Treatment Satisfaction in Patients with Highly-active Relapsing Multiple Sclerosis Treated with Cladribine Tablets: CLARIFY-MS Study Interim Analysis

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BB has received consultancy fees, speaker fees, research grants (non-personal), or honoraria from Actelion (Janssen/J&J), Bayer, Biogen, Celgene (BMS), MedDay, Merck KGaA (Darmstadt, Germany), Novartis, Roche, Sanofi-Genzyme, and Teva. **RH** has received institutional research grants and fees for lectures and advisory boards from Biogen, Merck KGaA (Darmstadt, Germany), and Sanofi-Genzyme. **DL** has participated in speaker bureau for Almirall, Bayer, Biogen, Merck KGaA (Darmstadt, Germany), Novartis, Roche, Sanofi, and Teva; has received consultancy fees from Bayer, Biogen, Merck KGaA (Darmstadt, Germany), Novartis, and Teva; and has received research grants from Bayer, Biogen, Merck KGaA (Darmstadt, Germany), and Novartis. All fees paid into DL's university. **AS** has served on the advisory boards for Merck KGaA (Darmstadt, Germany), Novartis, and Sanofi-Genzyme, and has been invited to speak on behalf of Almirall, Biogen, Excemed, Merck KGaA (Darmstadt, Germany), and Teva. **FP** has received research grants from Genzyme, Merck KGaA (Darmstadt, Germany), and Novartis, and fees for serving as Chair of DMC in clinical trials with Parexel. **JL-S** has accepted travel compensation from Biogen, Merck KGaA (Darmstadt, Germany), and Novartis. Her institution receives the honoraria for talks and advisory board commitment as well as research grants from Biogen, Celgene (BMS), Merck KGaA (Darmstadt, Germany), Novartis, Roche, Sanofi-Genzyme, and Teva. **XM** has received speaking honoraria and travel expenses for scientific meetings, has been a steering committee member of clinical trials or participated in advisory boards of clinical trials in the past 3 years with Actelion (Janssen/J&J), Alexion, Bayer, Biogen, Celgene (BMS), EMD Serono, Excemed, Genzyme, MedDay, Merck KGaA (Darmstadt, Germany), MSIF, Nervgen, NMSS, Novartis, Roche, Sanofi-Genzyme, Teva Pharmaceutical, and TG Therapeutics. **KS** has received honoraria for speaking, consulting and serving for advisory boards for Biogen, Celgene (BMS), Merck KGaA (Darmstadt, Germany), Novartis, Roche, and TG Therapeutics. **MV** has received speaking honoraria and travel expenses for participation in scientific meetings, or participated in advisory boards in the past years with Biogen, Merck KGaA (Darmstadt, Germany), Novartis, Roche, Sanofi-Genzyme, and Teva Pharmaceutical. **KR** has received speaking honoraria and travel expenses for participation in scientific meetings, and participated in advisory boards in the past years with Bayer, Biogen, Merck KGaA (Darmstadt, Germany), Novartis, Roche, Sanofi-Genzyme, and Teva Pharmaceutical. **EKH** has received honoraria/research support from Actelion (Janssen/J&J), Biogen, Celgene (BMS), Genzyme, Merck KGaA (Darmstadt, Germany), Novartis, Roche, and Teva; has served on advisory boards for Actelion (Janssen/J&J), Biogen, Celgene (BMS), Genzyme, Merck KGaA (Darmstadt, Germany), Novartis, and Roche; and has been supported by Czech Ministry of Education, program PROGRES Q27/LF1. **FP** has served on scientific Advisory Boards for Almirall, Bayer, Biogen, Celgene (BMS), Merck KGaA (Darmstadt, Germany), Novartis, Roche, Sanofi, and Teva; he also received speaker honoraria from the same companies and research grants for his department from Biogen and Merck KGaA (Darmstadt, Germany). **NA**, **AN**, and **BK** are employees of Merck KGaA, Darmstadt, Germany.

