Turkish Journal of Neurology

Turk J Neurol 2025;31(3):354-358
Doi: 10.55697/tnd.2025.293

CASE REPORT

Long-term cladribine experience in relapsing-remitting multiple sclerosis

Ömer Faruk Turan, Furkan Sarıdaş, Emine Rabia Koç

Department of Neurology, Uludağ University Faculty of Medicine, Bursa, Türkiye

ABSTRACT

We present the case of a 40-year-old male patient who was diagnosed with multiple sclerosis (MS) at age 16. Initially, he was treated with glatiramer acetate, but he later received cladribine due to high disease activity. After participating in the CLARITY study in 2007, he achieved 10 years of clinical and radiological stability (NEDA-3) with a single cladribine treatment. In 2019, relapse symptoms of optic neuritis and a new enhancing lesion on an MRI scan prompted the initiation of a second cladribine treatment cycle. Despite the appearance of a new asymptomatic lesion prior to the second-year dose, therapy was continued without modification. The patient remained free of relapses, disability progression, and radiological activity for the following three years. This case illustrates cladribine's potential for long-term efficacy, even with intermittent disease activity, and supports its use as a viable option for sustained disease control in relapsing MS.

Keywords: Cladribine, long-term experience, relapsing-remitting multiple sclerosis.

Multiple sclerosis is an immune-related demyelinating disease of the central nervous system with neuroinflammation and neurodegeneration.[1] Cladribine is an oral immune-reconstitution disease-modifying therapy approved for treating relapsing remitting multiple sclerosis. It has a unique dosing regimen compared to other disease-modifying therapies. It includes a short course of treatment at the beginning of the first and second months of two consecutive treatment years at a total cumulative dose of 3.5 mg/kg. Given the subsequent sustained efficacy, no further treatment is required until the end of the fourth year. Early initiation of cladribine treatment at high disease activity should be considered. However, the optimal treatment strategy during the follow-up period after cladribine treatment remains to be determined. Herein, we reported a 40-year-old male patient treated with cladribine with a 15-year follow-up.

CASE REPORT

A 40-year-old male patient was admitted to our clinic. The patient had no history of any disease, no medications, and no family history of autoimmune disease. The patient was married with two children and was working as an accountant. At the age of 16 years, demyelinating plaques were detected on magnetic resonance imaging (MRI) performed due to weakness that first developed in the right arm and leg and, three months later, in the left arm and leg. A diagnosis of MS was made. Glatiramer acetate treatment was started. For five years, three attacks developed under this treatment. The patient was included in the CLARITY study[1] in 2007 due to high disease activity after a one-year voluntary interruption of therapy. The patient was attack-free for 10 years after the last dose of cladribine. In 2019, due to a new optic neuritis attack, and a new contrasting lesion detected on MRI, a second course of cladribine therapy was initiated. Before

Correspondence: Ömer Faruk Turan, MD. Uludağ Üniversitesi Tıp Fakültesi Nöroloji Anabilim Dalı, 16059 Nilüfer, Türkiye.
E-mail: fturan@uludag.edu.tr
Received: September 16, 2024 **Accepted:** May 05, 2025 **Published online:** September 15, 2025
Cite this article as: Turan ÖF, Sarıdaş F, Koç ER. Long-term cladribine experience in long-term cladribine experience in relapsing-remitting multiple sclerosis. Turk J Neurol 2025;31(3):354-358. doi: 10.55697/tnd.2025.293.

