Impact of Cladribine Tablets on Serum Neurofilament Light Chain Levels in Patients with Relapsing Multiple Sclerosis: Results from a US-based Real-world Study

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RESEARCH IN CONTEXT

1. **In this observational study, a reduction in serum neurofilament light chain levels (sNfL) was observed over 2 years following treatment with cladribine tablets (CladT) in patients with relapsing multiple sclerosis (pwRMS). These findings further support sNfL as a valuable biomarker for monitoring RMS treatment response**
2. **These outcomes from a single-center cohort align with previously published results from MAGNIFY-MS study (NCT03364036)[1]**

OBJECTIVES

To assess the impact of cladribine tablets (CladT) on serum neurofilament light chain levels (sNfL) by evaluating the magnitude of changes in normalized sNfL (Z-scores) concentration in a single-center cohort of patients with relapsing multiple sclerosis (pwRMS).

INTRODUCTION

CladT (3.5 mg/kg cumulative dose over 2 years), a high-efficacy therapy (HET) approved for RMS, reduces relapses, disease progression, and magnetic resonance imaging (MRI) activity in pwRMS[2]

sNfL is a biomarker of neurological damage, and many studies have reported its promise in potentially predicting clinical relapses, future disability, brain atrophy, and response to treatment with disease-modifying therapies (DMTs)[3,4]

Additional data on the effects of CladT could further support the clinical application of sNfL

METHODS

- This retrospective, observational, single-center study included pwRMS who initiated CladT and had 1 sNfL assessment at baseline (index date: 1st dose of CladT) and 2 measurements post-CladT treatment. Assessments were conducted at 6, 12, 18, and 24+* months
- The primary endpoint was the change in sNfL levels from the index date to post-index measurements, assessed using Z-scores adjusted for age and body mass index. Key secondary endpoints included changes in sNfL concentration and the percentage of pwRMS free from relapse and MRI activity (T1 gadolinium-enhancing and new/enlarging T2 lesions)
- Data were analyzed descriptively

*pwRMS who completed assessments at and after 24 months were labeled as 24+ months. The median (interquartile range [IQR]) follow-up time was 19.2 months (15.9; 25.8).

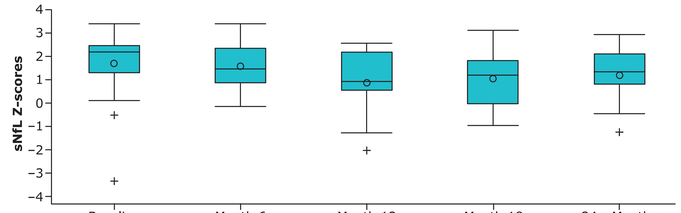
RESULTS

Table 1. Baseline demographics and disease characteristics

Characteristics	N=26
Mean (SD) age, years	41.3 (9.05)
Female, n (%)	21 (80.8)
Mean (SD) time since MS diagnosis, years[a]	9.3 (6.8)
Presence of relapse in the 12 months before the index date[b], n (%)	
• Yes	1 (3.8)
• No	23 (88.5)
• Unknown	2 (7.7)
Presence of MRI activity in the 12 months before the index date[b], n (%)	
• Yes	11 (42.3)
• No	10 (38.5)
• Unknown	5 (19.2)
Most common recent DMT prior to initiating CladT, n (%)	
• Platform DMTs[c]	7 (26.9)
• Oral DMTs[d]	7 (26.9)
• Infusible HETs[e]	12 (46.2)

[a]Time since diagnosis is unknown for 2 pwRMS (7.7%). [b]The index date was defined as the date of the first CladT dose. [c]Platform DMTs include interferon beta-1a, interferon beta-1b, glatiramer acetate, and peginterferon beta-1a. [d]Oral DMTs include teriflunomide, fingolimod, dimethyl fumarate, and diroximel fumarate. [e]HETs comprise natalizumab and ocrelizumab.
CladT, cladribine tablets; DMT, disease-modifying therapy; HET, high-efficacy therapy; MRI, magnetic resonance imaging; MS, multiple sclerosis; pwRMS, patients with relapsing multiple sclerosis; SD, standard deviation.
Please refer to **Supplementary Table 1** for more details on baseline demographics and disease characteristics.

