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Patient and Physician Perspectives on the Wearing-Off Effect in Multiple Sclerosis: Results From Structured Interviews

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KEY FINDINGS & CONCLUSIONS

- Perception and comprehension of the WOE differ between plwMS and clinicians, indicating the need for effective health communication and further work to elucidate the mechanisms of WOE
- Fatigue was reported as the most bothersome symptom by both patients and clinicians; some patients indicated fatigue as a trigger to other symptoms such as weakness and cognitive difficulties
- Clinicians' perceptions of the WOE were variable, suggesting that the care or attention provided by clinicians could be influenced by their perceived importance of the WOE
- Studies with a larger sample size are needed to further characterize the mechanisms and patient impact of the WOE among plwMS receiving DMTs

This study was sponsored by Novartis Pharma AG, Basel, Switzerland.

Poster Presented at the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum, February 29–March 2, 2024.

INTRODUCTION

- The wearing-off effect (WOE) refers to symptoms such as fatigue, cognitive dysfunction, sensory symptoms, and pain that occur toward the end of treatment cycles and can influence patient satisfaction[1,2]
- Studies have reported the wearing-off phenomenon in people living with multiple sclerosis (plwMS) receiving various disease-modifying therapies (DMTs)[1-7]
- Limited information is available on peoples' and clinicians' perspectives regarding the wearing-off phenomenon of DMTs in MS

OBJECTIVE

- To identify the key symptoms reported by plwMS and observed by clinicians due to the WOE associated with MS DMTs, and to better understand plwMS and physician perspectives on the WOE

METHODS

- Qualitative interviews were conducted among plwMS and clinicians treating MS (NCT05627271)
- Participants from the UK, USA, and Germany were recruited to participate in a one-time, semi-structured, virtual one-on-one interview; interviews were based on a modified version of a previously published questionnaire[2]
- The interviews were recorded and transcribed; all transcripts were checked for completeness and accuracy
- Both plwMS and clinicians were interviewed on disease experience, relapse and remission, and WOE symptoms
- In addition, patients were interviewed on their symptom experience and experience with their neurologist
- Clinicians were also asked on their perspective around the WOE
- Both plwMS and clinicians were requested to score the severity of each reported symptom on a scale of 0 (not severe) to 10 (extremely severe)
- Participants were also asked to fill in a short sociodemographic and clinical questionnaire shared via email
- Key inclusion/exclusion criteria for participants are outlined in **Figure 1**

Figure 1. Key inclusion/exclusion criteria

Eligibility criteria for plwMS	Eligibility criteria for clinicians
Key inclusion criteria	**Key inclusion criteria**
• Patients receiving DMTs (natalizumab, ocrelizumab, or ofatumumab) and aged ≥18 years • Confirmed diagnosis of RRMS • Experienced WOE symptoms[a]	• Specialists in neurology who have prescribed DMTs at least once during the last year • Treated ≥16 patients with MS in the last month • Treated patients who have experienced WOE
Key exclusion criteria	**Key exclusion criteria**
• Currently participating in an interventional MS clinical trial	• Currently involved as an HCP in an MS trial or receives funding from one of the drug manufacturers of the DMTs included in the survey

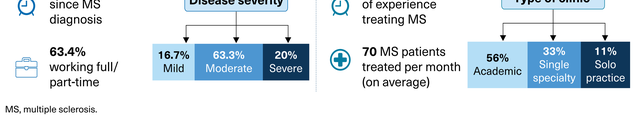
[a]Participants who experienced WOE symptoms toward the end of treatment cycles were recruited to minimize association bias.
DMT, disease-modifying therapy; HCP, healthcare professional; MS, multiple sclerosis; plwMS, people living with MS; RRMS, relapsing-remitting MS; WOE, wearing-off effect.

RESULTS

Sociodemographic and clinical characteristics

- Responses from 30 plwMS (n=10 per country) and 9 clinicians (n=3 per country) were collected during the survey
- Sociodemographic and clinical characteristics of patients and clinicians are summarized in **Figure 2**

Figure 2. Sociodemographic and clinical characteristics



MS, multiple sclerosis.