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[1]INSERM U 1215, University of Bordeaux, Bordeaux, France and [2]Department of Neurology, University Hospital, Bordeaux, France; [3]Orbis Medisch Centrum, Maastricht University Medical Center, Maastrict, The Netherlands; [4]Department of Psychology, Royal Holloway, University of London, Egham, UK; [5]Foundation IRCCS Neurological Institute C. Besta, Milan, Italy; [6]Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden; [7]University of Newcastle, Newcastle, NSW, Australia and [8]Division of Neurology, John Hunter Hospital, Newcastle, NSW, Australia; [9]Department of Neurology-Neuroimmunology Centre of Multiple Sclerosis of Catalonia (Cemcat), University Hospital Vall d'Hebron, Barcelona, Spain; [10]Center for Neurology, Lodz, Poland; [11]Charles University and University Hospital, Hradec Králové, Czech Republic; [12]Medical University of Lublin, Lublin, Poland; [13]Charles University, Prague, Czech Republic; [14]Azienda Ospedaliera-Universitaria, "Policlinico Vittorio Emanuele", Catania, Italy; [15]Merck KGaA, Darmstadt, Germany

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CONCLUSIONS

The convenience of cladribine tablets and side effect profile were well received by patients.

There were few serious adverse events in the first 6 months following cladribine tablets treatment; no grade 4 lymphopenia was observed.

This interim analysis of CLARIFY-MS found that, at 6 months, patients were generally satisfied with cladribine tablets.

INTRODUCTION

- MS, a chronic disabling disease requiring long-term treatment and regular monitoring, is associated with negative effects on HRQoL.
- In the CLARITY study, treatment with cladribine tablets was associated with reduced healthcare resource consumption and a decreased need for medical and societal support.[1]
  - Data from CLARITY also indicated that treatment with cladribine tablets lead to improved HRQoL outcomes, although further investigation was required.[2]
- CLARIFY-MS (NCT03369665) aims to assess the impact of cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years) on HRQoL and treatment satisfaction in patients with highly-active RMS, using TSQM v1.4.

OBJECTIVES

To present interim 6-month data on treatment satisfaction (via TSQM v1.4) and safety in the CLARIFY-MS study of CT3.5 in patients with highly-active RMS.

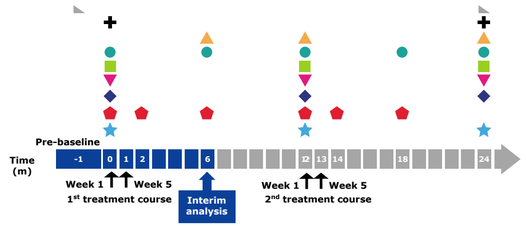
CT3.5, cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years); **HRQoL**, health-related quality of life; **MS**, multiple sclerosis; **RMS**, relapsing multiple sclerosis; **TSQM**, Treatment Satisfaction Questionnaire for Medication

METHODS

Inclusion criteria	Exclusion criteria
Aged ≥ 18 years	Lymphocyte count not within normal range
Highly-active RMS	Presence or suspicion of progressive multifocal leukoencephalopathy or other diseases of the central nervous system
EDSS score ≤ 5.0	Positive for human immunodeficiency virus, or hepatitis C antibody test or hepatitis B antigen test
Female patients must not be pregnant, lactating, or breastfeeding	Moderate or severe renal impairment
All patients must be willing to use contraception	Hypersensitivity to cladribine tablets or other excipients listed in the SmPC
	Active malignancy
	History or presence of tuberculosis

- The interim analysis at 6 months used TSQM v1.4 to assess patient-reported treatment satisfaction (a score of 100 is the best possible rating).
- **Safety:** Treatment-emergent AEs, serious AEs, and lymphocyte counts were recorded.
- Subgroup analysis was carried out by prior DMT treatment status.

METHODS



Assessments

- **HRQoL (MSQoL-54)**
- Hematology/chemistry as per SmPC
- Fatigue and mood symptoms (FSS HADS)
- Cognition (BICAMS)
- Relapse count
- Disability (EDSS 9-HPT, T25FW)
- Treatment satisfaction (TSQM-I)
- Employment status
- MRI

Statistical Analysis

- CLARIFY-MS is an ongoing phase IV, open-label, single-arm, multicenter, 2-year study.
- Patients with RMS received CT3.5, with 2 weeks of active treatment per course (week 1 and 5 of each year).

Primary Endpoint

- Improvement in HRQoL at 24 months, assessed by MSQoL-54.