Figure 1. sNfL Z-scores over 24+ months post-CladT initiation

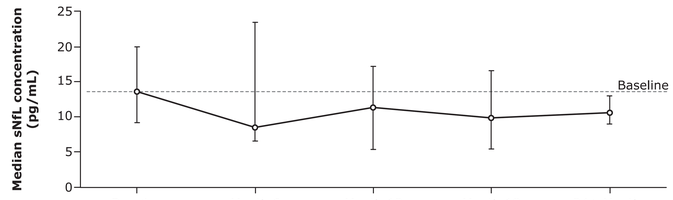


	Baseline	Month 6	Month 12	Month 18	24+ Months
n=	26	15	14	16	10
Mean ± SD	1.70 ± 1.40	1.58 ± 1.11	0.89 ± 1.44	1.07 ± 1.16	1.18 ± 1.24
Median	2.20	1.48	0.94	1.20	1.35
Q1; Q3	1.31; 2.46	0.88; 2.33	0.58; 2.20	−0.01; 1.79	0.81; 2.10

Box: IQR; —: median; o: mean; +: values outside whisker plot. Whisker: minimum and maximum values.
CladT, cladribine tablets; IQR, interquartile range; Q, quartile; SD, standard deviation; sNfL, serum neurofilament light chain.

- The median (IQR) sNfL Z-score at baseline was 2.20 (1.3; 2.5), which decreased to 1.35 (0.8; 2.1, n = 10) at 24+ months (**Figure 1**), resulting in a median change of −36.8% (−135.7; 4.5; **Supplementary Figure 1**).

Figure 2. sNfL concentration over 24+ months post-CladT initiation

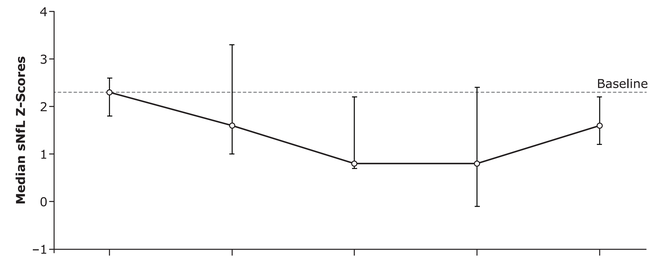


	Baseline	Month 6	Month 12	Month 18	24+ Months
n=	26	15	14	16	10
Median	13.60	8.48	11.35	9.86	10.60
Q1; Q3	9.16; 20.00	6.55; 23.50	5.33; 17.20	5.39; 16.60	8.96; 13.00

Error bars represent Q1 and Q3 values.
CladT, cladribine tablets; Q, quartile; sNfL, serum neurofilament light chain.

- At 24+ months, the median (IQR) sNfL concentration was 10.6 pg/mL (9.0; 13.0) compared with 13.6 pg/mL (9.2; 20.0) at baseline (**Figure 2**)

Figure 3. sNfL Z-score over 24+ months after switching from infusible HETs[a] to CladT



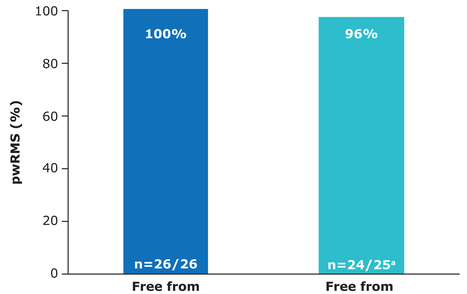
	Baseline	Month 6	Month 12	Month 18	24+ Months
n=	12	7	7	8	5
Median	2.33	1.55	0.84	0.82	1.55
Q1; Q3	1.77; 2.64	0.95; 3.26	0.71; 2.20	−0.05; 2.43	1.17; 2.20

[a]Infusible HETs comprise natalizumab and ocrelizumab. Error bars represent Q1 and Q3 values.
CladT, cladribine tablets; HET, high-efficacy therapy; Q, quartile; sNfL, serum neurofilament light chain.

