

The Wearing-off Effect of Two Anti-CD20 Therapies in Patients With Multiple Sclerosis: Ofatumumab and Ocrelizumab

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KEY FINDINGS & CONCLUSIONS

- A larger proportion of patients with multiple sclerosis (MS) treated with ocrelizumab (OCR) vs ofatumumab (OMB) experienced an increase in MS symptoms during the index treatment cycle, potentially indicating a wearing-off effect
- On Quality of Life in Neurological Disorders (Neuro-QoL) scales, patients taking OMB, compared with those taking OCR, showed significantly less worsening in fatigue, mobility, and cognition over the course of a treatment cycle
- The longer dosing interval associated with OCR may contribute to a higher reported incidence of wearing-off symptoms, characterized by increased symptoms prior to the next scheduled dose, although true disease activity cannot be ruled out



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This study was sponsored by Novartis Pharmaceuticals Corporation. Poster presented at the Consortium of Multiple Sclerosis Centers (CMSC) Annual Meeting • May 28-31, 2025 • Phoenix, AZ, USA

INTRODUCTION

- Anti-CD20 therapies are part of the standard of care for patients with relapsing forms of multiple sclerosis (MS)
- In a 2022 prospective study, 61% of patients with MS taking ocrelizumab (OCR; an anti-CD20 agent administered via biannual infusions) experienced a wearing-off effect, defined as worsening of or an increase in MS symptoms toward the end of a treatment cycle prior to the next dose. These wearing-off symptoms generally resolved after the next dose¹
- Further studies are needed to explore the potential wearing-off effect of OCR and other anti-CD20 therapies such as ofatumumab (OMB; administered via monthly injections)

OBJECTIVE

- To quantify worsening of MS symptoms over a treatment cycle with OCR and OMB, using validated Quality of Life in Neurological Disorders (Neuro-QoL) scales assessing MS symptoms (i.e., fatigue, mobility, depression, cognition) and direct questions on symptom worsening or increasing

METHODS

- This is a non-interventional, primary data collection study (**Figure 1**) among adult patients with MS treated with OCR or OMB in clinical practice settings across the United States
- Data were collected by Accelerated Cure Project, a patient-founded national nonprofit organization dedicated to accelerating advances towards a cure for MS
- Index treatment cycle was defined as the patients' first treatment cycle with OCR or OMB following recruitment
 - OCR: after ≥1 year of OCR treatment
 - OMB: after ≥6 months of OMB treatment
- The study outcome was defined as changes in patient-reported outcomes (PROs) from the start to the end of the index treatment cycle

Patient-Reported Outcomes

- A global wearing-off question ("Have you ever experienced an increase in MS symptoms between two consecutive OMB/OCR treatment administrations?"), based on the Toorop questionnaire,¹ was asked at enrollment. Response options were "Never," "Sometimes," "Usually," or "Always"

- The global wearing-off question ("Are you experiencing an increase in MS symptoms currently?"), based on the modified Toorop questionnaire,¹ was asked at the end of the index treatment cycle. Response options were "Yes," "No," or "Unsure"
- Four Neuro-QoL domain-specific scales were assessed at the beginning and end of the index treatment cycle:
 1. Fatigue
 2. Mobility
 3. Depression
 4. Cognition

Statistical Analysis

- The overall proportion of patients reporting an increase in symptoms for the global wearing-off question was calculated. Findings were also stratified across key patient and treatment subgroups
- For each of the Neuro-QoL scales, the proportion of patients whose scores worsened more than 0.5 times the standard deviation (SD) of baseline scores was calculated²
- For each scale question, the change in the proportion of patients selecting any of the three most severe response categories (i.e., unfavorable outcomes) between the start and end of the treatment cycle was assessed

