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Real-World Outcomes With Cladribine Tablets in People With Relapsing Multiple Sclerosis

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CONCLUSIONS

This real-world study evaluating data for up to 3 years following initiation of cladribine tablets for RMS adds to a growing body of evidence highlighting cladribine's clinical benefits: reduced ARRs, reduced MRI activity, and fewer hospitalisations due to MS relapse/symptoms

INTRODUCTION

- Multiple sclerosis (MS) is a chronic, neurodegenerative disorder of the central nervous system characterised by inflammation and demyelination[1,2]
- Early control of MS symptoms has been associated with improved long-term outcomes, therefore, the therapeutic options available aim to minimise the risk of relapse and disease progression as the primary goal of MS care[1-4]
- Cladribine tablets are indicated for the treatment of relapsing MS (RMS) in adults in the US[5]
- This cohort study adds to the growing body of evidence highlighting clinically relevant outcomes before and after initiation of cladribine treatment in patients with RMS

OBJECTIVE

- **Compare clinical outcomes in people with RMS 1 year prior to and 1 year after initiation of cladribine tablets**
- **Determine clinical outcomes up to 3 years after initiation of cladribine tablets in a real-world cohort study**

METHODS

Study Design

- A single-centre, longitudinal, retrospective, observational cohort study of de-identified medical records was carried out at The University of Texas Southwestern Medical Center in Dallas, TX, US, in people with RMS

Eligibility Criteria

- People aged ≥18 years with RMS treated with ≥1 course of cladribine tablets from April 2019 to April 2022 were included in this analysis
- People with primary progressive MS or clinically isolated syndrome were excluded from the study

Study Outcomes

- Annualised relapse rates (ARRs) 1 year prior to and up to 3 years after initiation of cladribine tablets
- Magnetic resonance imaging (MRI) activity 1 year prior to and up to 3 years after initiation of cladribine tablets
- Hospitalisations and urgent care/emergency department (ED) visits 1 year prior to and up to 3 years after initiation of cladribine tablets
- Reasons for discontinuation of cladribine tablets and delay between treatment courses during years 1 and 2

Statistical Analysis

- Wilcoxon signed-rank test was used to compare outcomes (ARRs, MRI activity, hospitalisation, and urgent care/ED visits) 1 year prior to and 1 year after initiating cladribine tablets
- Descriptive statistics and frequency counts were used for patient demographics, number of prior disease-modifying therapies (DMTs) used, primary reason for delay in cladribine treatment between the first and second courses, and years 2 and 3 data

RESULTS

Baseline Demographics and Disease Characteristics

- A total of 233 people were enrolled in this study, out of which 164 people treated with ≥1 course of cladribine tablets were included in the present analyses (Year 2: n=91; Year 3: n=49) (**Table 1**). The median follow-up time for all patients was 1.8 years

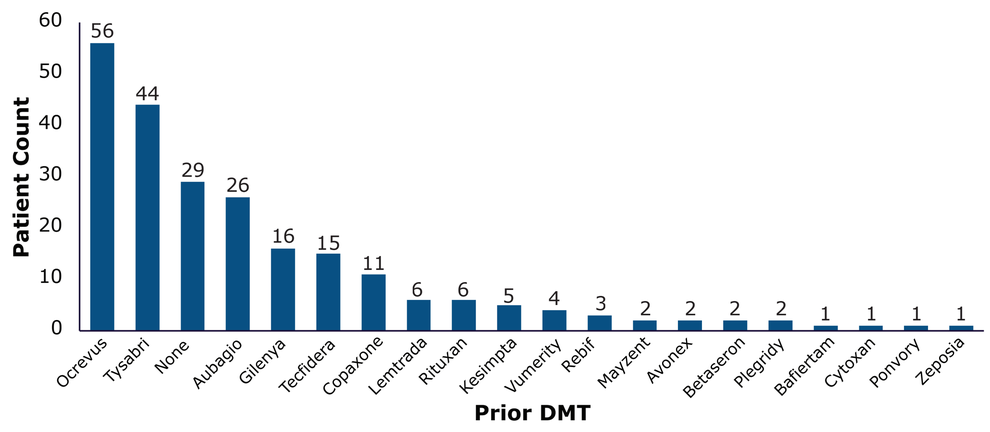
Table 1. Baseline Demographics and Disease Characteristics (N=233)*