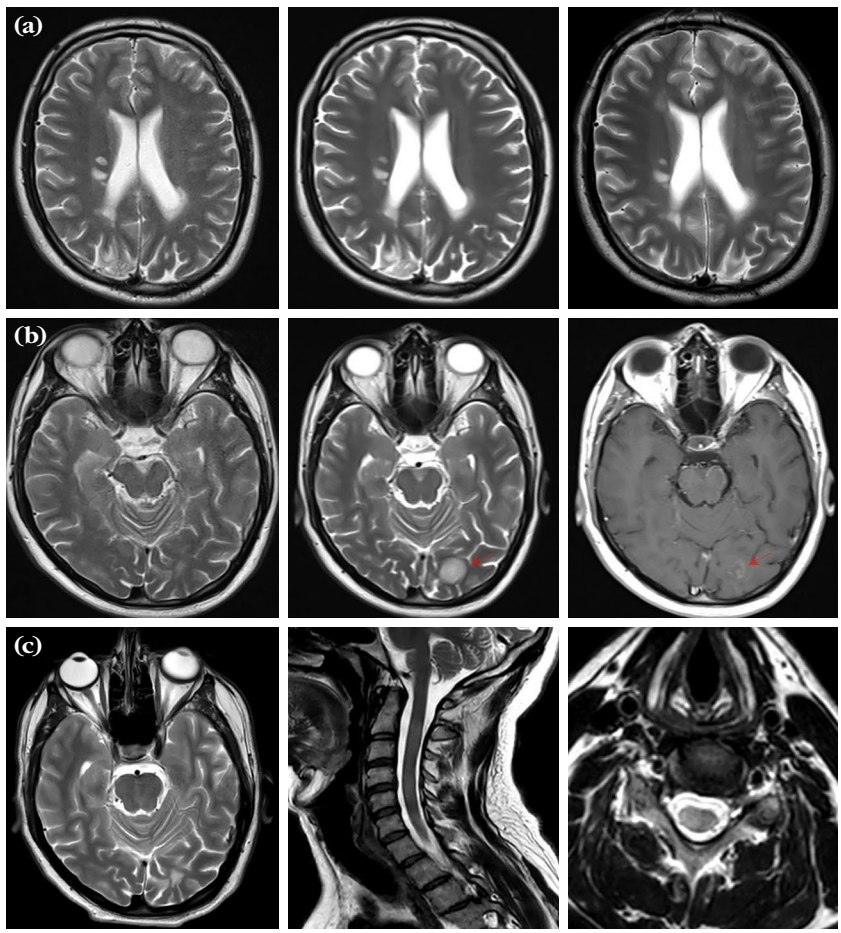

Figure 1. Follow-up magnetic resonance imagings in the last five years. **(a)** Supratentorial region (2019, 2021, and 2024, respectively). **(b)** Infratentorial region (2019, 2021, and 2021, respectively; arrow indicates the newly contrasted lesion). **(c)** Lesion regression and cervical demyelinating diffuse lesions (2024).

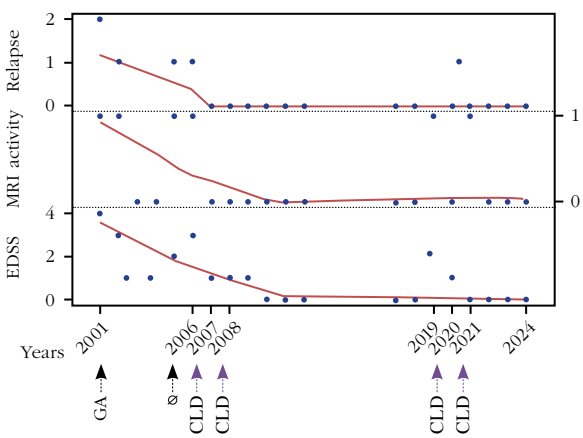

Figure 2. Twenty-four-year disease course of a case of relapsing-remitting multiple sclerosis. The patient received two cycles of cladribine, the first 3.5 mg/kg for a total of four weeks in 2007 and 2008, and the second 3.5 mg/kg for a total of four weeks in 2020 and 2021.

GA: Glatiramer acetate 40 mg/mL administered three times a week; CLD: Oral cladribine dose.

the second-year dose of the second cladribine cycle, a new contrasting lesion with no clinical equivalent was detected on the control MRI's preparatory phase (Figure 1). Treatment was not changed, and cladribine was continued. Thereafter, the patient was followed without progression, attacks, and radiological activity (Figure 2). The results of the current assessment and examination are presented in Table 1. Written informed consent was obtained from the patient.

