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Effectiveness, Self-Reported Adherence, and Safety of Cladribine Tablets in Patients With Relapsing Multiple Sclerosis After Suboptimal Response to Prior Injectable Disease-Modifying Therapy: 12-Month Interim Analysis From the US-Based Phase 4 CLICK-MS Study

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CONCLUSIONS

- **Results of this 12-month interim analysis of cladribine tablets in patients with RMS include an ARR of 0.017 with only 1 reported relapse, stable EDSS, high self-reported adherence, treatment satisfaction and favorable tolerability with no new safety signals**
- **Results from the CLICK-MS study may help inform treatment decisions in real-world clinical practice**

INTRODUCTION

- MS is a chronic autoimmune, neurodegenerative, and inflammatory disorder of the central nervous system[1,2]
- Cladribine tablets (3.5 mg/kg cumulative dose over 2 years) are approved for treating forms of RMS in adults including RRMS and active SPMS[3]
- Real-world data on the effectiveness, adherence, and safety of cladribine tablets in patients switching from injectable disease-modifying therapies (DMTs) are limited
- This observational study provides 12-month results for effectiveness, patient-reported treatment adherence, treatment satisfaction, and safety of cladribine tablets in patients with RRMS or SPMS who had a prior suboptimal response to an injectable DMT in a real-world setting

OBJECTIVE

- **To evaluate the effectiveness, patient-reported treatment adherence, and safety of cladribine tablets in patients with RMS who had a suboptimal[a] response to an injectable DMT in a real-world setting**

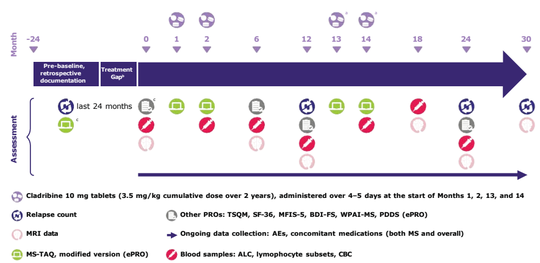
[a]Suboptimal as per protocol: lack of effectiveness, intolerability, poor adherence.

METHODS

Study Design

- CLICK-MS (NCT03933215) is an ongoing, observational, single-arm, phase 4, US-based study (**Figure 1**)
- These analyses were conducted with data collected up to January 27, 2023

Figure 1. CLICK Study Design



[a]Treatment in the second year may be delayed for up to 6 months for some patients, according to ALC. This is accounted for in the study duration. [b]Duration between stopping previous DMT and starting cladribine tablets was variable and at the discretion of the treating physician. [c]First assessment is for prior DMT.

Eligibility Criteria

- Patients aged ≥18 years with RRMS or active SPMS treated with ≥1 course of cladribine tablets who switched after a suboptimal response to an injectable DMT
- To participate in the study, all patients are required to meet the US Prescribing Information criteria for treatment with cladribine tablets

Study Endpoints

- The primary endpoint of this study is 24-month annualized relapse rate (ARR) after initiating treatment with cladribine tablets
- Key secondary endpoints include expanded disability status scale (EDSS) score, adherence as assessed by the MS treatment adherence questionnaire (MS-TAQ), and safety

Statistical Analysis

- The 12-month interim analysis is based on baseline, 6-month, and 12-month data
- Population estimates of the ARR, its corresponding 95% CI, and descriptive statistics were based on the average of patients' ARR values. The ARR over 12 months for a patient is calculated as the patient's number of relapses per routine clinical practice divided by the patient's number of days on study, multiplied by 365.25
- Descriptive statistics are shown for EDSS, MS-TAQ, and baseline characteristics
- The most recent prior DMT was examined
- Serious TEAEs, discontinuations due to TEAEs, the most commonly reported TEAEs ≥4%, and lymphopenia are shown