- In pwRMS switching from infusible HETs (natalizumab and ocrelizumab) to CladT, the median (IQR) sNfL Z-score at baseline was 2.3 (1.8; 2.6, n = 12), which decreased to 1.6 (1.2; 2.2) at 24+ months (n = 5; **Figure 3**), resulting in a median change of −35.2% (−118.3; −20.0)

Please refer to **Supplementary Figure 2** for percent change in sNfL Z-score by infusible HETs.

Figure 4. pwRMS free of relapse, and MRI activity through 20 months of follow-up[a]



[a]In 1 patient with MRI activity, the median sNfL Z-score was 3.4 at baseline which reduced to 2.0 at 24+ months. This patient had MRI activity prior to starting CladT and new lesions were seen in year 3 after starting CladT.
CladT, cladribine tablets; MRI, magnetic resonance imaging; pwRMS, patients with relapsing multiple sclerosis; sNfL, serum neurofilament light chain.

- All pwRMS remained relapse-free, and 96% were free of MRI activity during the follow-up period of 20 months (mean ± SD: 20 ± 8.8 months) after the initiation of CladT (**Figure 4**)

CONCLUSIONS

- **In this study which included pwRMS transitioning from infusible HETs, CladT-treated pwRMS exhibited a reduction in sNfL levels (Z and raw scores)**
- **There were no incidences of relapses among all pwRMS and no MRI activity in 96% of pwRMS**
- **Larger studies are warranted to assess the impact of CladT on sNfL in a US-based population of pwRMS**

SCAN FOR AFFILIATIONS, DISCLOSURES, AND SUPPLEMENTARY MATERIALS

References: 1. De Stefano N, et al. Oral Presentation at CMSC 2024. DMT 01.
2. Mavenclad. Prescribing information. EMD Serono, Inc; 2024.
3. Carolina Ferreira-Atuesta, et al. *Front Neurosci.* 2021;15:642384.
4. Thebault S, et al. *Sci Rep.* 2020;10(1):10381.

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(Updated: 24 March 2025)

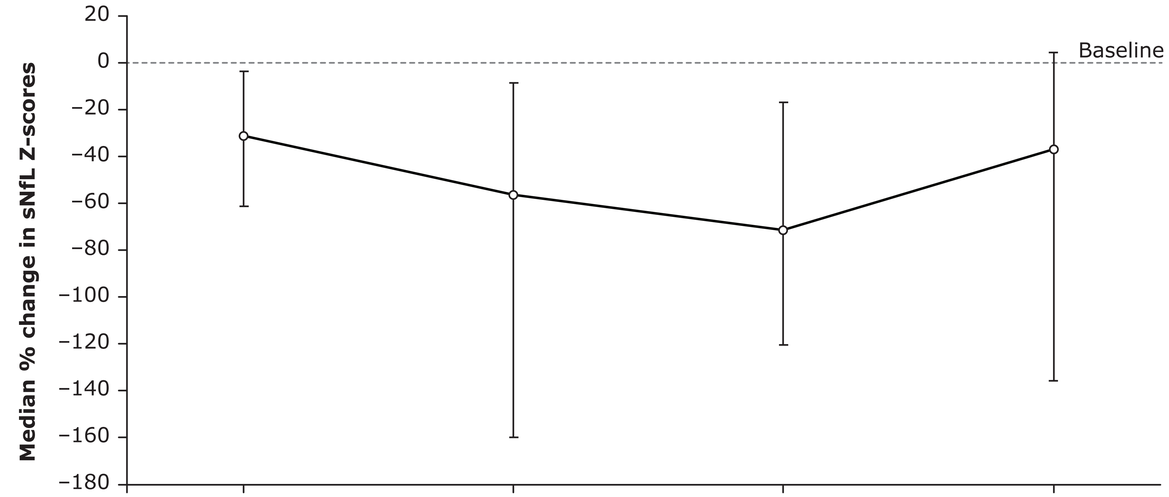
SUPPLEMENTARY MATERIAL

Supplementary Table 1. Baseline demographics and disease characteristics

Characteristics	N=26
Reason for discontinuing prior treatment, n (%)	
• Lack of efficacy	6 (11.5)
• Intolerance	20 (38.5)
• Safety concerns	7 (13.5)
• Subject preference	2 (3.8)
• Other	3 (5.8)
• Unknown	15 (28.8)
Number of pwRMS with at least one sNfL measurement per time window	
• Baseline	26 (100.0)
• Month 6 (±3 months)	15 (57.7)
• Month 12 (±3 months)	14 (53.8)
• Month 18 (±3 months)	16 (61.5)
• 24+ Months	10 (38.5)
CladT discontinuation, n (%)	1 (3.8)

CladT, cladribine tablets; pwRMS, patients with relapsing multiple sclerosis; sNfL, serum neurofilament light chain.
Table updated in poster after presentation at ACTRIMS 2025 (Updated: 24 March 2025).

