Baseline demographics, disease characteristics, and clinical measures of patients with relapsing MS in ENLIGHTEN: a phase 3b study of ozanimod on cognitive processing speed

DMT32

John DeLuca,[1,2] Jon V. Riolo,[3] Chun-Yen Cheng,[3] Robert T. Naismith,[4] Sibyl Wray,[5] Ann Bass,[6] Edward Fox,[7] Emily Riser,[8] Diego Silva,[3] Robert Zivadinov[9]

[1]Kessler Foundation, West Orange, New Jersey, and Departments of Physical Medicine and Rehabilitation, and Neurology; [2]Rutgers - New Jersey Medical School, Newark, New Jersey; [3]Bristol Myers Squibb, Princeton, New Jersey; [4]Washington University School of Medicine, St Louis, Missouri; [5]Hope Neurology, Knoxville, Tennessee; [6]Neurology Center of San Antonio, San Antonio, Texas; [7]Central Texas Neurology Consultants, Round Rock, Texas; [8]Alabama Neurology Associates, Birmingham, Alabama; [9]Buffalo Neuroimaging Analysis Center, Department of Neurology, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, The State University of New York, Buffalo, New York

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Introduction

- In patients with multiple sclerosis (MS), slowed cognitive processing speed (CPS) emerges as an early deficit[1]
- The Symbol Digit Modalities Test (SDMT) assesses CPS[2] and is the most sensitive individual cognitive measure for use in MS[3]
- Ozanimod, a sphingosine 1-phosphate (S1P) receptor modulator that binds with high affinity selectively to S1P receptor subtypes 1 and 5,[4] is approved in multiple countries for the treatment of adults with either relapsing forms of MS (RMS) or moderately to severely active ulcerative colitis[5,6]
- In the phase 3 SUNBEAM trial, patients taking ozanimod 0.92 or 0.46 mg once daily showed a nominally significant ($P < 0.05$) improvement in the SDMT over interferon ß-1a 30 µg weekly; however, SUNBEAM did not evaluate the SDMT as a primary endpoint[7]
- The ongoing ENLIGHTEN trial was designed to assess changes in CPS, measured with the SDMT, over 3 years in patients with early MS treated with ozanimod 0.92 mg

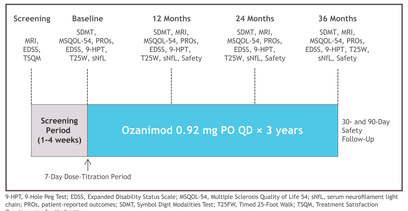
Objective

- To describe baseline demographics, MS disease characteristics, clinical and radiologic measures, cognitive assessments, and patient-reported outcomes of patients enrolled in ENLIGHTEN and who had received ≥ 1 dose of ozanimod as of November 3, 2021

Methods

Study design

- ENLIGHTEN (NCT04140305) is a single-arm, multicenter, longitudinal, open-label, phase 3b study of ozanimod 0.92 mg currently recruiting in the United States and Canada
- Eligible patients must be 18-65 years of age at screening, have a diagnosis of MS per the 2010 or 2017 McDonald criteria within the last 5 years, have taken ≤ 1 MS disease-modifying therapy (none within 1 month of entry), have an Expanded Disability Status Scale (EDSS) score of ≤ 3.5, have had no relapses within 30 days before screening, and have < 10 gadolinium-enhancing (GdE) lesions on baseline brain MRI scan
- Planned recruitment is 250 patients
  - As of the November 3, 2021 data cutoff, 95 patients were enrolled, of whom 82 had received ≥ 1 dose of ozanimod and are included in this analysis; 143 patients have enrolled as of May 5, 2022
- The study will run for 3 years; interim analyses may occur annually as appropriate



9-HPT, 9-Hole Peg Test; EDSS, Expanded Disability Status Scale; MSQOL-54, Multiple Sclerosis Quality of Life 54; sNfL, serum neurofilament light chain; PROs, patient-reported outcomes; SDMT, Symbol Digit Modalities Test; T25FW, Timed 25-Foot Walk; TSQM, Treatment Satisfaction Questionnaire for Medication.

Endpoints[a]

Primary Endpoint	• SDMT
Secondary Endpoints	• EDSS • Clinical relapse • MRI brain volume • MRI lesion count and volume • Patient-reported outcomes: Treatment Satisfaction Questionnaire for Medication Version 1.4 (TSQM-v1.4), Work Productivity and Activity Impairment-Multiple Sclerosis version 2.0 (WPAI-MS), Multiple Sclerosis Quality of Life-54 (MSQOL-54), Fatigue Severity Scale (FSS), Hospital Anxiety and Depression Scale (HADS), Timed 25-Foot Walk (T25FW), Nine-Hole Peg Test (9-HPT)
Exploratory Endpoints	• Brief Visuospatial Memory Test-Revised (BVMT-R) and California Verbal Learning Test-Second Edition (CVLT-II), serum neurofilament light chain (sNfL)

[a]Only the endpoints for which baseline data are reported in this poster are listed.