DISCUSSION

The results of the CLARITY study on the efficacy of cladribine on the disease showed that short-term treatment significantly reduced the relapse rate and the risk of progression of disability and improved imaging (MRI) results,[2] and the extension study further proved its sustained efficacy.[3] In follow-up analyses of both studies,

TABLE 1
Last examinations, 2024

Laboratory tests	Examination	Result	Comment
Serum panel	Glucose, AST, ALT, urea, creatinine, electrolytes	Normal	Normal
	Gamma glutamyl transferase (IU/L)	29	Normal
	Alkaline phosphatase (IU/L)	89	Normal
Lipid panel (mg/dL)	Low density lipoprotein	112	Normal
	High density lipoprotein	35	Low*
	Triglyceride	182	High*
	Total cholesterol	183	Normal
CBC ($\times 10^9$/L)	White blood cells	7.52	Normal
	Neutrophil	4.110	Normal
	Lymphocyte	2.720	Normal
	Monocyte	0.503	Normal
	Eosinophil	0.147	Normal
	Basophil	0.042	Normal
	Hemoglobin	14.5	Normal
	Platelets	253.9	Normal
Immunological tests	Serum IgA (g/L)	2.64	Normal
	Serum IgM (g/L)	1.16	Normal
	Serum IgG (g/L)	12.4	Normal
	CD19 (%)	26.8	Normal
Vitamins	25-OHD (µg/L)	24.2	Low*
	Vitamin B12 (ng/L)	447	Normal
	Folate (µg/L)	3.8	Normal
Viral serology	Anti-HBs (mIU/mL)	0.73	Negative
	Anti-HCV (IU/mL)	0.05	Negative
	HIV Ag/Ab	0.12	Negative
	Anti-HBc total Ab (mIU/mL)	0.15	Negative
	HBsAg (mIU/mL)	0.20	Negative
	VZV IgG (mIU/mL)	70.5	Negative
	HIV Ag/Ab	0.12	Negative
	EBV-VCA IgG (U/mL)	67.58	Positive*
	EBV-EBNA IgG (U/mL)	24.15	Negative
	CMV IgG (AU/mL)	54	Negative
Thyroid panel	sT3 (ng/L)	2.97	Normal
	sT4 (ng/L)	1.07	Normal
	TSH (mU/L)	3.22	Normal
	Anti-TG Ab (IU/mL)	2.2	Normal
	Anti-TPO Ab (U/mL)	1.1	Normal
Evoked potentials			
Lower extremity SEP	Right P40 responses absent. Other waves within normal limits.*		
Upper extremity SEP	Normal		
VEP	Slightly prolonged right P100 latency (121.8 µV)*		

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; CBC: Complete blood count; 25-OHD: 25-Hydroxyvitamin D; Anti-HBs: Antibody to hepatitis B surface antigen; Anti-HCV: Anti-hepatitis C virus antibodies; HIV Ag/Ab: Human immunodeficiency virus antigen-antibodies Anti-HBc: Antibody to hepatitis B core antigen; EBV: Epstein-Barr virus; VCA: Viral capsid antigen; IgG: Immunoglobulin G; EBNA: Epstein-Barr Nuclear antigen; CMV: Cytomegalovirus; TSH: Thyroid-stimulating hormone; Anti-TG: Anti-Thyroglobulin antibody; Anti-TPO: Anti-Thyroid Peroxidase antibody; SEP: Somatosensory evoked potentials; VEP: Visual evoked potential; * Abnormal results.

no evidence of disease activity (NEDA-3) showed sustained benefit for up to six years.[3,4] Data from the CLARITY/CLARITY Extension cohort of the recently announced CLASSIC-MS study showed that after a median of 10.9 years, 80.7% of patients did not require an ambulatory device at any time.[4] At the four-year follow-up, approximately two-thirds of patients reported no subsequent disease-modifying therapy (DMT) use; half showed no evidence of reactivation, and one-third achieved both conditions. It was revealed that the risk of reaching an Expanded Disability Status Scale score of 6 and the likelihood of using another DMT afterward was lower, the time to first DMT afterward was longer, and better results were achieved during the four years after the last dose.[4] However, they observed that the percentage of patients with NEDA-3 decreased numerically as the bridging interval between CLARITY and CLARITY-EXT exceeded 48 weeks.

