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37th Congress of ECTRIMS | October 13–15, 2021

MASTER-2 trial: Cladribine tablets in patients with relapsing-remitting multiple sclerosis or active secondary progressive multiple sclerosis after suboptimal response to prior infusion/oral disease-modifying therapy (interim baseline results)

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CONCLUSIONS

Treatment switching is common in the management of MS. How patients with relapsing forms of MS will respond to cladribine tablets, following suboptimal response to another DMT, is unclear

134 MASTER-2 study patients have been treated with cladribine tablets as of July 2021. Baseline demographics, disease characteristics and PROs are broadly representative of pwMS in the US. Mean age of enrolled patients is 49 years, with a mean 12.1 years since MS diagnosis, and most patients are diagnosed with RRMS

With the ever-increasing landscape of MS DMTs, real-world evidence in the US around switching, adherence, and PROs of DMTs will be critical in supporting optimal decision-making in MS treatment

BACKGROUND

- Most patients with MS (>50%) experience suboptimal response to a DMT in at least one of the three key measures of efficacy outcomes: relapse, disability progression, and lesion activity on MRI[1]
- Cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years) are approved for the treatment of relapsing-forms of MS, including RRMS and active SPMS, according to the USPI,[2] but it remains unclear how patients will respond to therapy following suboptimal response to other DMTs

