Comparative Assessment of Switching Outcomes for Patients With Multiple Sclerosis Receiving Cladribine Tablets vs Fingolimod, Dimethyl fumarate, and Teriflunomide

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CONCLUSIONS

- **In this real-world study, fewer patients receiving cladribine tablets switched to another disease-modifying therapy (DMT) over 2 years compared with patients receiving fingolimod, dimethyl fumarate, or teriflunomide**
- **Odds of switching and hazard for time to switching were significantly greater with fingolimod, dimethyl fumarate, and teriflunomide vs cladribine tablets**

BACKGROUND

- Cladribine tablets are the first and only FDA-approved treatment for relapsing remitting multiple sclerosis (RRMS) and active secondary progressive multiple sclerosis (SPMS) that provides 2 years of proven efficacy with a maximum of 20 days of oral treatment over 96 weeks
- Comparative data for cladribine tablets vs other oral disease-modifying therapies (DMTs) in patients with multiple sclerosis (MS) are emerging

OBJECTIVE

- **To evaluate treatment switching within 1- and 2-year follow-up in patients in the United States with MS treated with cladribine tablets vs fingolimod, dimethyl fumarate, and teriflunomide**

METHODS

- This administrative claims study used data from the Komodo Healthcare Map™ database
- Inclusion criteria were: ≥2 MS diagnoses ≥30 days apart between 4/1/2018 and 12/31/2022; ≥1 claim for cladribine tablets, fingolimod, dimethyl fumarate, or teriflunomide between 4/1/2019 and 12/31/2020 (initiation date = index); no index DMT 1 year before index (baseline); age ≥18 years; and continuous enrollment with healthcare insurance from baseline to 2 years after index (follow-up)
- In each comparison, propensity score weighting was used to balance covariates, including age, sex, index year, race/ethnicity, geographic region, insurance, Charlson Comorbidity Index (CCI) score, MS severity, baseline relapses, MS-related hospitalizations, baseline medications, and MS-related comorbidities
- Weighting by odds ratio (OR) was used to estimate the average treatment effect among those treated with cladribine tablets
- The proportions of patients switching to another DMT within 1 and 2 years (weighted ORs with 95% CIs) and time to switch (weighted proportional hazards Cox regression model hazard ratios [HRs]) were compared across DMTs. Covariates remaining unbalanced after weighting were included in the models

RESULTS

- A total of 269 patients initiating cladribine tablets, 677 initiating fingolimod, 2314 initiating dimethyl fumarate, and 1449 initiating teriflunomide met the eligibility criteria (**Figure 1**)

Figure 1. Patient Selection and Attrition

Have 2 MS diagnoses separated by at least 30 days between 4/1/2018 and 12/31/2022
N=749,396

Have at least one claim for cladribine tablets, fingolimod, dimethyl fumarate, teriflunomide between 4/1/2019 and 12/31/2020
N=92,476 (12.34%)

Have 12 months of continuous medical and pharmacy eligibility (allowing a 30-day gap) before the index date and 24 months post-index
N=19,520 (21.11%)

Age ≥18 years on the index date and resident of 50 states+ Washington DC and known insurance status at index date
N=18,958 (97.12%)

Exclude patients with any code that could indicate pregnancy in the 12 months before or 24 months after index date
N=18,429 (97.21%)

Exclude patients with a place of service code of hospice, inpatient mental health, or inpatient rehabilitation in the 12 months before index date
N=18,253 (99.04%)

Exclude patients with any prior claims for the index medication in the 12 months prior to the index date
N=4711 (25.81%)

Exclude patients with any cladribine infusion claims or prescribing consistent with off-label cladribine tablets use
N=4709 (99.96%)

Cladribine tablets N=269 (5.71%) | **Dimethyl fumarate N=2314 (49.14%)** | **Fingolimod N=677 (14.38%)** | **Teriflunomide N=1449 (30.77%)**

RESULTS (cont.)

