Self-Reported Adherence and Interval Safety from the US Phase IV MASTER-2 and CLICK-MS Studies of Cladribine Tablets in Patients with Relapsing Forms of Multiple Sclerosis After Suboptimal Response to Prior Disease-Modifying Therapy

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CONCLUSIONS

Treatment adherence and patient satisfaction outcomes were similar in patients switching to cladribine tablets from injection, oral, or infusion DMTs

Self-reported adherence to cladribine tablets was high: ≥96.5% adherence for the full dose for year 1

No new or unexpected safety findings were reported following treatment with cladribine tablets

Regardless of the route of administration of the DMT used prior to cladribine tablets, treatment adherence and safety results were generally promising. These results can help inform treatment decisions in real-world clinical practice when a patient is experiencing suboptimal response to a DMT

BACKGROUND

- Cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years) are approved in the US for the treatment of relapsing forms of MS
- Real-world data on treatment patterns, adherence, effectiveness, and the safety of cladribine tablets in US patients switching from other DMTs are limited

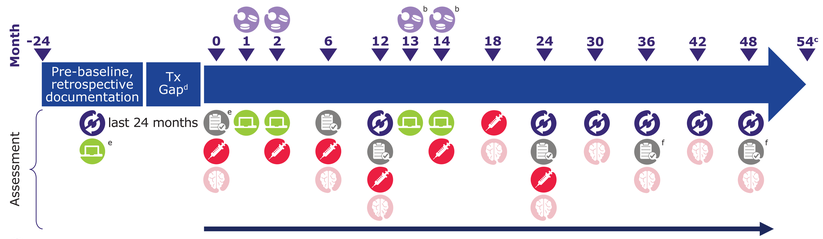
OBJECTIVE

- To evaluate interim treatment patterns, adherence, and the safety of cladribine tablets in patients switching from alternative DMTs due to suboptimal response enrolled in two US-based Phase IV studies

METHODS

- CLICK-MS (NCT03933215) and MASTER-2 (NCT03933202) are ongoing US-based, 54-month studies
- These single-arm, observational studies examine real-world clinical and patient-reported outcomes of treatment with cladribine tablets in patients with relapsing RRMS or active SPMS following suboptimal responses to prior injectable (CLICK-MS), oral, or infusion (MASTER-2) DMTs
- To participate in the study, all patients are required to meet the USPI criteria for treatment with cladribine tablets
- These are ongoing studies, and data queries are taking place currently

CLICK-MS AND MASTER-2 STUDY DESIGN[a]



- The primary outcome of both the CLICK-MS and MASTER-2 studies is 24-month ARR. Key secondary outcomes include treatment adherence and TEAEs
- These analyses were conducted with data collected up to either August 1, 2022 (CLICK-MS: includes all enrolled/dosed patients through ≥ 6 months), or July 7, 2022 (MASTER-2: preview of baseline analysis and safety)

Primary endpoint: ARR over 24 months

[a]Since the publication of the study design,[1] the study duration has been extended to 54 months from 30 months to further collect data on safety, relapse, MRI, and PDDS. [b]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. [c]If Year 2 treatment is delayed, follow-up may continue up to 54 months. [d]Duration between stopping previous DMT and starting cladribine tablets was variable and at the discretion of the treating physician. [e]First assessment is for prior DMT. [f]PDDS only.

RESULTS

- A total of 233 patients treated with cladribine tablets were included in the analysis: 63 switching from an injectable DMT (CLICK-MS), 102 from an oral DMT (MASTER-2), and 68 from an infusion DMT (MASTER-2)

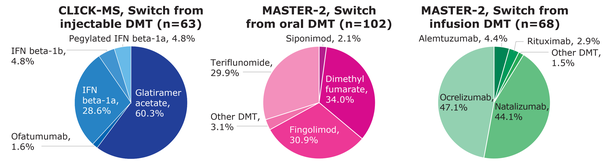
Demographics and baseline disease characteristics