CT3.5, cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years); **EDSS**, Expanded Disability Status Scale; **HRQoL**, health-related quality of life; **MRI**, magnetic resonance imaging; **MSQoL-54**, Multiple Sclerosis Quality of Life-54; **RMS**, relapsing multiple sclerosis; **TSQM**, Treatment Satisfaction Questionnaire for Medication

RESULTS

Table 1. Patient Characteristics

	Treatment naïve n=137	Prior use of DMT n=345	Total study cohort N=482
Mean age, years ± SD	35.4 ± 11.46	38.2 ± 9.83	37.4 ± 10.39
Female, n (%)	91 (66.4)	247 (71.6)	338 (70.1)
Relapses in prior 12 months, n (%)			
0	0 (0)	7 (2.0)	7 (1.5)
1	40 (29.2)	233 (67.5)	273 (56.6)
2	87 (63.5)	94 (27.2)	181 (37.6)
>2	10 (7.3)	11 (3.2)	21 (4.4)
Use of DMT in prior 6 months, n (%)	0 (0)	284 (82.3)	284 (58.9)
Median EDSS	2.0	2.5	2.5

Table 2. Global Satisfaction Score at 6 Months

	Treatment naïve n=137	Prior use of DMT n=345	Total study cohort N=482
n (%)	121 (88.3)	313 (90.7)	434 (90.0)
Mean ± SD	**69.5 ± 18.71**	**70.8 ± 18.40**	**70.4 ± 18.48**
Adjusted estimate*	**68.7**	**70.2**	**70.0**
95% confidence interval	(62.06, 75.39)	(66.36, 73.97)	(66.59, 73.46)

* Estimated by Least Squares Means by fitting a mixed-effects linear model adjusting for age (years), EDSS at baseline, and within-country correlation. Estimate for covariate fixed effects: Age: -0.2 per year / EDSS: -3.8 for > 3 vs ≤ 3. Global Satisfaction score includes: Item 7: To what extent do the side effects interfere with your mental function (i.e., ability to think clearly, stay awake, etc.)? Item 8: To what degree have medication side effects affected your overall satisfaction with the medication? Item 9: How easy or difficult is it to use the medication in its current form?

- Adjusted for age and EDSS, the global satisfaction score was **70.2 for prior DMT patients**, **68.7 for treatment naïve patients,** and **70.0 for the total study cohort**.

Table 3. Side Effects and Convenience at 6 Months

	Treatment naïve n=137	Prior use of DMT n=345	Total study cohort N=482
Side effects score			
n (%)	121 (88.3)	313 (90.7)	434 (90.0)
Mean ± SD	**92.7 ± 17.85**	**91.5 ± 17.63**	**91.9 ± 17.68**
Convenience score			
n (%)	121 (88.3)	313 (90.7)	434 (90.0)
Mean ± SD	**88.0 ± 13.71**	**86.1 ± 13.51**	**86.6 ± 13.57**

- **Treatment naïve** scores: side effects, **92.7**; convenience, **88.0**.
- **Prior use of DMT** scores: side effects, **91.5**; convenience, **86.1**.
- **Total study cohort** scores: side effects, **91.9**; convenience, **86.6**.

Table 4. Effectiveness at 6 Months

	Treatment naïve n=137	Prior use of DMT n=345	Total study cohort N=482
n (%)	121 (88.3)	313 (90.7)	434 (90.0)
Mean ± SD	**65.1 ± 20.99**	**66.1 ± 21.23**	**65.8 ± 21.14**
Median	66.7	66.7	66.7

- At 6 months, patients have received half of the therapeutic dose of cladribine tablets:
- **Treatment naïve** score: **65.1**.
- **Prior use of DMT** score: **66.1**.
- **Total study cohort** score: **65.8**.

DMT, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **SD**, standard deviation; **TEAE**, treatment-emergent adverse event

Table 5. Safety - TEAEs by Decreasing Frequency Observed in more than 2% of the Total

System Organ Class / Preferred Term, n (%)	Treatment naïve n=137	Prior use of DMT n=345	Total study cohort N=482
Patients with at least 1 event	**82 (59.9)**	**193 (55.9)**	**275 (57.1)**
Headache	21 (15.3)	42 (12.2)	63 (13.1)
Lymphopenia	5 (3.6)	35 (10.1)	40 (8.3)
Nasopharyngitis	14 (10.2)	16 (4.6)	30 (6.2)
Upper respiratory tract infection	9 (6.6)	11 (3.2)	20 (4.1)
Back pain	6 (4.4)	11 (3.2)	17 (3.5)
Urinary tract infection	1 (0.7)	15 (4.3)	16 (3.3)
Nausea	4 (2.9)	11 (3.2)	15 (3.1)
Fatigue	9 (6.6)	5 (1.4)	14 (2.9)
Alopecia	3 (2.2)	10 (2.9)	13 (2.7)
Influenza	5 (3.6)	7 (2.0)	12 (2.5)
Bronchitis	2 (1.5)	9 (2.6)	11 (2.3)
Oral herpes	4 (2.9)	7 (2.0)	11 (2.3)
Lymphocyte count decreased	1 (0.7)	9 (2.6)	10 (2.1)
Pain in extremity	4 (2.9)	6 (1.7)	10 (2.1)

