February 2024

Improved Cognitive Processing Speed in Patients Treated With Cladribine Tablets for Multiple Sclerosis: MAGNIFY-MS 2-year Findings

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CONCLUSIONS

- **Meaningful improvement in SDMT performance was detected in patients treated with cladribine tablets**
- **Cognitive benefit was already evident at M6, and became more pronounced by M18 when patients had received the full treatment course**
- **At M24, the estimated rate of stability or confirmed improvement was more than 95% (assessed with an 8-point score change in SDMT)**

INTRODUCTION

- Most people with multiple sclerosis (MS) experience cognitive impairment that can affect quality of life and employment[1]
- The Symbol Digit Modality Test (SDMT), a measure of cognitive processing speed (CPS), is widely accepted as a monitoring tool for cognitive impairment in clinical trials

OBJECTIVES

To investigate cognitive performance in patients with highly active relapsing MS, treated with cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years) in the 2-year MAGNIFY-MS study (NCT03364036)

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METHODS

- CPS was assessed with SDMT scores on individual levels (4- and 8-point score change)[2] or on the group level (4-point score change)[3]
- Time to first confirmed improvement (SDMT score changes from Baseline [BL] ≥4 or ≥8) or time to first worsening (SDMT score changes from BL ≤-4 or ≤-8) were measured at Month [M] 6, 12, 18, and 24 after treatment initiation and analyzed using the Kaplan–Meier method. Alternative SDMT key forms were used at each visit
- Improvement or worsening was confirmed if observed consistently over two consecutive visits, which were ≥166 days apart. Patients without confirmed improvement or worsening were grouped into the stable category
- All analyses were exploratory and were performed on the full analysis set, or by subgroups: high relapse activity (HRA) vs non-HRA; treatment-naïve vs treatment-experienced
- HRA was defined as follows: at least 2 relapses in the previous year (i.e., the number of historical relapses within 12 months prior to BL ≥2) regardless of prior use of disease-modifying therapies
- Mixed models for repeated measures (MMRM) adjusted for age, combined unique active lesions, Expanded Disability Status Scale score, and SDMT score at BL were used for group-level analyses, presenting least squares means with 95% confidence interval

RESULTS

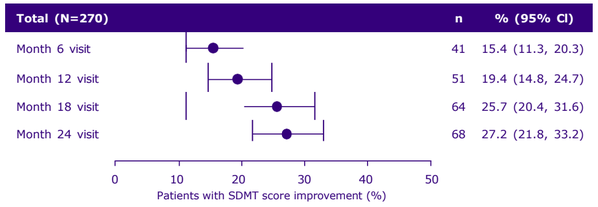
Table 1. Patient Characteristics

	HRA n=165	Non-HRA n=105	Treatment-naïve n=117	Treatment-experienced n=153	All patients N=270
Female, n (%)	107 (64.8)	73 (69.5)	76 (65.0)	104 (68.0)	180 (66.7)
Age ≤40 years, n (%)	93 (56.4)	59 (56.2)	68 (58.1)	84 (54.9)	152 (56.3)
EDSS score >3 at BL, n (%)	43 (26.1)	23 (21.9)	28 (23.9)	38 (24.8)	66 (24.4)
Median number of relapses within 12 months prior to BL (IQR)	2 (2, 2)	1 (1, 1)	2 (2, 2)	1 (1, 2)	2 (1, 2)
Patients with ≥1 annualized CUA lesion count during BL period, n (%)	88 (53.3)	57 (54.3)	62 (53.0)	83 (54.2)	145 (53.7)

For full demographics, see De Stefano N, et al. *Neurol Neuroimmunol Neuroin lamm*. 2022;9(4):e1187
BL, baseline; **CUA**, combined unique active; **EDSS**, Expanded Disability Status Scale; **HRA**, high relapse activity; **IQR**, interquartile range