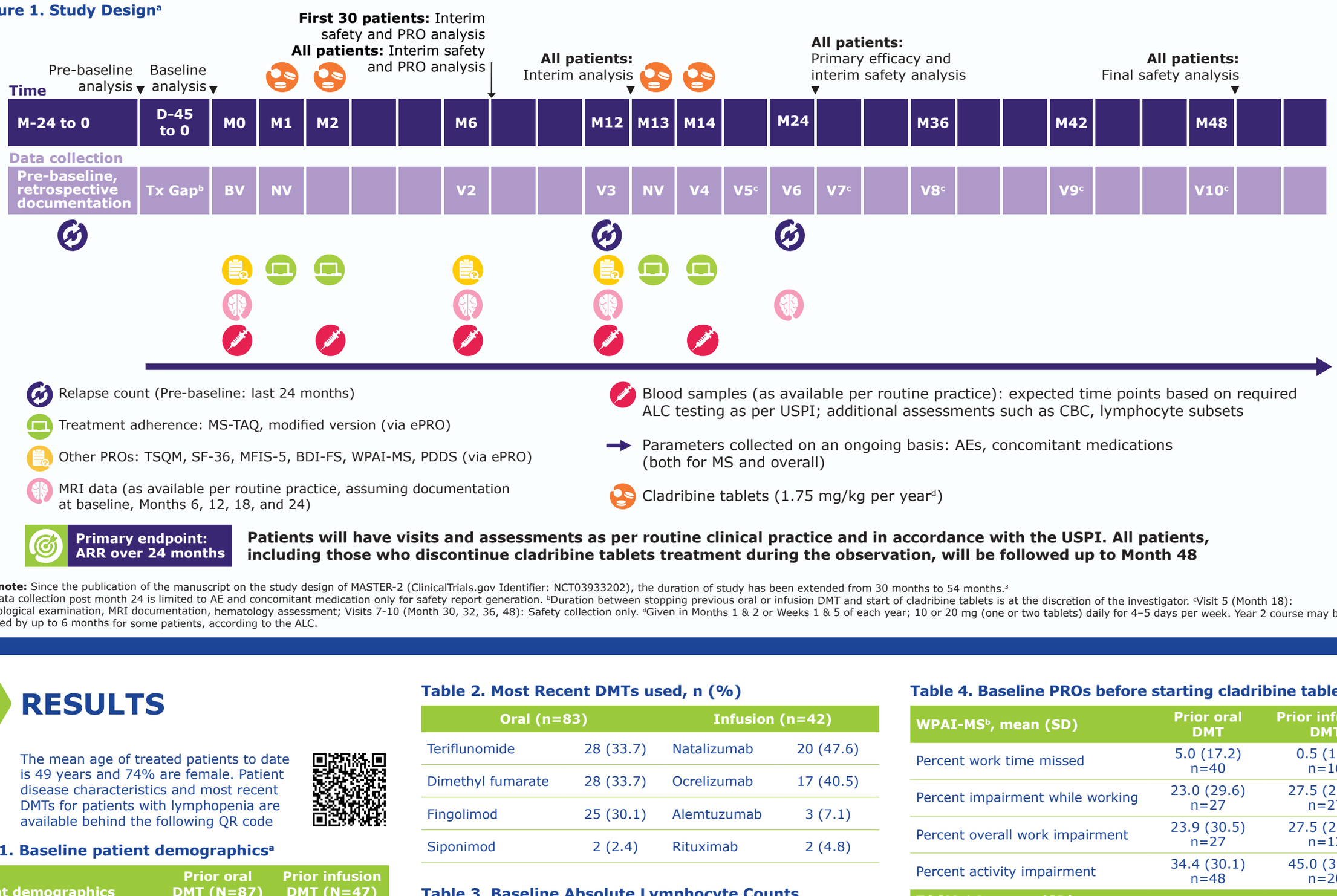
OBJECTIVES

- To examine baseline data from patients with RRMS or active SPMS who transition to cladribine tablets after suboptimal response to prior **oral** or **infusion** DMTs in the MASTER-2 study

METHODS

- MASTER-2 (ClinicalTrials.gov Identifier: NCT03933202) is a single arm, observational, 54 month (to allow for up to a 6 month delay of Year 2 treatment), Phase 4 trial in the US, beginning in 2019, expected to enroll and treat 325 patients across 65 sites and end in 2026[3]
- Patients included were adults diagnosed with RRMS or active SPMS with suboptimal response to prior oral or infusion DMT. Full inclusion/exclusion criteria have previously been published and are available using the following QR code

Figure 1. Study Design[a]



Footnote: Since the publication of the manuscript on the study design of MASTER-2 (ClinicalTrials.gov Identifier: NCT03933202), the duration of study has been extended from 30 months to 54 months.[3]
[a]All data collection post month 24 is limited to AE and concomitant medication only for safety report generation. [b]Duration between stopping previous oral or infusion DMT and start of cladribine tablets is at the discretion of the investigator. [c]Visit 5 (Month 18): Neurological examination, MRI documentation, hematology assessment; Visits 7-10 (Month 30, 32, 36, 48): Safety collection only. [d]Given in Months 1 & 2 or Weeks 1 & 5 of each year; 10 or 20 mg (one or two tablets) daily for 4–5 days per week. Year 2 course may be delayed by up to 6 months for some patients, according to the ALC.

RESULTS

The mean age of treated patients to date is 49 years and 74% are female. Patient disease characteristics and most recent DMTs for patients with lymphopenia are available behind the following QR code

Table 1. Baseline patient demographics[a]

Patient demographics	Prior oral DMT (N=87)	Prior infusion DMT (N=47)
Female, n (%)	67 (77.0)	32 (68.1)
Age (yrs)		
Mean (SD)	51 (11.3)	47 (12.5)
Min, Max	20, 74	22, 68
Race, n (%)		
White	73 (83.9)	39 (83.0)
Black/African American	9 (10.3)	4 (8.5)
Other	5 (5.7)	2 (2.3)

[a]This presentation reports interim baseline data (July 2021). Variable patient numbers for certain measures are due to ongoing data collection and cleaning

Table 2. Most Recent DMTs used, n (%)

Oral (n=83)		Infusion (n=42)	
Teriflunomide	28 (33.7)	Natalizumab	20 (47.6)
Dimethyl fumarate	28 (33.7)	Ocrelizumab	17 (40.5)
Fingolimod	25 (30.1)	Alemtuzumab	3 (7.1)
Siponimod	2 (2.4)	Rituximab	2 (4.8)

Table 3. Baseline Absolute Lymphocyte Counts

	Prior oral DMT (N=63)	Prior infusion DMT (N=36)
Baseline ALC in cells/μL, mean (SD)	1.458 (0.849)	2.338 (1.454)
Elevated, n (%)	1 (15.6)	5 (13.9)
Within normal range, n (%)	43 (68.3)	31 (86.1)
Grade 1, n (%)	8 (12.7)	0
Grade 2, n (%)	3 (4.8)	0
Grade 3, n (%)	5 (7.9)	0
Grade 4, n (%)	0	0

Note: per protocol all treatment decisions, including timing of initiation of treatment with cladribine tablets, are at the discretion of the investigator

Table 4. Baseline PROs before starting cladribine tablets[a]

