Real-World Treatment Patterns and Effectiveness of Cladribine Tablets in Patients with Relapsing Forms of Multiple Sclerosis in the United States

Y. Song[1], Y. Wang[2], S.L. Wong[3], D. Yang[1], M. Sundar[2], N.L. Tundia[3]

[1]Analysis Group, Inc., Boston, MA, USA; [2]Analysis Group, Inc., Los Angeles, CA, USA; [3]EMD Serono, Billerica, MA, USA

CONCLUSIONS

During the 2 years following the initiation of cladribine tablets, patients had a lower relapse rate, lower MS disease severity, no worsening of disability, less corticosteroid use, and lower all-cause and MS-related healthcare resource utilization driven by a reduction in outpatient visits

Over 2 years of follow-up, patients treated with cladribine tablets for RMS had a low rate of switching to other DMTs

INTRODUCTION

- Cladribine tablets are approved for the treatment of relapsing multiple sclerosis (RMS) in the United States (US).
- Cladribine tablets (3.5 mg/kg cumulative dose over 2 years) are administered as two treatment courses of 4–5 days in the first and second months of Year 1 and 2.
  - According to the US label, no additional course of cladribine tablets is needed in Year 3 and 4.
- The efficacy and safety of cladribine tablets have been demonstrated in several clinical trials, such as the CLARITY[1] and CLARITY Extension[2] studies.
- There is now emerging evidence of the real-world treatment patterns and effectiveness of cladribine tablets in patients with RMS.

OBJECTIVES

To assess the real-world treatment patterns and effectiveness of cladribine tablets in patients with RMS in the US.

METHODS

- The study used de-identified insurance claims data from the US Symphony Integrated Dataverse (IDV), from January 1, 2017 to December 31, 2021.
- Eligibility criteria: (a) ≥1 MS diagnosis; (b) ≥1 prescription claim of cladribine tablets (index date: date of first claim); (c) ≥18 years of age at index date; and (d) continuous claims activity (i.e., having ≥1 pharmacy, hospital, or medical claim for each quarter) for 12 months before the index date (baseline period) and 24 months after the index date (follow-up period).
  - Patients with evidence of pregnancy during the baseline period and the first 18 months of the follow-up period were excluded.
- MS disease severity,[3,4] Expanded Disability Status Scale-Derived Disability Indicators (EDSS-DDI),[5] and corticosteroid use were assessed during Years 1 and 2 of the follow-up period.
- Treatment switching was defined as the presence of ≥1 claim for another disease-modifying therapy (DMT) that was not followed by re-initiation of cladribine tablets.
- MS relapse was described using: (a) annualized relapse rates (ARR) in Years 1 and 2 of the follow-up period as well as in the entire follow-up period; and (b) time to first MS relapse during the follow-up period.

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).

METHODS

Statistical Analyses

- Baseline characteristics were described using counts and proportions for categorical variables and means and standard deviations for continuous or count variables.
- ARR, MS disease severity, EDSS-DDI, corticosteroid use, and all-cause and MS-related healthcare resource utilization (HRU) were described in Years 1 and 2 of the follow-up period, and were also compared with the baseline level using z-tests based on the mean and standard error of the longitudinal changes. The longitudinal changes represent the effectiveness of cladribine tablets.
- Additionally, ARR during the 2-year follow-up period was described and compared with the baseline level.

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RESULTS

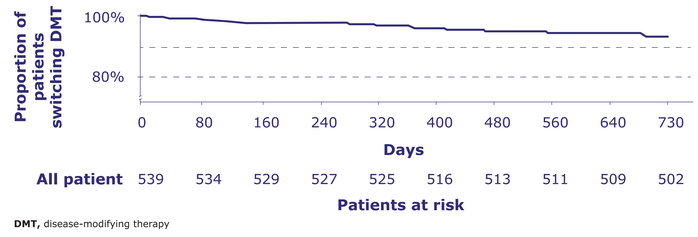
Table 1. Patient Characteristics

Baseline Characteristics	Overall Sample (N = 539)
Age at index date (years), mean ± SD	49.9 ± 11.1
Female, n (%)	418 (77.6)
Geographic region, n (%)	
South	204 (37.8)
Northeast	138 (25.6)
Midwest	132 (24.5)
West	63 (11.7)
Unknown	2 (0.4)
MS-related treatment and medical device use	
Corticosteroid, n (%)	261 (48.4)
Number of DMTs, mean ± SD	0.7 ± 0.6
DMT use, n (%)	314 (58.3)
Comorbidity	
Charlson Comorbidity Index, mean ± SD	0.4 ± 0.9