	CLICK-MS	MASTER-2	
	Switch from injectable DMT (n=63)	Switch from oral DMT (n=102)	Switch from infusion DMT (n=68)
Female, n (%)	49 (77.8)	82 (80.4)	47 (69.1)
Age, years Mean (SD) Min, Max	50 (12.3) 22, 68	51 (10.7) 20, 74	48 (12.4) 22, 71
Race, n (%) White Black/African American Other[a]	53 (84.1) 7 (11.1) 3 (4.8)	85 (83.3) 12 (11.8) 5 (4.9)	55 (80.9) 6 (8.8) 7 (10.3)
Diagnosis, n (%) RRMS Active SPMS PPMS[b]	60 (95.2) 2 (3.2) 1 (1.6)	95 (93.1) 7 (6.9) 0	59 (86.8) 8 (11.8) 0
Elapsed time since diagnosis, years, mean (SD)	14.0 (10.35)[c]	11.9 (7.18)	13.7 (9.31)
Number of previous DMTs, mean (SD)	1.9 (1.12)	3.0 (1.73)[d]	3.6 (1.88)[e]
Relapse in prior 24 months, n (%) 0 1 ≥2	36 (62.1) 18 (31.0) 4 (6.9)	60 (69.0) 23 (26.4) 4 (4.5)	35 (70.0) 13 (26.0) 2 (4. 0)
ARR in prior 24 months, mean (SD)	0.2 (0.32)	0.18 (0.320)	0.17 (0.279)

[a]Includes Asian, Multiple, and Other; [b]The patient with PPMS was mistakenly enrolled in the study. The patient received 1 week of cladribine tablets treatment, then discontinued from the study because of protocol deviation. There were no AEs reported; [c]n=62; [d]n=99; [e]n=66.
Proportions may not add up to 100% due to missing data

- Mean (SD) overall ARRs in the 24 months prior to the study were 0.2 (0.32), 0.18 (0.320), and 0.17 (0.279) for patients switched from injectable, oral, and infusion DMTs, respectively
- Mean (SD) number of combined unique lesions at baseline were 8.3 (14.17), 3.6 (9.36), and 9.3 (15.22), respectively (see Supplemental material for additional details)
- Baseline ALC levels were within normal ranges for most patients (74.6%, 73.5%, and 70.6% of patients, respectively) (see Supplemental material for additional details)
- Commonly reported prior DMTs were dimethyl fumarate, ocrelizumab, glatiramer acetate, fingolimod, and natalizumab

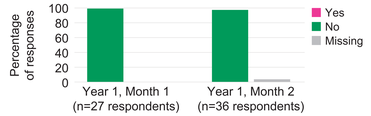
Most recent prior DMT



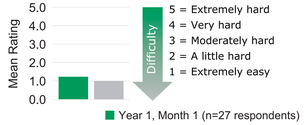
- Adherence rates to the full first year treatment dose (1.75 mg/kg), as self-reported by patients on the MS-TAQ, were ≥97.2% (n=35) and ≥96.5% (n=88) among MS-TAQ respondents in CLICK-MS and MASTER-2, respectively

CLICK-MS: MS-TAQ for cladribine tablets

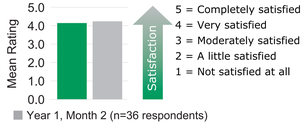
Did you miss or forget to take any cladribine tablets during this treatment week?



Overall, how hard or easy do you feel it is to take cladribine tablets as recommended by your physician during your treatment week?

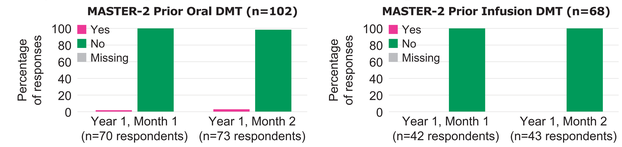


Overall, how satisfied are you with how things have been with your cladribine tablet treatment during your treatment week?



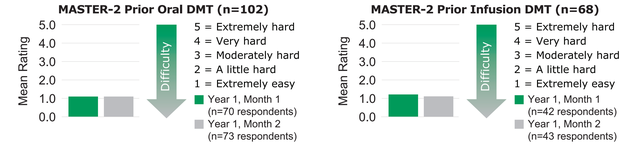
MASTER-2: MS-TAQ for cladribine tablets

Did you miss or forget to take any cladribine tablets during this treatment week?



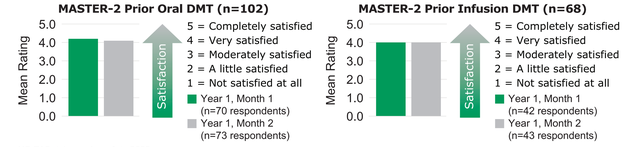
MS-TAQ data are from July 2022

Overall, how hard or easy do you feel it is to take cladribine tablets as recommended by your physician during your treatment week?



MS-TAQ data are from July 2022

Overall, how satisfied are you with how things have been with your cladribine tablet treatment during your treatment week?