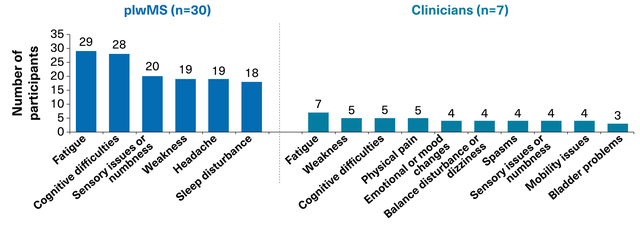
Patient and clinician perspectives on the WOE

- All patients recognized ≥1 WOE-associated symptoms, irrespective of the type, route of administration, and frequency of DMT received, whereas 7 of 9 clinicians reported observing WOE in their practice
- Most patients (22/30) were able to differentiate WOE from relapse-related symptoms
- Clinician perspectives on WOE were variable, describing it as psychosomatic manifestations, lack of efficacy, or placebo effect

Commonly reported WOE symptoms

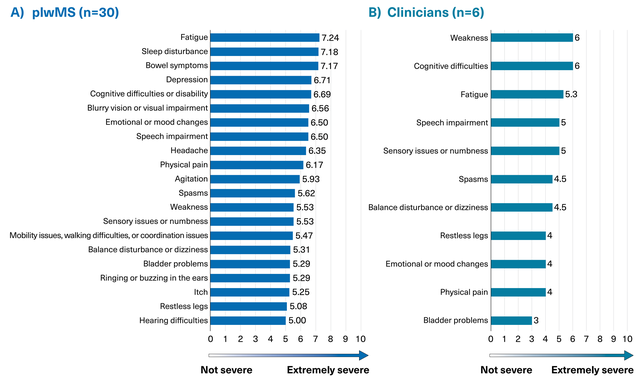
- Fatigue was the most common WOE symptom reported by patients (29/30) and clinicians (7/7; **Figure 3**) and was also described as the most bothersome symptom
- Other common symptoms reported by patients were cognitive difficulties (28/30) and sensory dysfunction or numbness (20/30)
- In comparison, clinicians most often identified weakness, cognitive difficulties, or pain (5/7 each) as related to WOE
- Fatigue was the most spontaneously reported symptom (without the need for probing) among patients; some patients also identified fatigue as a potential trigger for other symptoms such as weakness and cognitive difficulties (8/30)
- Patients perceived fatigue as the most severe WOE symptom, whereas clinicians perceived weakness and cognitive difficulties as the most severe WOE symptoms (**Figures 4A** and **4B**)

Figure 3. Commonly reported WOE-associated symptoms by plwMS and clinicians



plwMS, people living with multiple sclerosis; WOE, wearing-off effect.

Figure 4. Severity[a] of WOE symptoms perceived by plwMS and clinicians



[a]All values are represented as average. Participants were asked to score the severity of each reported symptom on a scale of 0 (not severe at all) to 10 (extremely severe).
plwMS, people living with multiple sclerosis; WOE, wearing-off effect.

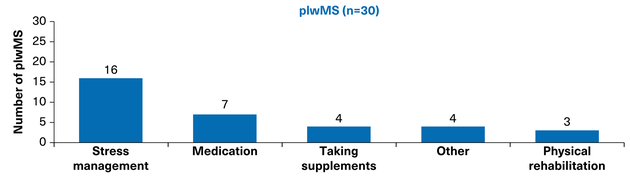
Time to onset of WOE-associated symptoms

- Patients mostly reported experiencing WOE-associated symptoms within 4 to 7 days prior to the next dose; however, most were unsure or said the time to resolution of WOE-associated symptoms varied after the last administration of DMT
- Clinicians perceived that the time to onset of WOE symptoms and time to symptom resolution after receiving the next DMT treatment varied across patients

