)
Other	84 (13.2)
Type of MS, n (%)	
Relapsing-remitting	573 (90.0)
Secondary progressive	45 (7.1)
Primary progressive	19 (3.0)
Disease duration, years	
Mean (SD) [Range]	14.4 (9.5) [1-51]

[a]Some responses missing due to non-response or desire not to disclose. DMT, disease-modifying therapy; MS, multiple sclerosis.

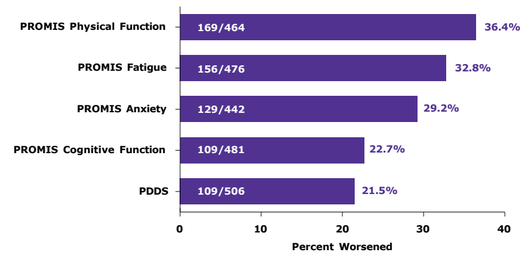
RESULTS (cont.)

- PROs and clinical outcomes in relapse free, DMT-treated patients who were in the study from ≥12 months

Proportion of Patients With Worsened PROs Score Independent of Relapse

- Clinically meaningful worsening was observed in PROMIS scores in 36.4% of patients in physical function (minimal clinically important difference [MCID]≥2.3)[2], 32.8% in fatigue (MCID≥3.4)[3], 29.2% in anxiety (MCID=5.0), 22.7% in cognitive function (MCID=5.0), and 21.5% in PDDS (**Figure 2**)

Figure 2. Proportion of Patients Who Worsened on PROs Over ≥12 Months



PDDS, Patient Determined Disease Steps; PROs, patient-reported outcomes; PROMIS, Patient-Reported Outcomes Measurement Information System

PROMIS Fatigue Score

- Approximately 33% of DMT-treated patients for whom we had 1 year of follow-up time had worsened PROMIS Fatigue Scores (MCID≥3.4) compared to baseline (**Table 2**)
- Patients worsened independent of relapse activity in PROMIS Fatigue score across sex, race, ethnicity, and type of MS

Table 2. Characteristics of Patients Who Worsened Independent of Relapse: PROMIS Fatigue (n=156)

Characteristics	Patients who worsened (n/N=156/475)
Sex, n (%)	
Female	131 (33.8)
Male	24 (28.9)
Race, n (%)	
White or Caucasian	122 (32.4)
Black or African American	23 (31.5)
Two or more races	6 (42.9)
Ethnicity, n (%)	
Not Hispanic	127 (33.0)
Hispanic	6 (31.6)
Other	18 (31.0)
Type of MS, n (%)	
Relapsing-remitting	141 (33.5)
Secondary progressive	9 (25.7)
Primary progressive	5 (33.3)

MS, multiple sclerosis; PROMIS, Patient-Reported Outcomes Measurement Information System.

- Worsening (higher score) was observed in PROMIS Fatigue score across all classes of DMTs. Higher scores indicate more fatigue (**Table 4**)[a]

