Evaluating Cognitive Outcomes in Multiple Sclerosis: Real-World Impact of Ozanimod on Processing Speed Using BICAMS

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INTRODUCTION

Cognitive impairment is a prevalent and debilitating aspect of multiple sclerosis (MS).

The **Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS)** has emerged as a validated screening tool for cognitive impairment in patients with MS, comprising three tests: the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test-II (CVLT-II), and the Brief Visuospatial Memory Test-Revised (BVMT-R).

Ozanimod, a selective sphingosine-1-phosphate (S1P) receptor modulator approved for the treatment of relapsing remitting MS (RRMS), has shown promising results on cognitive outcomes in clinical trials.

AIM

This single-center study aims to **evaluate changes in cognitive function in patients with RRMS receiving ozanimod in routine clinical practice**, with particular attention to processing speed as measured by the SDMT component of BICAMS.

By analyzing real-world data, this investigation aims to establish cognitive outcomes as potential therapeutic targets, providing insights into a treat-to-target approach for optimizing treatment strategies in MS clinical practice.

METHODS

This was a real-world monocentric cohort study conducted at University of Foggia, Italy, including patients with a confirmed diagnosis of RRMS according to revised McDonald criteria, who initiated ozanimod therapy from October 2022 to October 2024, aged > 18 years and who actively attended the center and scheduled visits during the study period.

Cognitive evaluation was performed at timepoints 0, 1 and 2. Time 0 was the first BICAMS available within 3 months before therapy start, and Time 1 and Time 2 were evaluations each carried out within a range from 6 to 9 months from the previous one.

Changes in cognitive outcomes from baseline to follow-up were analyzed using paired t tests for normally distributed data or Wilcoxon signed-rank tests for non-normally distributed data. A multiple linear regression model was employed to assess the impact of various clinical and demographic factors on changes in SDMT z-scores from baseline to follow-up.

RESULTS

A total cohort of 67 patients, 50 (74.6%) female, was enrolled. Mean time on ozanimod was 17.7 ± 3.0 months. Baseline characteristics are shown in Table 1.

The analysis indicated a significant improvement in SDMT Z-scores from Time 0 to Time 1, with a moderate effect size (Cohen's d = 0.42) and a statistically significant t test result (p overall= 0.0003) (Fig. 1).

The CVLT-II and BVMT-R tests showed minimal changes across time points.

A multiple linear regression analysis revealed that the baseline SDMT Z-score was a significant predictor of changes in SDMT Z-scores, with a coefficient of − 0.345 (p < 0.001) (Tab. 2). The model explained 32.4% of the variance in SDMT change (R-squared = 0.324, adjusted R-squared = 0.287) (Tab. 2).

None of the other variables (age, sex, disease duration, number of previous disease-modifying therapies, baseline expanded disability status scale [EDSS], relapses within 12 months from ozanimod prescription, and presence of Gadolinium enhancing lesions within 12 months from ozanimod prescription) were statistically significant predictors of SDMT change (Tab. 2).

All cohort (n = 67)	
Sex, female, n (%)	50 (74.6%)
Age, years, mean ± SD	47.8 ± 11.1
Patients with comorbidities, n (%)	29 (43.3%)
Disease characteristics	
Lag time, years, median (IQR)	1.0 (0.3–3.1)
Disease duration, years, median (IQR)	13.5 (7.1–21.8)
Baseline EDSS , median (IQR)	2.5 (2.0–4.0)
Patients naive to DMTs	7 (10.4%)
No. of previous DMTs, mean ± SD	1.9 ± 1.2
Patients with relapses in previous 24 months before ozanimod prescription, n (%)	35 (52.2%)
Patients with Gadolinium enhancing lesions within 12 months before ozanimod prescription, n (%)	11 (16.4%)
Time on treatment, months, mean ± SD	17.7 ± 3.0

Table 1. Baseline demographics and clinical characteristics. DMTs disease modifying therapies, EDSS Expanded Disability Status Scale, MRI magnetic resonance imaging, IQR interquartile range, n number, SD standard deviation.

Variable	Coefficient	95% CI	Standard error	p value
Age	− 0.015	(− 0.039, 0.009)	0.012	0.215
Sex (female)	0.234	(− 0.154, 0.622)	0.198	0.238
Disease duration	− 0.021	(− 0.056, 0.014)	0.018	0.245
Previous DMTs (n)	− 0.112	(− 0.283, 0.059)	0.087	0.198
Baseline EDSS	− 0.089	(− 0.238, 0.060)	0.076	0.243
Relapses within 12 months from ozanimod prescription	− 0.156	(− 0.419, 0.107)	0.134	0.245
MRI activity within 12 months from ozanimod prescription	0.078	(− 0.249, 0.405)	0.167	0.641
Baseline SDMT Z score	− 0.345	(− 0.519, − 0.171)	0.089	< 0.001*

*Table 2. Multiple linear regression analysis results. Dependent variable: change in SDMT Z-score from baseline to follow-up. R-squared: 0.324, adjusted R-squared: 0.287. *F-statistic: 8.45 (p < 0.001).*

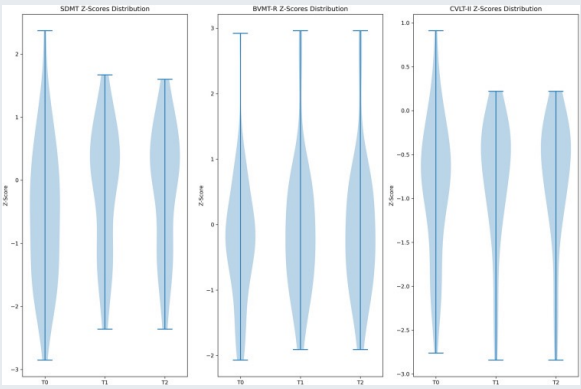

Figure 1. Violin plots representing BICAMS Z-scores at different time points. BVMT-R brief visuospatial memory test-revised, CVLT-II California Verbal Learning Test-II, SDMT symbol digit modalities, T0 Time 0, T1 Time 1, T2 Time 2

CONCLUSIONS

This real-world study suggests that **ozanimod treatment is associated with significant improvement in information processing speed**, independent of traditional prognostic factors.

These findings complement existing clinical trial data and warrant further investigation through larger, multicenter studies with extended follow-up periods to validate these cognitive benefits.

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DISCLOSURES

The authors have nothing to disclose.

CONTACT INFORMATION

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