- The overall mean (SD) age was 45 (11) years and 75.7% of patients were female. Most patients had commercial health insurance (63.6%), followed by Medicaid (26.7%), and Medicare (9.7%) (**Table 1**)

Table 1. Patient Baseline Demographic Characteristics

		Weighted Population			
	Overall	Cladribine tablets	Fingolimod	Dimethyl fumarate	Teriflunomide
Total, N	4709	269	264	253	255
Age at index (years)					
Mean (SD)	45 (11)	44 (11)	43 (12)	44 (12)	44 (11)
Sex, N (%)					
Female	3564 (75.7)	209 (77.7)	208 (78.8)	194 (76.7)	197 (77.3)
Male	1145 (24.3)	60 (22.3)	56 (21.2)	59 (23.3)	58 (22.7)
Index year, N (%)					
2019	2447 (52.0)	86 (32.0)	97 (36.7)	83 (32.8)	83 (32.5)
2020	2262 (48.0)	183 (68.0)	167 (63.3)	170 (67.2)	172 (67.5)
Race/ethnicity, N (%)					
White	2013 (42.7)	114 (42.4)	103 (39.0)	116 (45.8)	125 (49.0)
Black or African American	565 (12.0)	32 (11.9)	40 (15.2)	31 (12.3)	22 (8.6)
Asian or Pacific Islander	45 (1.0)	3 (1.1)	2 (0.8)	2 (0.8)	1 (0.4)
Hispanic or Latino	383 (8.1)	31 (11.5)	29 (11.0)	18 (7.1)	24 (9.4)
Other	164 (3.5)	10 (3.7)	8 (3.0)	9 (3.6)	8 (3.1)
Unknown	1539 (32.7)	79 (29.4)	81 (30.7)	77 (30.4)	75 (29.4)
Geographic region, N (%)					
Midwest	1150 (24.4)	60 (22.3)	52 (19.7)	53 (20.9)	53 (20.8)
Northeast	1179 (25.0)	70 (26.0)	61 (23.1)	67 (26.5)	71 (27.8)
South	1581 (33.6)	102 (37.9)	107 (40.5)	97 (38.3)	98 (38.4)
West	799 (17.0)	37 (13.8)	44 (16.7)	36 (14.2)	34 (13.3)
Insurance type at index, N (%)					
Commercial	2994 (63.6)	171 (63.6)	161 (61.0)	162 (64.0)	164 (64.3)
Medicare	456 (9.7)	32 (11.9)	32 (12.1)	31 (12.3)	32 (12.5)
Medicaid	1259 (26.7)	66 (24.5)	71 (26.9)	61 (24.1)	59 (23.1)

- Mean (SD) CCI score was 0.55 (1.11) (**Table 2**)

Table 2. Patient Baseline Clinical Characteristics

		Weighted Population			
	Overall	Cladribine tablets	Fingolimod	Dimethyl fumarate	Teriflunomide
Total, N	4709	269	264	253	255
Charlson Comorbidity Index score					
Mean (SD)	0.55 (1.11)	0.76 (1.33)	0.87 (1.75)	0.75 (1.34)	0.75 (1.41)
Baseline MS severity, N (%)					
MS relapse	1664 (35.3)	115 (42.8)	126 (47.7)	106 (41.9)	110 (43.1)
MS hospitalization	354 (7.5)	24 (8.9)	34 (12.9)	23 (9.1)	20 (7.8)
Baseline MS Severity Score					
Mean (SD)	4.3 (3.6)	5.7 (4.2)	6.1 (5.0)	5.4 (3.8)	5.5 (4.1)
Baseline MS Severity Score, N (%)					
Low (0-4)	2832 (60.1)	127 (47.2)	129 (48.9)	117 (46.2)	123 (48.2)
Moderate (5-10)	1554 (33.3)	100 (37.2)	85 (32.2)	108 (42.7)	94 (36.9)
High (≥11)	323 (6.9)	42 (15.6)	50 (18.9)	28 (11.1)	38 (14.9)
Dalfampridine use, N (%)	141 (3.0)	32 (11.9)	30 (11.4)	24 (9.5)	22 (8.6)
Overall DMT use, N (%)	1653 (35.1)	134 (49.8)	135 (51.1)	118 (46.6)	120 (47.1)
DMT use by drug class, N (%)					
Oral	139 (3.0)	17 (6.3)	12 (4.5)	4 (1.6)	9 (3.5)
Monoclonal antibody	222 (4.7)	61 (22.7)	62 (23.5)	47 (18.6)	51 (20.0)
Platform	1345 (28.6)	61 (22.7)	65 (24.6)	75 (29.6)	69 (27.1)