Figure 1. Study Design

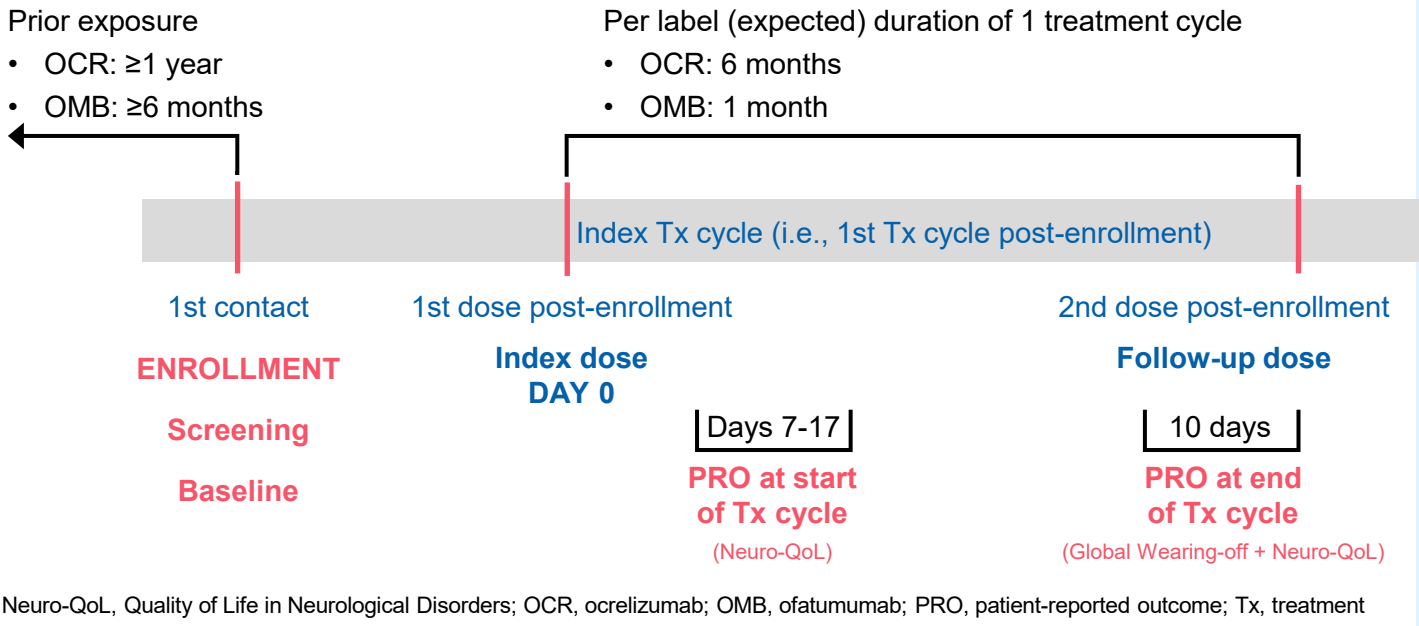