Table 4. PROMIS Fatigue Score and Characteristics of Patients by DMTs

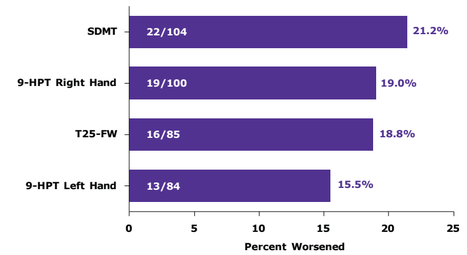
DMT	Patients Worsened, n/N (%)	Age, mean (SD) [range]	Disease duration, mean (SD) [range]	Baseline fatigue score, mean (SD)	Change from baseline to 12 months fatigue score, mean (SD)
Anti-CD20s	61/186 (32.8)	49.1 (10.5) [33-75]	12.9 (9.7) [1-39]	51.3 (10.1)	8.0 (4.0)
Natalizumab	16/45 (35.6)	44.5 (8.9) [25-65]	10.3 (6.9) [2-19]	51.7 (9.6)	8.9 (3.3)
Fumarates	14/54 (25.9)	54.7 (8.0) [45-69]	17.4 (8.1) [5-37]	48.8 (9.1)	7.3 (3.2)
Platform injectables	12/44 (27.3)	56.3 (8.0) [41-74]	15.9 (6.2) [7-25]	48.5 (12.1)	7.2 (3.2)
S1P modulators	19/45 (42.2)	51.2 (9.8) [29-70]	11.7 (9.1) [1-26]	48.7 (9.7)	8.1 (3.5)
Teriflunomide	13/34 (38.2)	56.5 (13.8) [30-76]	10.6 (8.1) [2-26]	51.4 (10.8)	9.2 (5.1)
Cladribine	5/19 (26.3)	48.8 (6.8) [37-54]	12.6 (6.8) [2-19]	58.0 (7.1)	6.3 (2.1)

[a]DMTs or classes of DMTs with <10 people were excluded from analysis.
DMTs, disease-modifying therapies; PROMIS, Patient-Reported Outcomes Measurement Information System.

Proportion of Patients With Worsened Clinical Outcomes Independent of Relapse

- 21.2% (22/104) had lower SDMT scores (MCID=4)[4]
- Clinically meaningful worsening was observed in 15.5% of patients for 9-HPT left hand, 18.8% for 9-HPT right hand, and 19.0% for T25-FW (**Figure 3**)

Figure 3. Proportion of Patients With Worsened Clinical Outcomes Over ≥12 Months



9-HPT; 9-Hole Peg Test; SDMT, Symbol Digit Modalities Test; T25-FW,Timed 25-Foot, Walk.

PROMIS Physical Function Score

- Approximately 36% of DMT-treated patients for whom we had 1 year of follow-up time had worsened PROMIS Physical Scores (MCID≥2.3) compared to baseline (**Table 3**)
- Patients worsened (lower scores) independent of relapse in PROMIS Physical Function across sex, race, ethnicity, and type of MS

Table 3. Characteristics of Patients Who Worsened Independent of Relapse: PROMIS Physical Function (n=169)

Characteristics	Patients who worsened (n/N=169/464)
Sex, n (%)	
Female	130 (34.5)
Male	37 (45.1)
Race, n (%)	
White or Caucasian	132 (35.9)
Black or African American	24 (34.3)
Two or more races	7 (50.0)
Ethnicity, n (%)	
Not Hispanic	134 (35.6)
Hispanic	9 (52.9)
Other	19 (33.3)
Type of MS, n (%)	
Relapsing-remitting	146 (35.7)
Secondary progressive	13 (37.1)
Primary progressive	8 (53.3)

MS, multiple sclerosis; PROMIS, Patient-Reported Outcomes Measurement Information System.

- Worsening (lower scores) was observed in PROMIS Physical Function score across all classes of DMTs. Higher scores indicate better physical function (**Table 5**)[a]

Table 5. PROMIS Physical Function Score and Characteristics of Patient by DMTs

DMT	Patients Worsened, n/N (%)	Age, mean (SD) [range]	Disease duration, mean (SD) [range]	Baseline Physical Function Score, mean (SD)	Change from baseline to 12 months Physical Function Score, mean (SD)
Anti-CD20s	72 (39.3)	50.3 (9.6) [31-75]	13.3 (9.1) [1-37]	44.5 (11.8)	−5.5 (2.8)
Natalizumab	14 (32.6)	49.9 (13.7) [25-78]	15.8 (8.0) [2-33]	46.7 (11.5)	−5.7 (3.8)
Fumarates	16 (30.8)	54.3 (8.2) [45-71]	17.1 (7.4) [3-33]	46.1 (10.0)	−6.1 (4.7)
Platform injectables	11 (26.2)	56.5 (5.6) [47-63]	14.2 (4.5) [7-21]	42.3 (9.3)	−5.0 (1.9)
S1P modulators	23 (52.3)	51.0 (10.5) [30-75]	14.6 (9.1) [1-36]	46.6 (11.6)	−6.1 (2.8)
Teriflunomide	11 (33.3)	58 (8.5) [44-76]	12.0 (9.4) [2-32]	42.4 (8.6)	−5.8 (4.6)
Cladribine	6 (31.6)	49.7 (12.0) [31-66]	18.5 (12.0) [6-38]	38.4 (7.7)	−7.2 (2.5)