WPAI-MS[b], mean (SD)	Prior oral DMT	Prior infusion DMT
Percent work time missed	5.0 (17.2) n=40	0.5 (1.9) n=16
Percent impairment while working	23.0 (29.6) n=27	27.5 (26.0) n=27
Percent overall work impairment	23.9 (30.5) n=27	27.5 (26.0) n=12
Percent activity impairment	34.4 (30.1) n=48	45.0 (30.7) n=20
TQSM-14[c], mean (SD)		
Global satisfaction	54.4 (22.50)	45.9 (26.10)
Effectiveness	58.5 (22.49)	45.0 (24.98)
Side effects	86.3 (26.74)	82.9 (26.83)
Convenience	77.9 (20.39)	62.0 (19.09)
MFIS-5[d], mean (SD)	9.2 (5.15) n=52	10.5 (4.83) n=22
BDI-FS[e], mean (SD)	1.9 (2.13) n=52	2.8 (2.92) n=23
PDDS[f], mean (SD)	2.2 (2.20) n=60	3.3 (2.56) n=28

[a]This presentation reports interim baseline data (July 2021). Variable patient numbers for certain measures are due to ongoing data collection and cleaning. [b]WPAI-MS scores are expressed as impairment percentages (higher percentage = greater impairment/less productivity). [c]TSQM score range 0–100. Higher score = higher satisfaction; oral, n=45, infusion n=19 except for global satisfaction which is n=20. [d]MFIS-5 scores range 0–20 (higher scores = greater impact of fatigue). [e]BDI-FS scores range 0–21 (higher scores = greater symptom severity). [f]PDDS scores range 0–8 (higher scores = higher level of disability).

Abbreviations: A, assessment; **AE,** adverse event; **ALC,** absolute lymphocyte count; **ARR,** annualized relapse rate; **BDI-FS,** Beck-Depression Inventory – Fast Screen; **BV,** baseline visit; **CBC,** complete blood count; **D,** day; **DMT,** disease modifying therapy; **EDSS,** Expanded Disability Status Scale; **ePRO,** electronic PRO; **IFN,** interferon; **M,** month; **MFIS-5,** Modified Fatigue Impact Scale – 5-item version; **MRI,** magnetic resonance imaging; **MS,** multiple sclerosis; **MS-TAQ,** MS Treatment Adherence Questionnaire; **NV,** no visit; **PDDS,** Patient Determined Disease Steps; **PRO,** patient reported outcome; **pwMS,** people with MS; **QoL,** quality of life; **RRMS,** relapsing-remitting MS; **SD,** standard deviation; **SF-36,** 36-Item Short Form Health Survey; **SPMS,** secondary progressive MS; **TSQM,** 14-Item Treatment Satisfaction Questionnaire for Medication; **USPI,** United States Prescribing Information; **V,** visit; **WPAI-MS,** Work Productivity Activity Impairment – MS; **Yrs,** years

References: 1. Gasperini C, et al. *Neurology* 2019;92:180-92. **2.** Mavenclad [package insert]. Rockland, MA: EMD Serono, Inc.; 2019. **3.** Miravalle AA, et al. *Neurodegener Dis Manag* 2021;11(2):99-111.

Acknowledgements: The MASTER-2 study is sponsored by EMD Serono, Inc., Rockland, MA, USA, an affiliate of Merck KGaA (CrossRef Funder ID: 10.13039/100004755), who reviewed and provided feedback on the poster. Writing and editorial support for the preparation of this poster was provided by Jenna Steere, PhD and Delisa O'Brien of Ashfield Healthcare Communications (New York, NY, USA); funding was provided by the study sponsor. The authors had full control of the poster and provided their final approval of all content.