Symbol Digit Modalities Test

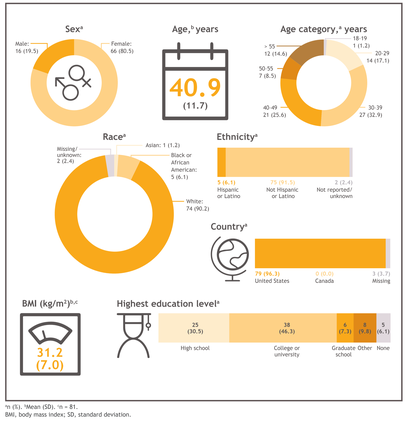
- An oral version of the SDMT is used in ENLIGHTEN
  - The SDMT is 1 of 3 tests of the Brief International Cognitive Assessment for MS (BICAMS; also includes the California Verbal Learning Test-Second Edition [CVLT-II] and the Brief Visuospatial Memory Test-Revised [BVMT-R])
- In the SDMT, various symbols are substituted for digits, and participants must match the appropriate symbol to the paired numerical digit using a key[2]
- Scoring is based on the correct number of responses given in 90 seconds, with higher scores indicating faster processing; a score change of ≥ 4 points or ≥ 10% is considered clinically meaningful[2]

Statistical analysis

- Continuous variables were summarized with descriptive statistics (n, mean, standard deviation [SD], median, minimum, and maximum)
- Frequency counts and percentage of participants within each category were provided for categorical data

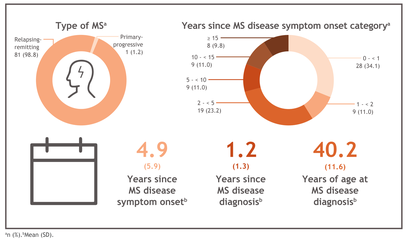
Results

Demographics (N = 82)



[a]n (%). [b]Mean (SD). [c]n = 81.
BMI, body mass index; SD, standard deviation.

Disease characteristics (N = 82)



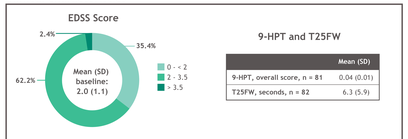
[a]n (%). [b]Mean (SD).

BICAMS cognitive assessments at baseline in patients with RMS currently enrolled in ENLIGHTEN are consistent with previously published values in a population with early MS[9]

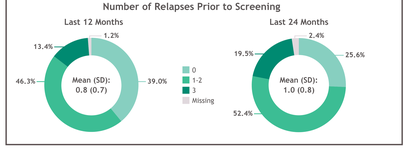
BICAMS	N = 82[a]
SDMT[a]	
n	77
Mean (SD)	53.3 (12.5)
CVLT-II[b]	
n	74
Mean (SD)	53.1 (9.8)
BVMT-R[c]	
n	68
Mean (SD)	23.6 (6.8)

[a]Higher SDMT scores indicate better performance; mean normative control score range: 60-70.[2,10,11]
[b]Higher CVLT-II scores indicate better performance; mean normative controls score range: 54-56.[10,11]
[c]Range of possible BVMT-R scores is 0-36, with higher scores indicating better performance. Mean normative controls score range: 27-28.[13]

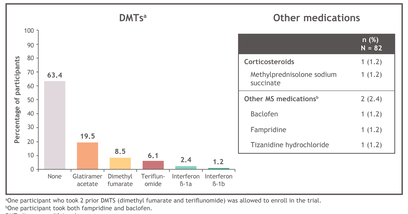
Clinical characteristics



9-HPT and T25FW	Mean (SD)
9-HPT, overall score, n = 81	0.04 (0.01)
T25FW, seconds, n = 82	6.3 (5.9)



Prior MS treatments



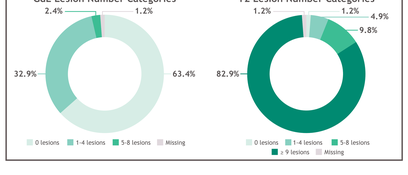
Other medications	n (%) N = 82
Corticosteroids	1 (1.2)
Methylprednisolone sodium succinate	1 (1.2)
Other MS medications[b]	2 (2.4)
Baclofen	1 (1.2)
Fampridine	1 (1.2)
Tizanidine hydrochloride	1 (1.2)

[a]One participant who took 2 prior DMTS (dimethyl fumarate and teriflunomide) was allowed to enroll in the trial.
[b]One participant took both fampridine and baclofen.
DMT, disease-modifying therapy.