[a]DMTs or classes of DMTs with <10 people were excluded from analysis.
DMTs, disease-modifying therapies; PROMIS, Patient-Reported Outcomes Measurement Information System.

References: 1. Giovannoni G, Mathews J. *Neurol Ther*. 2022;11(2):571-595. **2.** Kamudoni P, et al. *Mult Scler Relat Disord*. 2022;62:103753. **3.** Kamudoni P, et al. *Multi Scler Relat Disord*. 2021;54:103117. **4.** Benedict RH, et al. *Mult Scler*. 2017;23(5):721-733.

Acknowledgments: This study is sponsored by EMD Serono, an affiliate of Merck KGaA, who reviewed and provided feedback on this poster. Writing and editorial support for the preparation of this poster were provided by Syneos Health; funding was provided by the study sponsor. The authors had full control of the poster and provided their final approval of all content.

Disclosures: JE: creator, partner, and stockholder in Healthcare Impact Partners, LLC, and HIPnation Operations & Solutions, LLC; was on advisory boards and speaker panels for pharmaceutical companies including Biogen Idec, Teva, Mallinckrodt, Novartis, Genentech, Genzyme, EMD Serono, and Celgene. Also served as medical director at MS Center of Atlanta. **CT:** Has received research funding from Biogen, Sanofi, and EMD Serono and was on advisory boards for Biogen, Genentech, Sanofi, EMD Serono, TG Therapeutics, and Atara. **ER:** Nothing to disclose. **GP:** Has received grants (to the institution) from Biogen, EMD Serono, Roche/Genentech, Sanofi Genzyme, Novartis, AbbVie, and BMS; consultant and/or speaker bureau for Biogen, EMD Serono, Roche/Genentech, Sanofi Genzyme, Novartis, Janssen, BMS, TG Therapeutics, PRIME Education, and MSAA. **LF:** Has received consultancy fees from Genentech, Novartis, Bristol Myers Squibb, EMD Serono, TG Therapeutics, Sanofi, and Horizon Therapeutics; has received program sponsorship from EMD Serono; and has grant support from NIH/NINDS, PCORI, Genentech, and EMD Serono. **JS:** was on advisory boards for Biogen, Novartis, and Genentech. **JC:** Has received consultancy, advisory board, and speaker fees from Genentech, Novartis, Bristol Myers Squibb, EMD Serono and TG Therapeutics. **RZ:** Site investigator for Adamas, Biogen, EMD Serono, Genentech, Novartis, Sanofi, Sunpharma, and PCORI; consultant for Bayer, Biogen, Genentech, Celgene/BMS, EMD Serono, Genzyme, the healthcare business of Merck KGaA, Darmstadt, Germany, Sanofi, TEVA Neuroscience, and TG therapeutics; lecturer for Novartis, Genentech BMS, EMD Serono, and Sanofi; Adjudication Committee member for the clinical trial "Biotin in primary and secondary progressive MS" sponsored by PAREXEL and medDay pharmaceutical; grant reviewer for PCORI and Advancing Healthier Wisconsin. **TR:** Has received research support from Biogen, UCB; consulting fees from EMD Serono, Alexion, TG Therapeutics, Biogen. **EP, CC,** and **TL:** employees of EMD Serono.

Prepared for the ACTRIMS 2024 Meeting; February 29–March 2; West Palm Beach, FL, USA