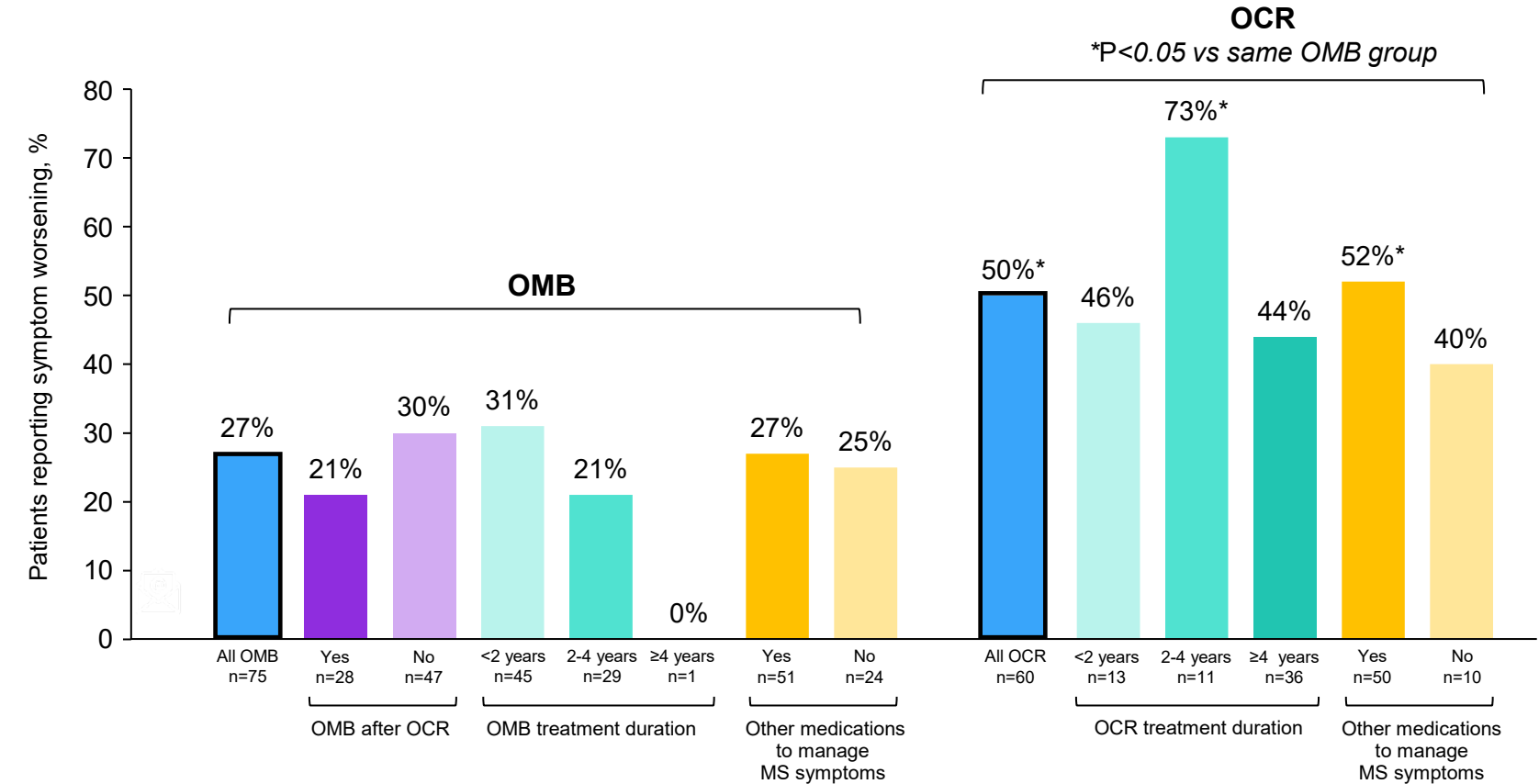