RESULTS

Baseline Demographics and Disease Characteristics

- A total of 62 patients with RMS who switched from an injectable DMT were treated with cladribine tablets (**Table 1**)
- The mean (SD) overall ARR 24 months prior to the study was 0.23 (0.301)
- The mean (SD) number of combined unique lesions at baseline was 8.1 (14.26)
- The majority of the patients (80.6%) had baseline ALC levels within normal range

Table 1. Baseline Demographics and Disease Characteristics

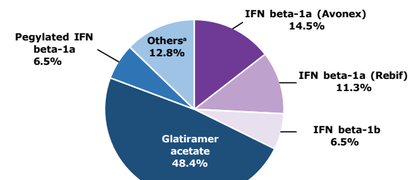
Characteristics	Switch from an injectable DMT to cladribine tablets 3.5 mg/kg (N=62)
Female, n (%)	49 (79.0)
Age, years	
Mean (SD)	49.1 (12.4)
Min, Max	22, 67
Race, n (%)	
White	52 (83.9)
Black/African American	7 (11.3)
Other	3 (4.8)
Diagnosis, n (%)	
RRMS	59 (95.2)
Active SPMS	2 (3.2)
PPMS[a]	1 (1.6)
Elapsed time since diagnosis, years, mean (SD)	13.9 (10.36)
Relapse in prior 24 months, n (%)	
0	33 (53.2)
1	20 (32.3)
2	3 (4.8)
≥3	0
ARR in prior 24 months, mean (SD)	0.23 (0.301)
Number of MRI lesions, mean (SD)	
T1 Gd+ lesions	0.2 (0.38)
New T2 lesions	0.5 (0.90)
Combined unique lesions	8.1 (14.26)
ALC (10^9/L), median (Q1; Q3)	1.9 (1.5; 2.5)
ALC (10^9/L), n (%)	
Below lower limit of normal	0
Within normal range	50 (80.6)
Above upper limit of normal	1 (1.6)
Missing	11 (17.7)

[a]The patient with PPMS was mistakenly enrolled in the study. The patient received 1 week of treatment with cladribine tablets, then discontinued from the study because of protocol deviation. There were no AEs reported.

Most Recent Prior DMT

- The most common injectable DMTs used prior to initiating cladribine tablets were glatiramer acetate (48.4%), IFN beta-1a (Avonex 14.5%, Rebif 11.3%) (**Figure 2**)

Figure 2. Common Prior Injectable DMTs Used (N=62)



[a]Other DMTs include dimethyl fumarate (3.2%), natalizumab (4.8%), ocrelizumab (1.6%), ofatumumab (1.6%), and teriflunomide (1.6%).

Annualized Relapse Rate

- The ARR 12 months post-initiation of cladribine tablets was 0.017, with only 1 patient experiencing relapse
- No relapses requiring treatment with glucocorticoids or hospitalization were reported over the 12-month period (**Table 2**)

Table 2. ARR at 12 Months Following Cladribine Tablet Initiation

ARR	Switch from an injectable DMT to cladribine tablets 3.5 mg/kg (N=62)
ARR documented, n (%)	51 (82.3)
ARR missing, n (%)	11 (17.7)
Total number of relapses over the 12-month period	1
Total time on study over 12-month period, days	21,177
Relapse rate (per patient-year on study)	0.017

EDSS for Cladribine Tablets

- At both 6 and 12 months following cladribine tablet initiation, median (Q1; Q3) EDSS score was stable at 2.0 (1.5; 3.0) for those who completed the EDSS assessment (n=14 [22.6%]) (**Table 3**)

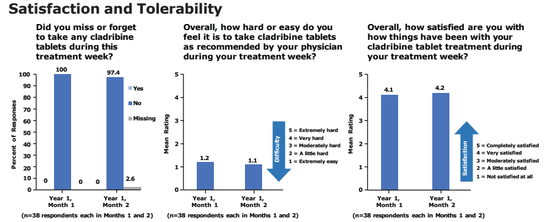
Table 3. EDSS Score Following Cladribine Tablet Initiation