	1 year prior to/ 1 year after	Year 2	Year 3
n	164	91	49
Mean age, years (SD)	45.0 (10.2)	44.9 (10.4)	45.5 (11.5)
Sex (female), n (%)	119 (72.6)	64 (70.3)	36 (73.5)
Race, n (%)			
White	128 (78.0)	73 (80.2)	41 (83.7)
Black or African American	32 (19.5)	17 (18.7)	8 (16.3)
Asian	4 (2.4)	1 (1.1)	-
Ethnicity, n (%)			
Hispanic	18 (11.0)	10 (11.0)	6 (12.2)
Non-Hispanic	146 (89.0)	81 (89.0)	43 (87.8)
Mean disease duration, years (SD)	11.6 (7.2)	12.0 (6.0)	11.2 (5.2)
Median number of prior treatments, n (range)	2 (1-9)	3 (1-9)	3 (1-9)
Median time between cladribine courses, years (range)	1.1 (0.88-2.4)	1.2 (0.88-2.4)	1.2 (0.88-2.4)

*The entire cohort consisted of 233 people, but given that each patient entered the UTSW practice at different timepoints, data analyses for ARRs, MRI, and hospitalisation were restricted to those who followed up for the full year before and after cladribine treatment (n=164). ARRs, annualised relapse rates; MRI, magnetic resonance imaging; UTSW, University of Texas Southwestern.

- The most common DMTs used prior to initiating cladribine tablets were ocrelizumab (n=56), natalizumab (n=44), and teriflunomide (n=26); 29 patients had no prior DMT treatment (**Figure 1**)
  - The most common reasons for switching to cladribine from the previous treatment were progressive MS, lack of efficacy, poor tolerability, viral infection, physician direction, or cost/access

Figure 1. Most Recent DMT Prior to Starting Cladribine Tablets (N=233)

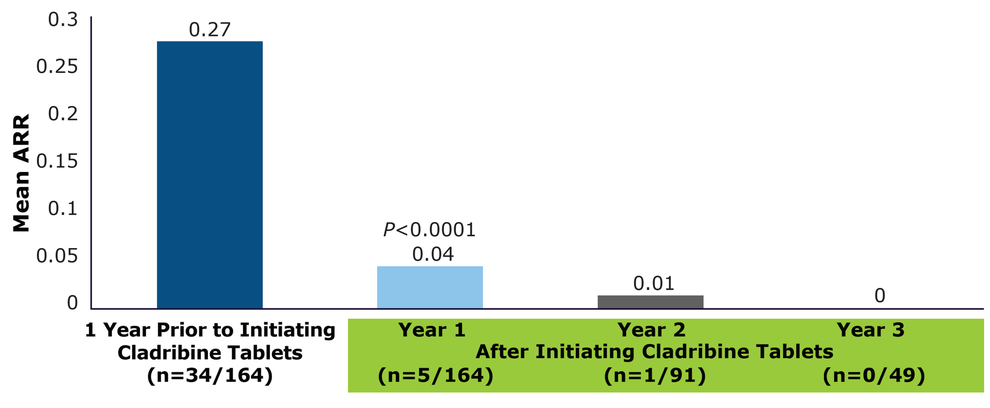


DMT, disease-modifying therapies.

Annualised Relapse Rates

- The mean (SD) ARR during the year prior to cladribine treatment was 0.27 (0.68; n=34/164 with relapse), which significantly decreased to 0.04 (0.28; n=5/164 with relapse; *P*<0.0001) on Year 1 after initiating cladribine tablets (**Figure 2**)
  - The mean (SD) ARR was 0.01 (0.08, n=1/91) at Year 2 after initiation of cladribine tablets
  - No relapses were reported during Year 3 (n=0/49) after initiation of cladribine tablets