Figure 2. Response to Global Wearing-off Question at the End of Index Treatment Cycle^a Across Key Patient and Treatment Subgroups

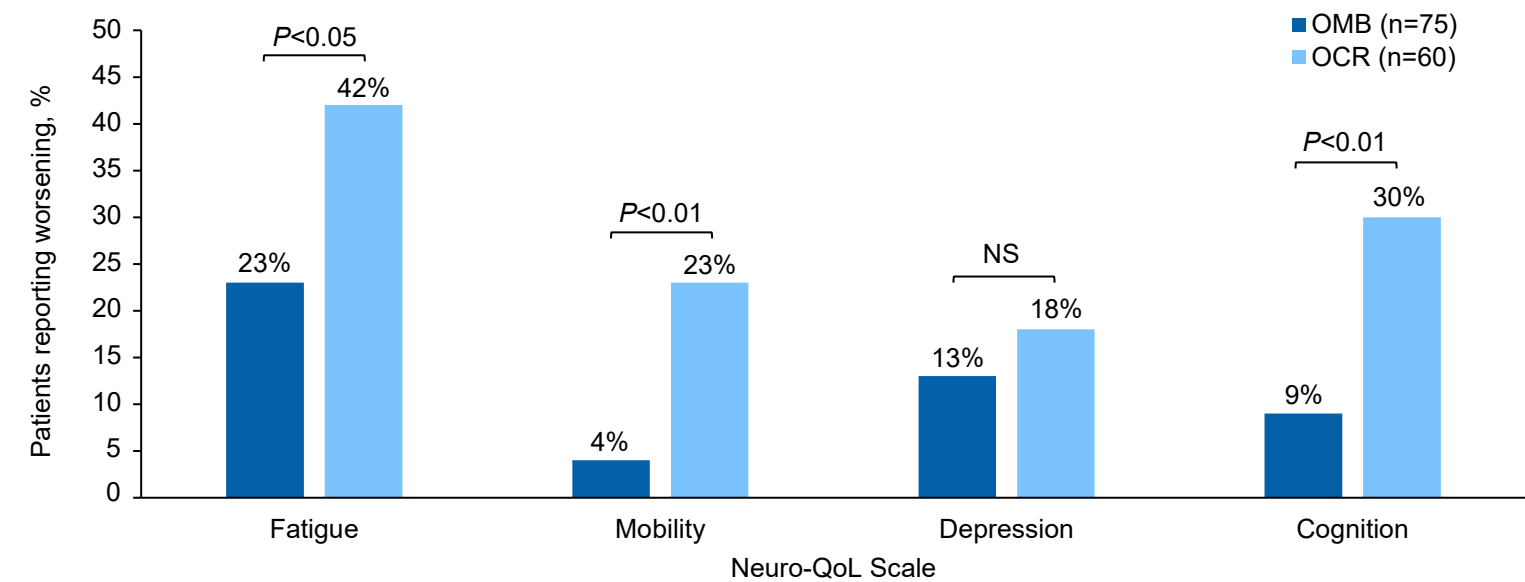


MS, multiple sclerosis; OCR, ocrelizumab; OMB, ofatumumab
^aAt the end of the index treatment cycle, patients were asked, "Are you experiencing an increase in MS symptoms currently?" Response options: Yes, No, Unsure

Neuro-QoL Scales

- Over the index treatment cycle, patients receiving OMB demonstrated significantly less worsening on the Neuro-QoL Fatigue, Mobility, and Cognition scales compared with those receiving OCR (all P<0.05) (**Figure 3**)
- Across all items from the Fatigue, Mobility, and Cognition scales (**Tables 2, 3, and 5**), OCR patients experienced substantially greater increases in the frequency of Neuro-QoL specific symptoms from the start to end of the index treatment cycle compared with OMB patients, who exhibited relatively smaller changes, suggesting that OMB is associated with less wearing-off and more consistent symptom control across these domains
- Across all items from the Depression scale (**Table 4**), compared with OCR patients, OMB patients exhibited slightly smaller or comparable increases in symptom frequency

Figure 3. PRO Worsening on Neuro-QoL During Index Treatment Cycle^a



Neuro-QoL, Quality of Life in Neurological Disorders; NS, not significant; OCR, ocrelizumab; OMB, ofatumumab; PRO, patient-reported outcome
^aWorsening was defined as a change greater than 0.5 times the standard deviation at the baseline Neuro-QoL assessment, which was conducted in the 10 days preceding the first treatment dose post-enrollment

Acknowledgments

The study was supported by Novartis Pharmaceuticals Corporation. Medical writing support was provided by Envision Pharma, Inc., and was funded by Novartis Pharmaceuticals Corporation. This poster was developed in accordance with Good Publication Practice (GPP 2022) guidelines. Authors had full control of the content and made the final decision on all aspects of this poster

Table 2. Neuro-QoL FATIGUE (% Responding "Sometimes," "Often," or "Always")

	Question	OMB (n=75)			OCR (n=60)		
		Cycle START	Cycle END	Δ	Cycle START	Cycle END	Δ
In the past 7 days...	I felt exhausted	62.7	66.7	4.0	66.7	75.0	8.3
	I felt that I had no energy	76.0	78.7	2.7	78.3	86.7	8.3
	I felt fatigued	81.3	86.7	5.3	83.3	81.7	-1.7
	I was too tired to do my household chores	56.0	60.0	4.0	51.7	68.3	16.7
	I was too tired to leave the house	50.7	52.0	1.3	38.3	56.7	18.3
	I was frustrated by being too tired to do the things I wanted	65.3	70.7	5.3	65.0	71.7	6.7
	I felt tired	50.7	52.0	1.3	46.7	65.0	18.3
	I had to limit my social activity because I was tired	42.7	44.0	1.3	36.7	45.0	8.3