Coping mechanisms

- The primary coping mechanisms recommended to patients included stress management, prescription of medications, taking supplements, physical rehabilitation, or others (including planning and preparation, wearing tight clothing, tips from patient support group; **Figure 5**)
- Many plwMS (18/30) were not willing to switch to a different DMT because of WOE symptoms
  - Seven plwMS were willing to switch; reasons for switching included preference for a more effective treatment, side effects, or physician recommendation
- In comparison, 6 of 9 clinicians were willing to switch to a different medication because they perceived the appearance of WOE symptoms as a lack of effect from the current medication

Figure 5. Coping mechanisms

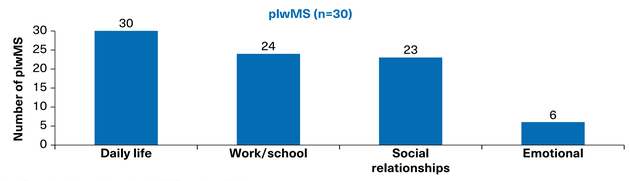


plwMS, people living with multiple sclerosis.

Impact of WOE on patient quality of life

- All patients reported that WOE negatively impacted their daily activities (**Figure 6**). When stratified by commonly reported WOE-associated symptoms, plwMS most frequently reported an impact on daily activities

Figure 6. Impact of WOE symptoms on patient quality of life



plwMS, people with multiple sclerosis; WOE, wearing-off effect.

Experience of plwMS with neurologist

- Overall, 25 of 30 plwMS discussed WOE-associated symptoms with their neurologists
- Among these 25 plwMS, 15 perceived that the attention received was appropriate

Strengths and limitations

- The questionnaire was designed to not ask questions on WOE directly but rather on the underlying symptoms at the beginning of the interview to minimize association bias
- Application of study results is limited by the small sample size and inclusion of participants from only three countries

References

1. Foley JF, et al. *Neurol Neuroimmunol Neuroinflamm*. 2020;7(3):e706.
2. Toorop AA, et al. *Mult Scler Relat Disord*. 2022;57:103364.
3. Fielding J, et al. *LB8384*. Poster presented at CMSC 2022.
4. Catherine D, et al. *Mult Scler Relat Disord*. 2020;41:102020.
5. Ratchford JN, et al. *Int J MS Care*. 2014;16(2):92–98.
6. van Kempen ZLE, et al. *Neurology*. 2019;93(17):e1579–e1586.
7. Labani A, et al. *Neuroimmunol Rep*. 2023;3:100167.

Abbreviations

DMT, disease-modifying therapy; **HCP**, healthcare professional; **MS**, multiple sclerosis; **plwMS**, people living with MS; **RRMS**, relapsing-remitting MS; **WOE**, wearing-off effect.

Disclosures

Enrique Alvarez received compensation for consulting from Alexion, Biogen, Celgene/BMS, EMD Serono/Merck, Genentech/Roche, Horizon/Amgen, Motric Bio, Novartis, Sanofi, Scionic, and TG Therapeutics, and for research from Atara, Biogen, Genentech/Roche, Novartis, Sanofi, TG Therapeutics, Patient-Centered Outcomes Research Initiative, National Multiple Sclerosis Society, National Institutes of Health, and Rocky Mountain MS Center. **Joanne Fielding** has received support for contracted research from Biogen Australia and Genzyme Corporation and honorarium from Novartis Pharmaceuticals, Australia. **Dorsa Khazaei**, **Cecilia Jimenez-Moreno**, and **Donald M. Bushnell** are employees of Evidera-PPD who received funding to complete this research study. **John Parratt** has received honoraria and research grants from Biogen, Novartis, Sanofi, Roche and Teva Pharmaceuticals. **Diogo Pata** was associated with Novartis during the study. **Ivan John Clement** is an employee of Novartis.

Acknowledgments

Medical writing support was provided by Venkateswarlu Bonala and Sreelatha Komatireddy and design support by Madhavi Kanithi, all of Novartis Healthcare Pvt. Ltd., Hyderabad, India. The final responsibility for content lies with the authors.