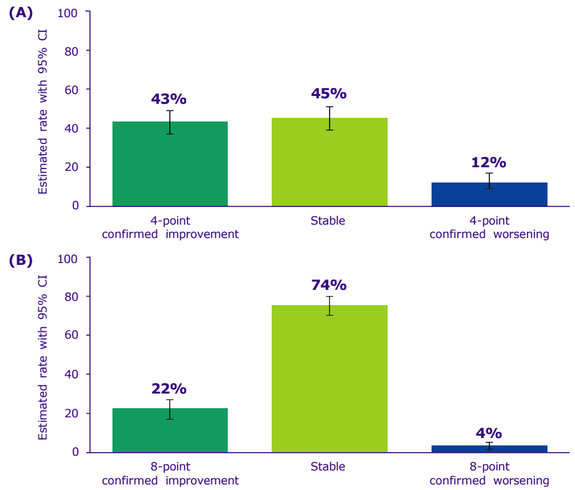
- In total, 270 patients were included in the study: 67% female, 56% aged ≤40 years, 61% with HRA, and 43% treatment-naïve (**Table 1**)
- A continued increase in the proportions of patients with CPS improvement (≥8 points) was observed over time (**Figure 1**)
- At M24, the rates of confirmed improvement, stable, and confirmed worsening, are shown in **Figure 2A** (4-point score change) and **Figure 2B** (8-point score change)
- No differences were observed between HRA/non-HRA or treatment-naïve/treatment-experienced subgroups
- For group-level MMRM analysis, SDMT scores increased first at M6, with continued percentage increase at M12, and reaching 4-point change at M18 (**Figure 3**)

Figure 1. Patients with ≥8-Point Improvement (Proportion Over Time)



CI, confidence interval; **SDMT**, Symbol Digit Modality Test

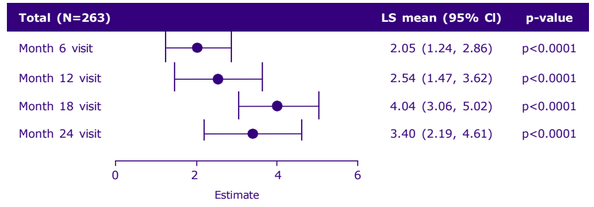
Figure 2. Kaplan-Meier Estimate of 4-Point (A) or 8-Point (B) Confirmed SDMT Score Changes at M24



CI, confidence interval; **SDMT**, Symbol Digit Modality Test

- Limitations: single-arm, open-label study
- Practice effects were mitigated with the use of alternate oral test forms and with 6 months between each assessment

Figure 3. Estimated LS Means Using MMRM for SDMT 4-Point Group Score Change from Baseline



CI, confidence interval; **LS**, least squares; **MMRM**, mixed models for repeated measures; **SDMT**, Symbol Digit Modality Test

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Cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years) are indicated for the treatment of patients with MS in the United States (relapsing forms of MS, including relapsing-remitting disease and active secondary progressive disease, in adults).

Disclosures: PV has received honoraria or consulting fees from AB Science, Biogen, Celgene (Bristol Myers Squibb), Imcyse, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, Sanofi, and Teva; and research support from Novartis, Roche, and Sanofi. **HW** is member of scientific advisory boards/steering committees for Bayer, Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, Sanofi, and Teva. He received speaker honoraria and travel support from Bayer, Biogen, CSL Behring, EMD Serono, Fresenius Medical Care, the healthcare business of Merck KGaA, Darmstadt, Germany, Omniamed, Novartis, Sanofi, and Teva. He received compensation as a consultant from Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Omniamed, Roche, and Sanofi. He has received research support from Bayer, Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Sanofi, and Teva, as well as the German Ministry for Education and Research (BMBF), German Research Foundation (DFG), Else Kröner Fresenius Foundation, Fresenius Foundation, Hertie Foundation, NRW Ministry of Education and Research, Interdisciplinary Center for Clinical Studies (IZKF) Münster, and RE Children's Foundation. **FB** is supported by the NIHR Biomedical Research Centre at UCLH and is a steering committee or Data Safety Monitoring Board member for ATRI/ACTC, Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, and Prothena. He is a consultant for Celltrion, Combinostics, IXICO, Janssen (J&J), the healthcare business of Merck KGaA, Darmstadt, Germany, Rewind Therapeutics, and Roche. Research agreements with Biogen, GE Healthcare, the healthcare business of Merck KGaA, Darmstadt, Germany, and Roche. 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He received research support from Biogen, Sanofi, and UCB, the European Union, and the Swiss National Foundation. He serves as associate editor of the European Journal of Neurology, on the editorial board for Clinical and Translational Neuroscience and as topic editor for the Journal of International Medical Research. **SH** serves on advisory boards for Bayer, Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, and Sanofi. 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Medical writing assistance was provided by Ruth Butler-Ryan of inScience Communications, Springer Healthcare Ltd, UK, and was funded by the healthcare business of Merck KGaA, Darmstadt, Germany.

Presented at ACTRIMS 2024 Forum | February 29–March 2 | West Palm Beach, FL, USA

Data collection and analysis was sponsored by the healthcare business of Merck KGaA, Darmstadt, Germany (CrossRef Funder ID: 10.13039/100009945)