Table 3. Neuro-QoL MOBILITY (% Responding "With some difficulty," "Much difficulty," or "Unable to do")

	Question	OMB (n=75)			OCR (n=60)		
		Cycle START	Cycle END	Δ	Cycle START	Cycle END	Δ
In the past 7 days...	Were you able to get on and off the toilet?	12.0	14.7	2.7	13.3	18.3	5.0
	Were you able to step up and down curbs?	22.7	24.0	1.3	23.3	30.0	6.7
	Were you able to get in and out of a car?	24.0	22.7	-1.3	20.0	30.0	10.0
	Were you able to get out of bed into a chair?	14.7	14.7	0.0	11.7	15.0	3.3
	Were you able to push open a heavy door?	21.3	26.7	5.3	28.3	35.0	6.7
	Were you able to run errands and shop?	30.7	30.7	0.0	33.3	46.7	13.3
	Were you able to get up off the floor lying on your back without help?	33.3	34.7	1.3	41.7	45.0	3.3
	Were you able to go for a walk of at least 15 minutes?	32.0	37.3	5.3	45.0	46.7	1.7

Table 4. Neuro-QoL DEPRESSION (% Responding "Sometimes," "Often," or "Always")

	Question	OMB (n=75)			OCR (n=60)		
		Cycle START	Cycle END	Δ	Cycle START	Cycle END	Δ
In the past 7 days...	I felt depressed	41.3	44.0	2.7	33.3	33.3	0.0
	I felt hopeless	32.0	32.0	0.0	21.7	20.0	-1.7
	I felt that nothing could cheer me up	28.0	30.7	2.7	20.0	25.0	5.0
	I felt that my life was empty	26.7	28.0	1.3	16.7	21.7	5.0
	I felt worthless	25.3	25.3	0.0	13.3	16.7	3.3
	I felt unhappy	46.7	48.0	1.3	35.0	38.3	3.3
	I felt I had no reason for living	17.3	14.7	-2.7	10.0	6.7	-3.3
	I felt that nothing was interesting	26.7	29.3	2.7	16.7	15.0	-1.7

Table 5. Neuro-QoL COGNITION (% Responding With Unfavorable Outcomes^a)

	Question	OMB (n=75)			OCR (n=60)		
		Cycle START	Cycle END	Δ	Cycle START	Cycle END	Δ
In the past 7 days...	I had to read something several times to understand it	44.0	48.0	4.0	48.3	55.0	6.7
	My thinking was slow	54.7	52.0	-2.7	46.7	60.0	13.3
	I had to work really hard to pay attention or I would make a mistake	45.3	50.7	5.3	46.7	48.3	1.7
	I had trouble concentrating	50.7	58.7	8.0	46.7	53.3	6.7
How much difficulty do you currently have...	Reading and following complex instructions?	25.3	26.7	1.3	25.0	30.0	5.0
	Planning for and keeping appointments that are not part of your weekly routine?	21.3	18.7	-2.7	23.3	23.3	0.0
	Managing your time to do most of your daily activities?	26.7	28.0	1.3	30.0	43.3	13.3
	Learning new tasks or instructions?	26.7	25.3	-1.3	28.3	35.0	6.7

Neuro-QoL, Quality of Life in Neurological Disorders; OCR, ocrelizumab; OMB, ofatumumab
^aFor questions beginning with "In the past 7 days...", unfavorable outcomes include "Sometimes," "Often," or "Always." For questions beginning with "How much difficulty do you currently have...", unfavorable outcomes include "Somewhat," "A lot," or "Cannot do"

Disclosures

Karishma Thakkar, Brandon Brown, and Abhijit Gadkari: Salary- Novartis Pharmaceuticals Corporation.
Hollie Schmidt and Mark Gilliland: Salary- Accelerated Cure Project, which received collaboration funding from Novartis for the conduct of the current study, and has received grants, collaboration funding, payments for use of assets, and/or in-kind contributions from Novartis and other MS biopharmaceutical companies. Julien St-Pierre, Raluca Ionescu-Iltu, and Francis Vekeman: Salary- STATLOG Inc., a consultancy company that received funds from Novartis for the conduct of the current study

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