Table 6. Safety - Serious Treatment-emergent Adverse Events

System Organ Class / Preferred Term, n (%)	Treatment naïve n=137	Prior use of DMT n=345	Total study cohort N=482
Patient with at least 1 event	**3 (2.2)**	**6 (1.7)**	**9 (1.9)**
Injury, poisoning and procedural complications	1 (0.7)	4 (1.2)	5 (1.0)
Medication error	0 (0.0)	1 (0.3)	1 (0.2)
Overdose	1 (0.7)	3 (0.9)	4 (0.8)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0 (0.0)	1 (0.3)	1 (0.2)
Ovarian cancer	0 (0.0)	1 (0.3)	1 (0.2)
Psychiatric disorders	1 (0.7)	0 (0.0)	1 (0.2)
Panic disorder	1 (0.7)	0 (0.0)	1 (0.2)
Reproductive system and breast disorders	0 (0.0)	1 (0.3)	1 (0.2)
Ovarian cyst	0 (0.0)	1 (0.3)	1 (0.2)
Vascular disorders	1 (0.7)	0 (0.0)	1 (0.2)
Aortic aneurysm	1 (0.7)	0 (0.0)	1 (0.2)

Safety – Lymphopenia at 6 Months

- Most post-baseline lymphopenias were of grade 1 or 2.
- There were 33 patients (6.8%) who experienced grade 3 lymphopenia.
  - Treatment naïve, n=3 (2.2%); prior use of DMT, n=30 (8.7%).
- No grade 4 lymphopenia was observed.

1. Ali S, et al. *Clin Drug Investig.* 2012;32:15–27. 2. Afolabi D, et al. *Mult Scler.* 2018;24:1461–1468.

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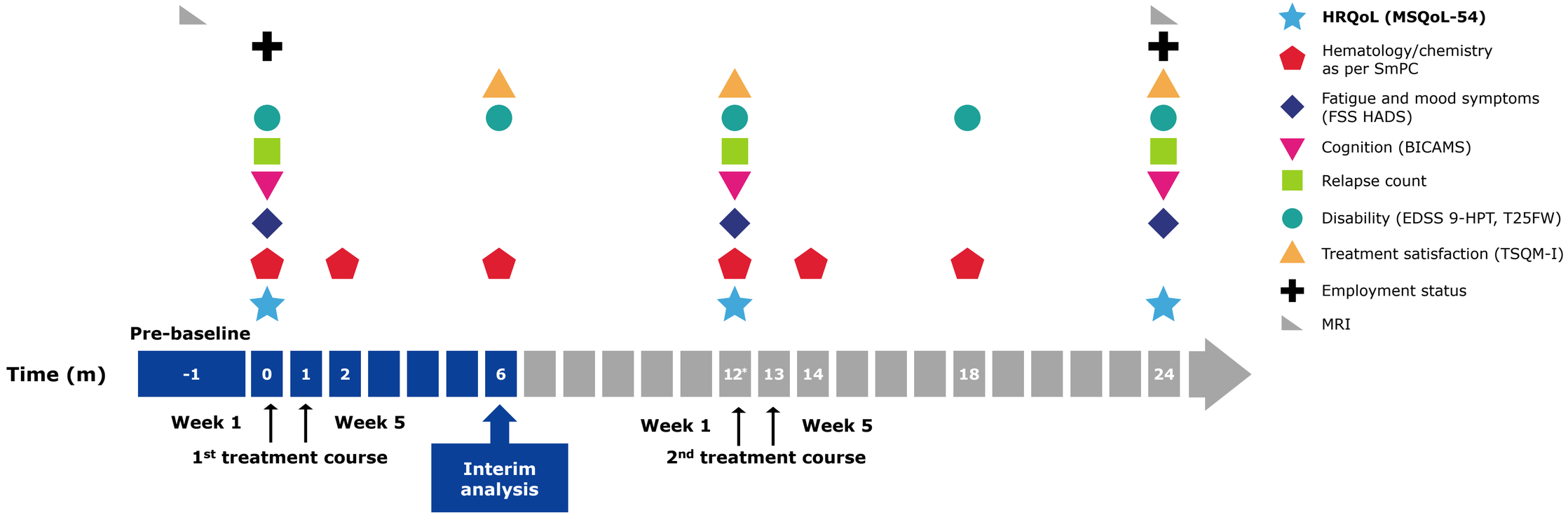
RESULTS



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