Figure 2. ARRs 1 Year Prior to and 1-3 Years After Initiating Cladribine Tablets



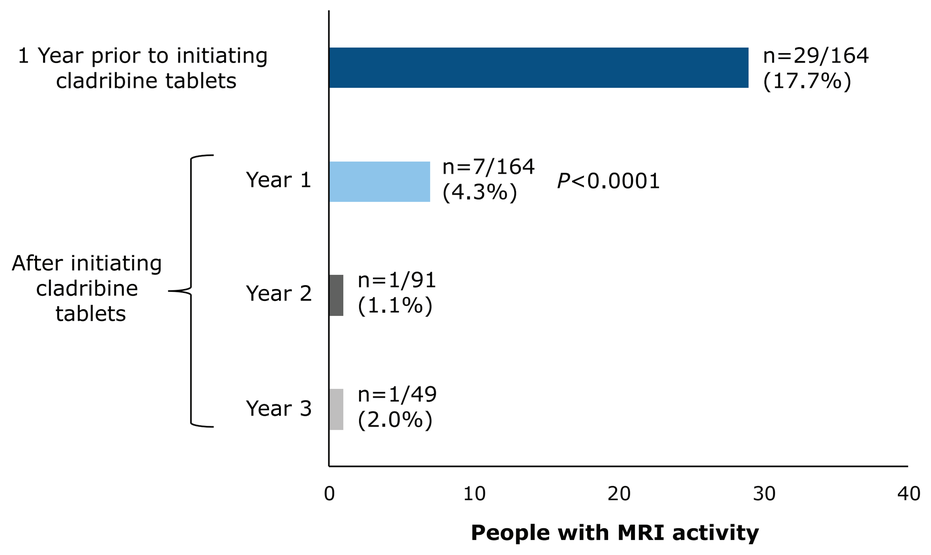
ARR, annualised relapse rate.

RESULTS (cont.)

MRI Activity

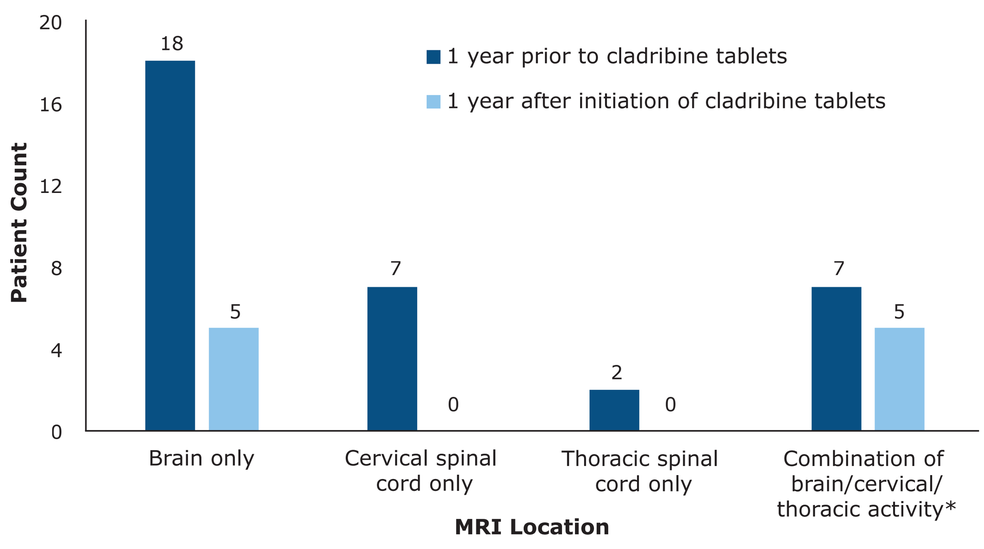
- The number of people with any MRI activity* significantly decreased after initiation of cladribine tablets (1 year prior: n=29/164 [17.7%]; Year 1: n=7/164 [4.3%]; *P*<0.0001), which continued throughout Year 2 (n=1/91; 1.1%) and Year 3 (n=1/49; 2.0%) (**Figure 3**)
  - Compared with 1 year prior to treatment, there was a considerable reduction in the percentage of people with new or enlarging T2 lesions 1 year after initiating the cladribine tablets (**Figure 4**)

Figure 3. MRI Activity 1 Year Prior to and 1-3 Years After Initiating Cladribine Tablets (n=164)



*Any T1 gadolinium enhancing lesion or any new or enlarging T2 lesions.
MRI, magnetic resonance imaging.

Figure 4. MRI Activity 1 Year Prior to and 1 Year After Initiating Cladribine Tablets (n=164)



*Categories are mutually exclusive.
Note: Some patients have more than one MRI.
MRI, magnetic resonance imaging.