DMT, disease-modifying therapy; MS, multiple sclerosis.

- For the weighted population, proportions of patients switching within 1 year were 3.7% on cladribine tablets, 17.8% on fingolimod, 28.9% on dimethyl fumarate, and 21.2% on teriflunomide (**Table 3**)
  - The ORs (95% CI) of 1-year switch vs cladribine tablets were fingolimod 5.66 (2.90-12.15), dimethyl fumarate 10.81 (5.66-22.87), and teriflunomide 7.34 (3.78-15.74) (**Table 4**)
  - The HRs (95% CIs) for time to switching at 1 year were statistically significant compared with cladribine tablets (fingolimod 5.21 [2.54-10.67], dimethyl fumarate 9.26 [4.91-17.45], and teriflunomide 6.65 [3.46-12.79]) (**Table 4**)

Table 3. Switching Outcomes Within 1 Year

	Cladribine tablets N (%)	Fingolimod N (%)	Dimethyl fumarate N (%)	Teriflunomide N (%)
Total, N	269	264	253	255
Switch within 1 year				
Total number of patients who switched	10 (3.7)	47 (17.8)	73 (28.9)	54 (21.2)
Name of DMT switched to				
Platform	**2 (0.7)**	**7 (2.6)**	**14 (5.5)**	**13 (5.1)**
Glatiramer	0 (0.0)	5 (2.0)	9 (3.4)	8 (3.1)
Interferon beta-1a	2 (0.7)	0 (0.0)	3 (1.4)	4 (1.7)
Interferon beta-1b	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.3)
Peginterferon beta-1b	0 (0.0)	1 (0.3)	1 (0.5)	0 (0.0)
Monoclonal antibodies	**6 (2.2)**	**23 (8.7)**	**28 (11.0)**	**23 (9.0)**
Alemtuzumab	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Natalizumab	0 (0.0)	3 (1.0)	7 (2.9)	7 (2.7)
Ocrelizumab	2 (0.7)	20 (7.5)	19 (7.5)	14 (5.7)
Ofatumumab	3 (1.1)	1 (0.2)	1 (0.5)	2 (0.6)
Oral	**2 (0.7)**	**17 (6.5)**	**31 (12.0)**	**18 (7.1)**
Cladribine tablets	0 (0.0)	2 (0.6)	1 (0.4)	2 (0.9)
Dimethyl fumarate	1 (0.4)	7 (2.8)	0 (0.0)	7 (2.9)
Diroximel fumarate	0 (0.0)	0 (0.0)	18 (7.0)	5 (1.8)
Fingolimod	0 (0.0)	0 (0.0)	4 (1.5)	1 (0.3)
Ozanimod	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.4)
Siponimod	0 (0.0)	1 (0.4)	2 (0.6)	2 (0.7)
Teriflunomide	1 (0.4)	6 (2.4)	6 (2.5)	0 (0.0)

DMT, disease-modifying therapy.