Therefore, a careful treatment strategy should be planned to prevent future disease progression. However, the answer to this question must be clarified, and prospective studies are required. As real-world data are presented, recommendations are emerging on what treatment should be preferred in stable disease course or activation after cladribine. Those without disease activity can be followed without treatment, or the reintroduction of cladribine tablets may provide a better treatment response and a lasting effect on disease control. However, the long-term efficacy/adverse effect profile is still unknown. Treatment is unclear in recurrent disease activity more than two years after the first course, and a clinical assessment is recommended. Currently, the general opinion is to reinitiate cladribine therapy after cure or switch to highly effective therapies (e.g., ocrelizumab or natalizumab).[5] An additional dose of cladribine should be considered in mild to moderate disease activity. In the case of acute severe relapse, a marked increase in disability, or high disease activity, consideration should be given to completing an entire course of two doses of cladribine for an additional two years or switching to another highly effective therapy.[6] In the absence of disease activity during follow-up after the period considered effective for treatment with cladribine, either retreatment or the treatment-free period may be extended under a structured close monitoring approach.[7] In our young patient who showed high disease activity meeting with cladribine treatment in the seventh year of the disease, we decided to repeat the cladribine course because relapse developed after 10 years of NEDA-3 after the last dose of the first course. The patient had radiological activation in the controls before the second dose of the second course, but we decided to continue cladribine treatment. We did not observe any disease activity in the following three-year period. This suggests that giving only two cycles of cladribine as immunomodulatory therapy did not result in a significant therapeutic deficit with close follow-up for more than 13 years.

In conclusion, this case demonstrates that cladribine can provide long-term disease control in patients with relapsing multiple sclerosis, even after an extended treatment-free period. The patient's stable clinical and radiological course for over a decade after initial cladribine treatment and subsequent disease stabilization after retreatment supports the efficacy and potential durability of this therapeutic approach. Furthermore, the absence of disease activity after reinitiating treatment suggests that retreatment with cladribine may be a viable option for patients experiencing reactivation. However, the optimal timing of treatment, long-term safety, and criteria for re-treatment require further investigation. Individualized treatment decisions and close clinical and radiological monitoring are essential.

Data Sharing Statement: The data that support the without findings of this high-efficacy study therapy are available from with the cor responding author upon reasonable request.

Author Contributions: Idea/concept, control/supervision, analysis and/or interpretation, literature review, critical review, references and fundings, materials: Ö.F.T.; Design, data collection and/or processing, literature review, writing the article, references and fundings, materials: F.S.; Data collection and/or processing, literature review, references and fundings, materials: E.R.K.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Giovannoni G, Comi G, Cook S, Rammohan K, Rieckmann P, Soelberg Sørensen P, et al. CLARITY Study Group. A placebo-controlled trial of oral cladribine for relapsing multiple sclerosis. N Engl J Med 2010;4;362:416-26. doi: 10.1056/NEJMoa0902533.

2. Kurne A, Karabudak R, Aydın ÖF. Steps in the pathogenesis of multiple sclerosis - I: From neuroinflammation to neurodegeneration. Turk J Neurol 2006;12:5-13.
3. Giovannoni G, Soelberg Sorensen P, Cook S, Rammohan K, Rieckmann P, Comi G, et al. Safety and efficacy of cladribine tablets in patients with relapsing-remitting multiple sclerosis: Results from the randomized extension trial of the CLARITY study. Mult Scler 2018;24:1594-604. doi: 10.1177/1352458517727603.
4. Giovannoni G, Boyko A, Correale J, Edan G, Freedman MS, Montalban X, et al. Long-term follow-up of patients with relapsing multiple sclerosis from the CLARITY/CLARITY Extension cohort of CLASSIC-MS: An ambispective study. Mult Scler 2023;29:719-730. doi: 10.1177/13524585231161494.
5. Ciron J, Bourre B, Castelnovo G, Guennoc AM, De Sèze J, Ben-Amor AF, et al. Holistic, long-term management of people with relapsing multiple sclerosis with cladribine tablets: Expert opinion from France. Neurol Ther 2024;13:503-18. doi: 10.1007/s40120-024-00589-7.
6. Petrou P, Achiron A, Cohen EG, Garty M, Magalashvili D, Karmon Y, et al. Practical recommendations on treatment of multiple sclerosis with Cladribine: An Israeli Experts Group Viewpoint. J Neurol 2023;270:88-5195. doi: 10.1007/s00415-023-11846-4.
7. Meuth SG, Bayas A, Kallmann B, Linker R, Rieckmann P, Wattjes MP, et al. Long-term management of multiple sclerosis patients treated with cladribine tablets beyond year 4. Expert Opin Pharmacother 2022;23:1503-10. doi: 10.1080/14656566.2022.2106783.