MS-TAQ data are from July 2022

Safety

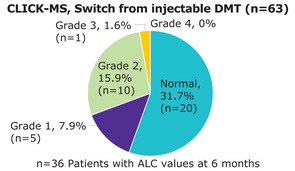
- Few patients (3.2%) in CLICK-MS experienced a serious TEAE, and no patients discontinued treatment due to TEAEs
- In MASTER-2, 8.2% of patients experienced a serious TEAE, and 4.7% discontinued treatment due to TEAEs

Rates of TEAEs

	CLICK-MS (n=63)		MASTER-2 (n=170)	
	n (%)	Rate per 100 patient-years	n (%)	Rate per 100 patient-years
Total patient-years		75.92		233.85
Any TEAE	28 (44.4)	0.83 (1.09)	80 (47.1)	2.72 (1.16)
Severe	2 (3.2)	0.03 (0.04)	16 (9.4)	0.22 (0.09)
Moderate	19 (30.2)	0.29 (0.38)	38 (22.4)	0.92 (0.39)
Mild	22 (34.9)	0.51 (0.67)	67 (39.4)	1.58 (0.68)
Any serious TEAE	2 (3.2)	0.03 (0.04)	14 (8.2)	0.17 (0.07)
TEAE leading to discontinuation	0	0	8 (4.7)	0.11 (0.05)

- The most commonly reported TEAEs (≥4% of patients in either study) were fatigue (8.2%), nausea (4.1%), and COVID-19 (4.1%) for MASTER-2 and urinary tract infection (4.8%) in CLICK-MS
- Overall, for CLICK-MS, grade 3 lymphopenia was observed in 11 of 63 patients (17.5%), and grade 4 lymphopenia was reported in 1 of 63 patients (1.2%)
  - At the 6-month visit, no patient in the CLICK-MS study had grade 4 lymphopenia

CLICK-MS: Lymphopenia grade at the 6-month visit



Grades of lymphopenia
Normal 1.0 to 4.8 x 10E9/L cells/L
Grade 1 Lymphopenia 0.8 to < 1.0 x 10E9/L cells/L
Grade 2 Lymphopenia 0.5 to < 0.8 x 10E9/L cells/L
Grade 3 Lymphopenia 0.2 to < 0.5 x 10E9/L cells/L
Grade 4 Lymphopenia <0.2 x 10E9/L cells/L

- Overall, for MASTER-2, grade 3 lymphopenia was observed in 29 of 170 of patients (17.1%), and grade 4 lymphopenia was reported in 9 of 170 of patients (5.3%)

Abbreviations: AE, adverse event; **ALC**, absolute lymphocyte count; **ARR**, annualized relapse rate; **BDI-FS**, Beck-Depression Inventory – Fast Screen; **CBC**, complete blood count; **DMT**, disease-modifying therapy, **ePRO**, electronic PRO; **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; **PRO**, patient-reported outcome; **RMS**, relapsing forms of MS; **RRMS**, relapsing-remitting MS; **SF-36**, 36-Item Short Form Health Survey; **SD**, standard deviation; **SPMS**, secondary progressive MS; **TEAEs**, treatment-emergent AEs; **TSQM**, 14-Item Treatment Satisfaction Questionnaire for Medication; **Tx**, treatment; **US**, United States; **USPI**, US Prescribing Information; **WPAI-MS**, Work Productivity Activity Impairment – MS.

References: 1. Miravalle AA, et al *Neurodegener Dis Manag* 2021;11:99–111.

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Baseline MRI

	CLICK-MS	MASTER-2	
	Switch from injectable DMT (n=63)	**Switch from oral DMT (n=102)**	**Switch from infusion DMT (n=68)**
Number of MRI lesions, mean (SD)			
T1 Gd+ lesions	0.2 (0.39)	0.3 (0.66)	0.1 (0.32)
New T2 lesions	0.5 (0.90)	0.7 (1.17)	1.2 (4.48)
Combined unique lesions	8.3 (14.17)	3.6 (9.36)	9.3 (15.22)

Baseline ALC characteristics

	CLICK-MS	MASTER-2	
	Switch from injectable DMT (n=63)	**Switch from oral DMT (n=102)**	**Switch from infusion DMT (n=68)**
n (%)	52 (82.5)	81 (79.4)	53 (77.9)
ALC (10^9/L)[a], median (Q1, Q3)	1.9 (1.5, 2.5)	1.4 (1.0, 2.0)	2.0 (1.4, 2.9)
ALC (10^9/L), n (%)			
Below lower limit of normal	3 (4.8)	1 (1.0)	0
Within normal ranges	47 (74.6)	75 (73.5)	48 (70.6)
Above upper limit of normal	2 (3.2)	5 (4.9)	5 (7.4)
Missing	11 (17.5)	21 (20.6)	15 (22.1)