EDSS Score	Switch from an injectable DMT to cladribine tablets 3.5 mg/kg (N=62)		
	Baseline	Month 6	Month 12
Observed values			
n (%)	24 (38.7)	14 (22.6)	14 (22.6)
Median (Q1; Q3)	2.0 (1.5; 3.0)	2.0 (1.5; 3.0)	2.0 (1.5; 3.0)
Change from baseline			
n (%)	-	14 (22.6)	13 (21.0)
Median (Q1; Q3)	-	0 (0; 0)	0 (0; 0.5)

MS-TAQ for Cladribine Tablets: Adherence Rates, Treatment Satisfaction and Tolerability

- Self-reported adherence rate for the full first year treatment course among MS-TAQ respondents was high at ≥97.4% (n=37/38) (**Figure 3**)
- High self-reported cladribine treatment satisfaction and favorable tolerability was reported among the MS-TAQ respondents for the full first year treatment course with a mean score ≥4.1

Figure 3. MS-TAQ for Cladribine Tablets: Adherence Rates, Treatment Satisfaction and Tolerability



Safety

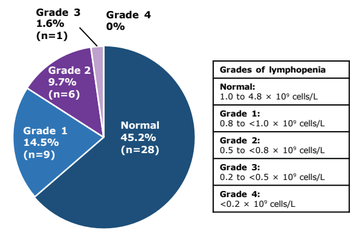
- Two (3.2%) patients experienced serious TEAEs (**Table 4**)
- No patient discontinued due to TEAEs during the observation period
- The most commonly reported TEAEs (≥4% of patients) were COVID-19 (6.5% [n=4]) and urinary tract infection (4.8% [n=3])
- At 12 months, grade 3 lymphopenia was reported in 1.6% of patients, and no grade 4 lymphopenia was reported in patients who switched from injectable DMTs (**Figure 4**)

Table 4. Rates of TEAEs in Patients Who Switched From an Injectable DMT to Cladribine Tablets

TEAEs	Switch from an injectable DMT to cladribine tablets 3.5 mg/kg (N=62)
Any TEAE, n (%)	31 (50.0)
Severe	2 (3.2)[a]
Moderate	19 (30.6)
Mild	25 (40.3)
Any serious TEAE, n (%)	2 (3.2)[a]
TEAE leading to discontinuation, n (%)	0

[a]One patient experienced both low ALC and suspected kidney infection, and another patient experienced gastritis. The 2 reported severe TEAEs and serious TEAEs are the same in this analysis.

Figure 4. Lymphopenia Grade at the 12-Month Visit[a]



[a]n=44 patients with ALC values at 12 months.

Abbreviations: AEs, adverse events; **ALC,** absolute lymphocyte count; **ARR,** annualized relapse rate; **BDI-FS,** Beck-Depression Inventory – Fast Screen; **CBC,** complete blood count; **DMT,** disease-modifying therapy; **EDSS,** Expanded Disability Status Scale; **ePRO**, electronic PRO; **IFN,** interferon; **MFIS-5,** Modified Fatigue Impact Scale – 5-item version; **MRI,** magnetic resonance imaging; **MS,** multiple sclerosis; **MS-TAQ,** MS Treatment Adherence Questionnaire; **PDDS**, Patient Determined Disease Steps; **PPMS,** primary progressive multiple sclerosis; **PRO**, patient-reported outcome; **RMS,** relapsing multiple sclerosis; **RRMS,** relapsing-remitting multiple sclerosis; **SF-36,** 36-Item Short Form Health Survey; **SPMS,** secondary progressive multiple sclerosis; **TEAEs,** treatment-emergent adverse events; **TSQM,** 14-Item Treatment Satisfaction Questionnaire for Medication; **Tx,** treatment; **WPAI-MS,** Work Productivity Activity Impairment – MS.

References: 1. Giovannoni G, Mathews J. *Neurol Ther*. 2022;11(2):571-595. **2.** Kamma E, et al. *J Neuroinflammation*. 2022;19(1):45. **3.** MAVENCLAD (cladribine) tablets [package insert]. EMD Serono, Inc.; 2022.

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