Table 4. Comparative Switching Outcomes Within 1 Year

Comparison of proportion of treatment switchs (1 year)			
	Odds ratio	**95% CI**	***P* value**
Cladribine tablets		Reference	
Fingolimod	5.66	2.90-12.15	<0.0001
Dimethyl fumarate	10.81	5.66-22.87	<0.0001
Teriflunomide	7.34	3.78-15.74	<0.0001
Comparison of time-to-switch at 1 year			
	Hazard ratio	**95% CI**	***P* value**
Cladribine tablets		Reference	
Fingolimod	5.21	2.54-10.67	<0.0001
Dimethyl fumarate	9.26	4.91-17.45	<0.0001
Teriflunomide	6.65	3.46-12.79	<0.0001

- Within 2 years, proportions of patients switching treatments were 10.4% on cladribine tablets, 26.9% on fingolimod, 43.5% on dimethyl fumarate, and 34.1% on teriflunomide (**Table 5**)
  - The ORs (95% CI) of 2-year switching vs cladribine tablets were fingolimod 3.25 (2.03-5.32), dimethyl fumarate 6.75 (4.29-10.92), and teriflunomide 4.65 (2.92-7.59) (**Table 6**)
  - HRs (95% CIs) for time to switching at 2 years were statistically significant compared with cladribine tablets (fingolimod 2.99 [1.89-4.71], dimethyl fumarate 5.45 [3.73-7.97], and teriflunomide 4.06 [2.73-6.06], respectively) (**Table 6**)

Table 5. Switching Outcomes Within 2 Years

	Cladribine tablets N (%)	Fingolimod N (%)	Dimethyl fumarate N (%)	Teriflunomide N (%)
Total, N	269	264	253	255
Switch within 2 years				
Total number of patients who switched	28 (10.4)	71 (26.9)	110 (43.5)	87 (34.1)
Name of DMT switched to				
Platform	**5 (1.9)**	**9 (3.6)**	**17 (6.8)**	**17 (6.7)**
Glatiramer	2 (0.7)	7 (2.6)	11 (4.4)	11 (4.4)
Interferon beta-1a	3 (1.1)	1 (0.3)	4 (1.6)	5 (1.9)
Interferon beta-1b	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.3)
Peginterferon beta-1b	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)
Monoclonal antibodies	**17 (6.3)**	**39 (15.0)**	**43 (17.0)**	**41 (16.0)**
Alemtuzumab	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Natalizumab	1 (0.4)	4 (1.4)	8 (3.3)	10 (4.0)
Ocrelizumab	6 (2.2)	32 (12.0)	29 (11.0)	23 (9.1)
Ofatumumab	9 (3.3)	3 (1.1)	6 (2.2)	7 (2.9)
Oral	**6 (2.2)**	**23 (8.6)**	**50 (20.0)**	**29 (11.0)**
Cladribine tablets	0 (0.0)	2 (0.9)	2 (0.7)	5 (1.8)
Dimethyl fumarate	2 (0.7)	8 (2.9)	0 (0.0)	8 (3.3)
Diroximel fumarate	1 (0.4)	1 (0.2)	32 (13.0)	6 (2.5)
Fingolimod	0 (0.0)	0 (0.0)	4 (1.7)	1 (0.5)
Ozanimod	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Siponimod	1 (0.4)	1 (0.5)	2 (0.6)	2 (0.8)
Teriflunomide	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

DMT, disease-modifying therapy.

Table 6. Comparative Switching Outcomes Within 2 Years

Comparison of proportion of treatment switch (2 years)			
	Odds ratio	**95% CI**	***P* value**
Cladribine tablets		Reference	
Fingolimod	3.25	2.03-5.32	<0.0001
Dimethyl fumarate	6.75	4.29-10.92	<0.0001
Teriflunomide	4.65	2.92-7.59	<0.0001
Comparison of time-to-switch at 2 years			
	Hazard ratio	**95% CI**	***P* value**
Cladribine tablets		Reference	
Fingolimod	2.99	1.89-4.71	<0.0001
Dimethyl fumarate	5.45	3.73-7.97	<0.0001
Teriflunomide	4.06	2.73-6.06	<0.0001

LIMITATIONS

- Limitations of this study include the relatively small sample size for patients receiving cladribine tablets and the lack of direct clinical measures of MS disease severity and relapse
- The observed results may not be generalizable to other patient populations due to potential differences in data source populations, indications, treatment practices, and endpoint definitions

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