DMT, disease-modifying therapy; **MS,** multiple sclerosis; **SD**, standard deviation

- A total of 539 eligible patients were included in the study (**Table 1**).
- Eligible patients had a mean age of 49.9 years at index date, with the majority being female (77.6%) and from the South (37.8%), Northeast (25.6%), and Midwest (24.5%).
- A total of 41.7% of patients had no evidence of DMT use.
- By the end of the 2-year follow-up period, 93% of patients did not have evidence of switching to another DMT (**Figure 1**).

Figure 1. Time to DMT Switch During the Follow-up Period



DMT, disease-modifying therapy

Table 2. Changes in Clinical Outcomes, Corticosteroid Use, and HRU in Years 1 and 2

Outcomes	Baseline	Year 1 vs Baseline		Year 2 vs Baseline	
	Mean ± SD or n (%)	Mean Change (95% CI)	p-value	Mean Change (95% CI)	p-value
Clinical outcomes					
ARR	0.39 ± 0.82	-0.24 (-0.33, -0.14)	**<0.001**	-0.21 (-0.31, -0.11)	**<0.001**
MS disease severity	3.47 ± 3.44	-1.45 (-1.73, -1.16)	**<0.001**	-1.35 (-1.65, -1.05)	**<0.001**
Number of disabilities per EDSS-DDI	1.09 ± 0.88	-0.03 (-0.09, 0.03)	0.347	-0.02 (-0.08, 0.05)	0.619
Corticosteroid use					
Use of corticosteroids	261 (48.4)	-15% (-20%, -10%)	**<0.001**	-14% (-19%, -8%)	**<0.001**
HRU					
All-cause HRU					
Inpatient admissions	0.27 ± 0.81	-0.10 (-0.18, -0.01)	**0.021**	-0.02 (-0.14, 0.10)	0.719
Outpatient visits	12.64 ± 16.47	-2.76 (-3.80, -1.72)	**<0.001**	-2.52 (-3.78, -1.26)	**<0.001**
Emergency room visits	0.34 ± 1.03	-0.07 (-0.16, 0.03)	0.153	-0.07 (-0.15, 0.01)	0.079
Rehabilitation services	1.87 ± 6.54	-0.20 (-0.78, 0.39)	0.511	-0.38 (-1.03, 0.28)	0.260
MS-related HRU					
Inpatient admissions	0.11 ± 0.39	-0.06 (-0.09, -0.03)	**0.001**	-0.02 (-0.07, 0.04)	0.543
Outpatient visits	6.14 ± 8.12	-1.55 (-2.09, -1.01)	**<0.001**	-2.13 (-2.79, -1.46)	**<0.001**
Emergency room visits	0.21 ± 0.76	-0.05 (-0.12, 0.02)	0.154	-0.06 (-0.14, 0.02)	0.119
Rehabilitation services	0.76 ± 3.99	-0.14 (-0.48, 0.19)	0.405	-0.29 (-0.67, 0.09)	0.132

ARR, annualized relapse rate; **CI,** confidence interval; **DMT,** disease-modifying therapy; **EDSS-DDI,** Expanded Disability Status Scale-Derived Disability Indicators; **HRU,** healthcare resource utilization; **MS,** multiple sclerosis; **SD,** standard deviation

Effectiveness of Cladribine Tablets (Table 2)

- In all, 81% of patients were relapse-free over the 2-year follow-up period.
- ARR decreased from 0.39 during baseline to 0.16 in Year 1 and 0.19 in Year 2 (both p<0.001). The ARR during the entire follow-up period was 0.17, which differed by -0.22 (p<0.001) from baseline.
- MS disease severity score decreased from 3.47 during baseline to 2.02 in Year 1 and 2.12 in Year 2 (both p<0.001).
- The number of disabilities per the EDSS-DDI remained similar during baseline (1.09) vs Year 1 (1.06, p=0.347) and Year 2 (0.90, p=0.619).
- Fewer patients used corticosteroids in Year 1 (33.4%) and Year 2 (34.9%) compared with baseline (48.4%; both p<0.001).
- All-cause and MS-related HRU was reduced in Years 1 and 2. Specifically, the number of annual all-cause outpatient visits was reduced from 12.64 during baseline to 9.88 in Year 1 and 10.12 in Year 2 (both p<0.001).
- Similarly, annual MS-related outpatient visits were reduced from 6.14 during baseline to 4.60 in Year 1 and 4.02 in Year 2 (both p<0.001).