Disclosures: EJF: Received compensation for research, consulting, speakers' bureau, and/or advisory work from AbbVie, Alexion, Biogen, Bristol Myers Squibb, Celgene, Chugai, EMD Serono, Inc., Rockland, MA, USA, an affiliate of Merck KGaA (CrossRef Funder ID: 10.13039/100004755), Genentech/Roche, MedDay, Novartis, Sanofi Genzyme, and TG Therapeutics; **ADB:** Research, advisory board, and speakers' bureau for Biogen, EMD Serono, Inc., Rockland, MA, USA, an affiliate of Merck KGaA (CrossRef Funder ID: 10.13039/100004755), Mallinckrodt, Novartis, Roche-Genentech, Sanofi-Genzyme, and TG Therapeutics; **JA:** Employee of EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA; **EE, LAL:** Employees of EMD Serono, Inc., Rockland, MA, USA, an affiliate of Merck KGaA; **DR:** Has received consultancy fees from Alexion, Biogen, Bristol Myers Squibb, EMD Serono, Inc., Rockland, MA, USA, an affiliate of Merck KGaA, Genentech, Greenwich Biosciences, Novartis, Sanofi Genzyme, Teva Neuroscience, Viela Bio. He has received honoraria or speaker fees from Acorda, Alexion, Biogen, Bristol Myers Squibb, EMD Serono, Inc., Rockland, MA, USA, an affiliate of Merck KGaA, Genentech, Mallinckrodt Pharmaceuticals, Novartis, Sanofi Genzyme, and Teva Neuroscience and has received research grant support from Biogen, EMD Serono, Inc., Rockland, MA, USA, an affiliate of Merck KGaA (CrossRef Funder ID: 10.13039/100004755), Genentech, GW Pharmaceuticals, Janssen, Mallinckrodt Pharmaceuticals, MedDay, MedImmune, Novartis, PCORI, Sanofi Genzyme, SunPharma and TG Therapeutics.

Presented at the 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) | 13–15 October 2021

Inclusion/Exclusion Criteria

Main inclusion criteria

- Age ≥18 years
- Diagnosed with RRMS or active SPMS for ≥12 months
- Suboptimal response (investigator-assessed) to previous treatment with an oral or infusion DMT, such as lack of effectiveness, intolerability or poor adherence
- Received last DMT for ≥1 month or last infusion ≥1 dose
- Decision to initiate cladribine tablets treatment made during routine clinical care (i.e. before enrollment)

Main exclusion criteria

- Previous cladribine treatment (any dose or formulation)
- Decision to transition from previous DMT made for administrative reasons only (e.g. relocation)
- Have any clinical condition or medical history noted as a contraindication on the cladribine tablets USPI

Patient Disease Characteristics

Patient demographics	Prior oral DMT (N=87)	Prior infusion DMT (N=47)
RRMS diagnosis, n (%)	80 (92.0)	41 (87.2)
SPMSb diagnosis, n (%)	6 (6.9)	6 (12.8)
Missing diagnosis, n (%)	1 (1.1)	0 (0.0)
Elapsed time since diagnosis (yrs), mean (SD)	11.7 (7.2)	12.9 (9.5)
No. of prior DMTs, mean (SD)	3.0 (1.68)	3.5 (1.76)
Relapse in prior 24 months, n (%)		
0	52 (65.8)	29 (67.4)
1	23 (29.1)	12 (27.9)
2	3 (3.8)	2 (4.7)
3	1 (1.3)	-
ARR in prior 24 months, mean (SD)	0.19 (0.30)	0.18 (0.29)
Number of MRI lesions in prior 24 months, mean (SD)		
T1 Gd+ lesions	0.6 (3.10)[c]	0.0 (0.10)[d]
New T2 lesions compared with most recent MRI	0.9 (2.28)[e]	0.9 (3.91)[d]
Newly enlarging T2 lesions compared with most recent MRI	0.0 (0.19)[f]	0.0 (0.05)[d]

[a]This presentation reports interim baseline data (July 2021). Variable patient numbers for certain measures are due to ongoing data collection and cleaning; [b]2 of the 12 patients were active; [c]n=42; [d]n=26; [e]n=43; [e]n=35

Most Recent DMT (Patients with Lymphopenia)

Lymphopenia Grade at Baseline	Most Recent Prior DMT (no. of patients)				
	Dimethyl Fumarate	Fingolimod	Siponimod	Teriflunomide	Total
Grade 1	2	5	1		**8**
Grade 2		2		1	**3**
Grade 3	1	4			**5**
Any	**3**	**11**	**1**	**1**	**16**

Note: per protocol all treatment decisions, including timing of initiation of treatment with cladribine tablets, are at the discretion of the investigator

Abbreviations: ARR, annualized relapse rate, **DMT,** disease-modifying therapy; **Gd+,** gadolinium enhancing; **MRI,** magnetic resonance imaging; **MS,** multiple sclerosis; **RRMS,** relapsing-remitting MS; **SD,** standard deviation; **SPMS,** secondary progressive MS; **USPI,** United States Prescribing Information; **yrs,** years