Supplementary Figure 1. Percentage change in sNfL Z-scores over 24+ months (vs baseline)

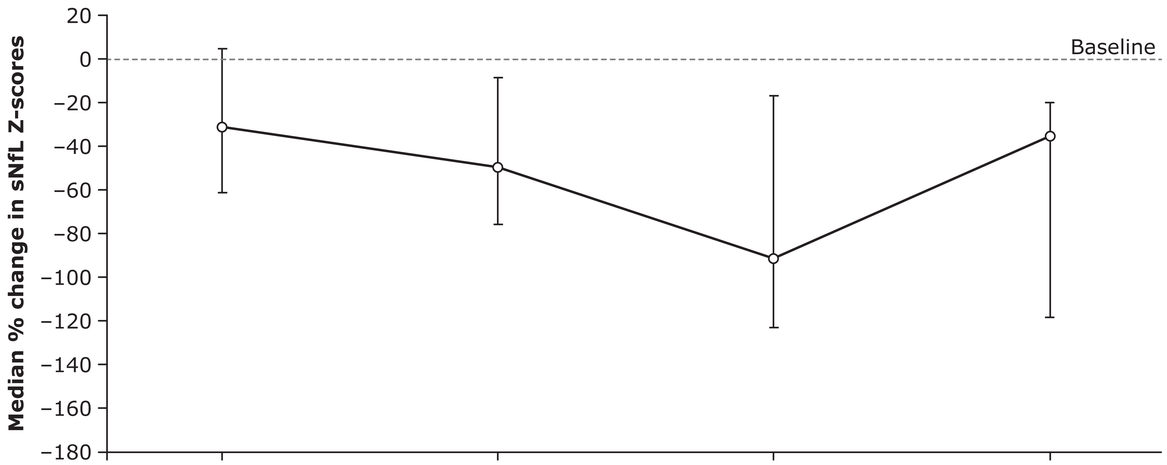


	Month 6	Month 12	Month 18	24+ Months
n=	15	14	16	10
% Median	−31.12	−56.23	−71.45	−36.82
Q1; Q3	−61.17; −3.72	−159.76; −8.66	−120.48; −16.82	−135.71; 4.53

Error bars represent Q1 and Q3 values.
Q, quartile; sNfL, serum neurofilament light chain.

- The median (IQR) % change in sNfL Z-score from baseline to 24+ months was −36.8% (−135.7; 4.5) in pwRMS treated with CladT

Supplementary Figure 2. Percentage change in sNfL Z-scores over 24+ months (vs baseline) – Infusible HETs[a]



	Month 6	Month 12	Month 18	24+ Months
n=	7	7	8	5
% Median	−31.12	−49.54	−91.40	−35.18
Q1; Q3	−61.17; 4.65	−75.80; −8.66	−122.86; −16.82	−118.26; −19.99

[a]Infusible HETs comprise natalizumab and ocrelizumab. Error bars represent Q1 and Q3 values.
HET, high-efficacy therapy; Q, quartile; sNfL, serum neurofilament light chain.

- The median (IQR) % change in sNfL Z-score from baseline was −35.2% (−118.3; −20.0) in pwRMS switching from a high efficacy infusible HET (natalizumab and ocrelizumab) to CladT

SUPPLEMENTARY MATERIAL

Author Affiliations

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JK is an employee of EMD Serono, Boston, MA, USA.

RP has received honoraria for education, consulting, and speaking fees from Biogen Inc., EMD Serono, Genentech, Novartis Pharmaceuticals Corp, Sanofi, and TG Therapeutics Inc.

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