Hospitalisations and Urgent Care/ED Visits

- Hospitalisations due to MS relapse/symptoms decreased following cladribine treatment (mean [SD] per person 1 year prior: 0.10 [0.49]; 1 year after: 0.02 [0.15]; 0 in Years 2 and 3) (**Table 2**)
  - Urgent care/ED visits due to MS relapse/symptoms also decreased following cladribine treatment initiation (1 year prior: 0.05 [0.23]; 1 year after: 0.01 [0.08]; 0 in Years 2 and 3)

Table 2. Hospitalisations and Urgent Care/ED Visits Due to MS Relapse/ Symptoms 1 Year Prior to and 1-3 Years After Initiating Cladribine Tablets

	1 Year Prior to Initiating Cladribine Tablets (n=164)	After Initiating Cladribine Tablets		
		Year 1 (n=164)	Year 2 (n=91)	Year 3 (n=49)
Hospitalisations due to MS relapse/symptoms, n	11	4	0	0
Mean (SD) per person	0.10 (0.49)	0.02 (0.15)	–	–
Urgent care/ED visits due to MS relapse/symptoms, n	9	1	0	0
Mean (SD) per person	0.05 (0.23)	0.01 (0.08)	–	–

ED, emergency department; MS, multiple sclerosis.

- Respiratory and cardiovascular problems were common reasons for hospitalisations and urgent care/ED visits after cladribine treatment (**Table 3**)

Table 3. Hospitalisations and Urgent Care/ED Visits Due to Non-MS Reasons 1 Year Prior to and 1-3 Years After Initiating Cladribine Tablets

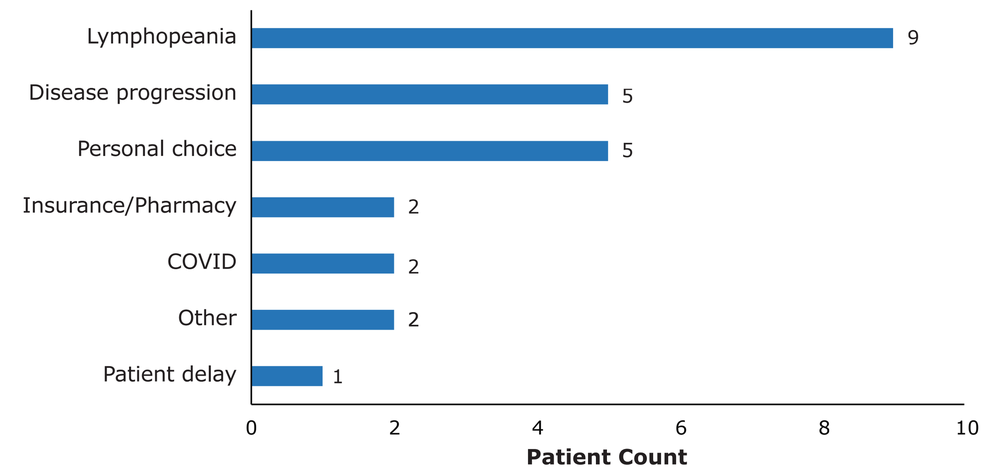
	1 Year Prior to Initiating Cladribine Tablets (n=164)	After Initiating Cladribine Tablets		
		Year 1 (n=164)	Year 2 (n=91)	Year 3 (n=49)
Hospitalisation reason, n (%)				
Respiratory problems	0	3 (1.83)	0	0
Cardiovascular problems	0	1 (0.61)	1 (1.10)	0
UTIs	0	0	0	0
Other	1 (0.61)	0	2 (2.20)	1 (2.04)
Urgent care/ED visit reason, n (%)				
Respiratory problems	1 (0.61)	3 (1.83)	1 (1.10)	0
Cardiovascular problems	0	1 (0.61)	1 (1.10)	0
UTIs	0	1 (0.61)	0	0
Other	5 (3.05)	6 (3.66)	3 (3.30)	0

ED, emergency department; MS, multiple sclerosis; UTIs, urinary tract infections.

Treatment Delay in Starting Second Course of Cladribine

- Reduced lymphocyte count was the primary reason for delays in starting a second course of cladribine treatment (**Figure 5**). There were 5 discontinuations, including 1 patient who switched to another DMT

Figure 5. Reasons for Delay in Second Cladribine Treatment Course (n=91)



References: 1. Giovannoni G, Mathews *J. Neurol Ther.* 2022;11(2):571-595. **2.** Ramo-Tello C, et al. *J Pers Med.* 2021;12(1):6. **3.** Gold R, et al. *Ther Adv Neurol Disord.* 2010;3(6):351-367. **4.** Bowen J, et al. *Adv Ther.* 2020;37(7):3163-3177. **5.** MAVENCLAD (cladribine) tablets. Package insert. EMD Serono, Inc.; 2022.

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