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METHODS

MS Relapses

- The following algorithm, adapted from previously published ones,[1,2] was applied to identify MS relapse:
  1) Inpatient claim with a principal diagnosis of MS (ICD-10-CM: G35), or
  2) Other type of clinical encounter (e.g., outpatient, physician office visit, other medical visit claim) with a principal or secondary diagnosis of MS (ICD-10-CM: G35) AND a pharmacy or medical claim for betamethasone, dexamethasone, methylprednisolone, prednisolone, prednisone, triamcinolone, or corticotrophin (within 7 days after the visit) or plasmapheresis (within 30 days after the visit)

- The following scenarios did not qualify as a relapse event:
  1) For inpatient encounters, an event meeting criterion 1) above was not considered as a relapse if the inpatient encounter had a medical claim for any infused DMT on the date of admission
  2) For non-inpatient encounters, an event meeting criterion 2) above was not considered as a relapse if ocrelizumab, alemtuzumab, or natalizumab was used on the same day or within 7 days prior to an injected/infused corticosteroid

- If multiple claims were present within a 30-day window, this was treated as a single relapse event; the first available service date within such a grouping was deemed as the date of MS relapse

- MS relapse was described using: (a) ARR in Years 1 and 2 of the follow-up period as well as in the entire follow-up period; and (b) time to first MS relapse during the follow-up period

ARR, annualized relapse rate; **DMT**, disease-modifying therapy; **ICD-10-CM**, International Classification of Diseases, 10th Version, Clinical Modification; **MS**, multiple sclerosis

REFERENCES: 1. Ollendorf DA, et al. *J Managed Care Pharm.* 2002;8:469–476. 2. Chastek BJ, et al. *J Med Econ.* 2010;13:618–625.

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METHODS

Subgroup Analysis

Methods

- A subgroup analysis was conducted among patients who had at least 4 claims of cladribine tablets during the follow-up period (i.e., as a proxy of patients who completed the full treatment courses for cladribine tablets)

Results

- The results were similar among a total of 316 patients who had at least 4 claims of cladribine tablets during the follow-up period (i.e., as a proxy of patients who completed the full treatment courses for cladribine tablets)

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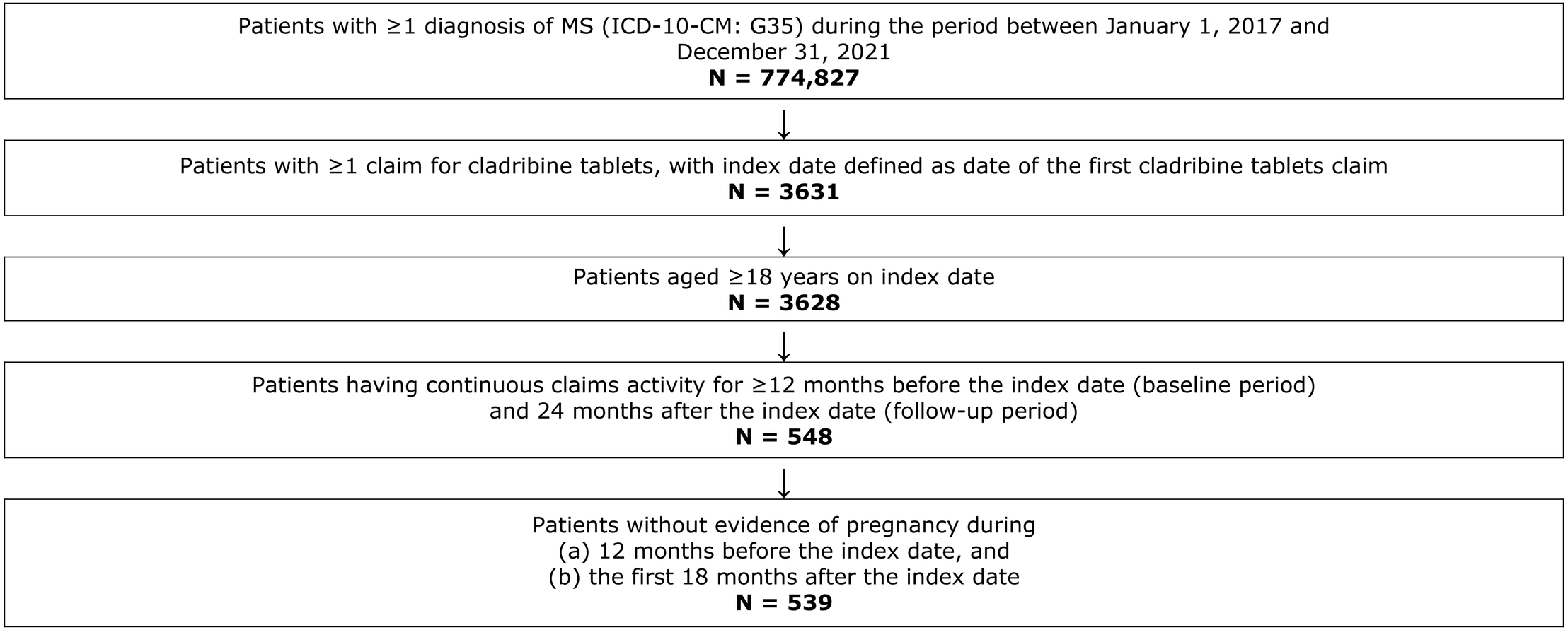
METHODS