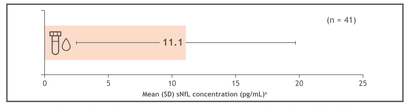
MRI characteristics

MRI parameter	Mean (SD) n = 81[a]
Number of GdE lesions	0.7 (1.3)
Number of T2 lesions	25.3 (19.0)
GdE lesion volume (cm³)	0.1 (0.1)
T2 lesion volume (cm³)	6.0 (8.6)
Unenhancing T1 lesion count	7.2 (9.0)
Unenhancing T1 lesion volume (cm³)	1.1 (2.4)
Normalized brain volume (cm³)	1516.1 (128.0)
Normalized cortical volume (cm³)	627.5 (72.3)
Normalized thalamic volume (cm³)	16.0 (2.1)

[a]Lesion data were missing for 1 patient.

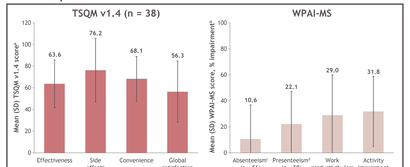


Biomarker



[a]In previously reported phase 3 trials of ozanimod, median baseline plasma NfL levels in patients with RMS were 13.4 and 14.7 pg/mL.[8]

Patient-reported outcomes



[a]Range of possible scores for TSQM is 0-100, with greater numbers indicating higher satisfaction.[14]
[b]Range of possible scores for the WPAI-MS is 0-100, with greater numbers indicating greater impairment.[15,16]
[c]Percentage of work time missed.
[d]Percentage of impairment while working.

Additional patient-reported outcomes	Mean (SD)
MSQOL-54[a]	
Physical health composite score,[b] n = 80	59.0 (20.5)
Mental health composite score,[c] n = 81	66.7 (19.8)
FSS total score[d], n = 82	4.4 (1.7)
HADS, total score[e], n = 82	12.8 (6.5)

[a]Range of possible scores is 0-100; higher scores indicate better QoL.[17]
[b]Previously reported mean physical health composite scores in patients with MS with mild symptoms: 26.0; severe symptoms: 77.8.[17]
[c]Previously reported mean mental health composite scores in patients with MS with mild symptoms: 50.0; severe symptoms: 78.8.[17]
[d]Range of possible scores is 1-7; higher scores indicate greater severity. Previously reported mean score in patients with MS: 4.8.[18]
[e]Range of possible scores is 0-42; higher scores indicate greater severity. Previously reported mean score in patients with MS: 13.57.[19]

Conclusions

- Detection of early improvements in cognitive processing speed is an important aspect of assessing therapeutic efficacy
- Findings from this study, once completed, will help to inform patients and caregivers on the early changes in SDMT performance and the effect of ozanimod on cognitive processing speed in patients with MS
- The ENLIGHTEN study is currently recruiting

References

1. Van Schependom J, et al. *Mult Scler J* 2015;21:83-91. 2. Benedict RHB, et al. *Mult Scler J* 2017;23:721-733. 3. Strober L, et al. *Mult Scler J* 2019;25:1781-1790. 4. Scott FL, et al. *Br J Pharmacol* 2016;173:1778-1792. 5. ZEPOSIA® ozanimod [package insert]. Princeton, NJ: Bristol Myers Squibb; December 2021. 6. ZEPOSIA® ozanimod [summary of product characteristics]. Utrecht, Netherlands: Celgene Distribution BV; December 2021. 7. Comi G, et al. *Lancet Neurol* 2019;18:1009-1020. 8. Harris S, et al. *Eur J Neurol* 2021;11:3722-2730. 9. Skoog E, et al. *Mult Scler Relat Dis* 2020;46. doi:10.1016/j.msard.2020.102577. 10. Sheridan LK, et al. *Arch Clin Neuropsychol* 2006;21:23-28. 11. Strober LB, et al. *Mult Scler Relat Disord* 2020;43. doi: 10.1016/j.msard.2020.102154. 12. Benedict RHB, et al. *BMC Neurol* 2012;12:55. 13. Ozturk A, et al. *J Mult Scler Res* 2021;1:1-6. doi:10.4274/jmsr.galenos.2021.6-5. 14. Atkinson MJ, et al. *Health Qual Life Outcomes* 2004;26:1-13. 15. Reilly MC, et al. *Pharmacoeconomics* 1993;4:353-365. 16. Reilly Associates. WPAI scoring. 2022. http://www.reillyassociates.net/WPAI_Scoring.html. 17. Vickrey BG, et al. *Qual Life Res* 1995;4:187-206. 18. Krupp LB, et al. *Arch Neurol* 1989;46:1121-1123. 19. Pais-Ribeiro JL, et al. *Neuropsychiatr Dis Treat* 2018;14:3193-3197.

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Email: John DeLuca jdeluca@kesslerfoundation.org

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