Flow Chart of Sample Selection



ICD-10-CM, International Classification of Diseases, 10th Version, Clinical Modification; **MS**, multiple sclerosis

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RESULTS

Changes in MS-Related Treatment and Medical Device Use, Clinical Characteristics, and HRU in Years 1 and 2

Outcomes	Baseline	Year 1	Year 1 vs. baseline		Year 2	Year 2 vs. baseline	
	Mean ± SD or n (%)	Mean ± SD or n (%)	Mean change (95% CI)	p-value	Mean ± SD or n (%)	Mean change (95% CI)	p-value
Clinical outcomes							
ARR	0.39 ± 0.82	0.16 ± 0.50	-0.24 (-0.33, -0.14)	**<0.001**	0.19 ± 0.62	-0.21 (-0.31, -0.11)	**<0.001**
MS disease severity	3.47 ± 3.44	2.02 ± 2.92	-1.45 (-1.73, -1.16)	**<0.001**	2.12 ± 3.01	-1.35 (-1.65, -1.05)	**<0.001**
Number of disabilities per EDSS-DDI	1.09 ± 0.88	1.06 ± 0.90	-0.03 (-0.09, 0.03)	0.347	0.90 ± 1.07	-0.02 (-0.08, 0.05)	0.619
Corticosteroid use							
Use of corticosteroids	261 (48.4%)	180 (33.4%)	-15% (-20%, -10%)	**<0.001**	188 (34.9%)	-14% (-19%, -8%)	**<0.001**
HRU							
All-cause HRU							
Inpatient admissions	0.27 ± 0.81	0.17 ± 0.73	-0.10 (-0.18, -0.01)	**0.021**	0.24 ± 1.28	-0.02 (-0.14, 0.10)	0.719
Outpatient visits	12.64 ± 16.47	9.88 ± 13.44	-2.76 (-3.80, -1.72)	**<0.001**	10.12 ± 14.15	-2.52 (-3.78, -1.26)	**<0.001**
Emergency room visits	0.34 ± 1.03	0.27 ± 0.87	-0.07 (-0.16, 0.03)	0.153	0.26 ± 1.02	-0.07 (-0.15, 0.01)	0.079
Rehabilitation services	1.87 ± 6.54	1.67 ± 6.53	-0.20 (-0.78, 0.39)	0.511	1.49 ± 6.55	-0.38 (-1.03, 0.28)	0.260
MS-related HRU							
Inpatient admissions	0.11 ± 0.39	0.05 ± 0.24	-0.06 (-0.09, -0.03)	**0.001**	0.09 ± 0.55	-0.02 (-0.07, 0.04)	0.543
Outpatient visits	6.14 ± 8.12	4.60 ± 6.74	-1.55 (-2.09, -1.01)	**<0.001**	4.02 ± 6.27	-2.13 (-2.79, -1.46)	**<0.001**
Emergency room visits	0.21 ± 0.76	0.16 ± 0.59	-0.05 (-0.12, 0.02)	0.154	0.14 ± 0.72	-0.06 (-0.14, 0.02)	0.119
Rehabilitation services	0.76 ± 3.99	0.62 ± 4.21	-0.14 (-0.48, 0.19)	0.405	0.47 ± 2.19	-0.29 (-0.67, 0.09)	0.132

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