Improvements in QoL at 1 Year in Patients Treated With Cladribine Tablets for Highly Active Relapsing MS: An Interim Analysis of CLARIFY-MS

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CONCLUSIONS

This 1-year interim analysis demonstrates a significant improvement in the physical and mental health component scores of MSQoL-54 at 1 year representing half of the indicated 2-year treatment course of cladribine tablets.

No new safety concerns were observed, with no new severe or opportunistic infections that could have an impact on the established benefit:risk profile of cladribine tablets in relapsing MS.

INTRODUCTION

- In CLARITY, patients with relapsing multiple sclerosis (MS) taking cladribine tablets (3.5 mg/kg or 5.25 mg/kg) reported significantly improved EQ-5D index scores compared with placebo (p=0.001 and p=0.022, respectively).[1]
  - Positive, yet non-significant, differences in Multiple Sclerosis Quality of Life-54 questionnaire (MSQoL-54) scores were also detected between cladribine tablets and placebo; however, the sample size was limited.[1]
- CLARIFY-MS (NCT03369665) aims to further explore changes in physical and mental health functioning (MSQoL-54) after initiation of treatment with cladribine tablets.

OBJECTIVES

Main objective of this interim analysis is to evaluate the change in quality of life (QoL) for patients with highly active relapsing MS at 1 year after initiating treatment with cladribine tablets.

METHODS

- CLARIFY-MS study is a 2-year, open-label, single-arm, multicenter, phase IV study.
- Inclusion criteria:
  - Aged ≥18 years old;
  - Expanded Disability Status Scale (EDSS) score ≤5.0;
  - Diagnosed with highly active relapsing MS, defined as one relapse in the previous year and ≥1 T1 gadolinium enhancing lesion or ≥9 T2 lesions, while on therapy with other disease-modifying therapies (DMTs); or ≥2 relapses in the previous year, whether on DMT treatment or not.
- Patients were recruited as per the European label, and eligible patients received cladribine tablets 3.5 mg/kg cumulative dose over 2 years.
- A subgroup analysis of MSQoL-54 component scores was conducted for treatment naïve/prior DMT, and before/after the start of the COVID-19 pandemic.

Endpoints for the Current Interim Analysis:

Changes in MSQoL-54 physical health and mental health component scores at 12 months from Baseline

TSQM v1.4 component scores at Months 6 and 12

Frequency of TEAEs, serious AEs, and lymphocyte counts by Month 12

AE, adverse event; **MSQoL-54**, Multiple Sclerosis Quality of Life-54 questionnaire; **TEAEs**, treatment-emergent adverse events; **TSQM**, Treatment Satisfaction Questionnaire for Medication.

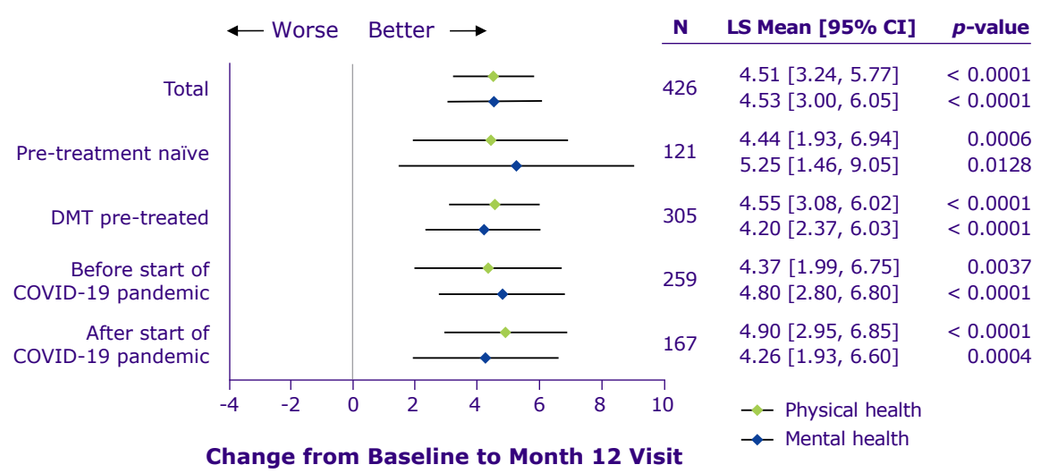
RESULTS

Table 1. Patient Characteristics

	Treatment naïve N=135	Prior DMT N=347	Total N=482
Age (years), mean ± SD	35.4 ± 11.51	38.2 ± 9.83	37.4 ± 10.39
Female, n (%)	90 (66.7)	248 (71.5)	338 (70.1)
Relapses in prior 12 months, n (%)	135 (100)	340 (98.0)	475 (98.5)
DMT in prior 6 months, n (%)	0 (0)	286 (82.4)	286 (59.3)
EDSS, median (min, max)	2.0 (0, 5.0)	2.5 (0, 5.0)	2.5 (0, 5.0)
MSQoL-54 component scores, mean ± SD			
Physical health	62.4 ± 19.64	59.3 ± 19.65	60.1 ± 19.67
Mental health	61.9 ± 21.71	60.9 ± 21.64	61.2 ± 21.64

DMT, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **MSQoL-54**, Multiple Sclerosis Quality of Life-54 questionnaire; **N**, total number of patients; **n**, number of occurrences; **SD**, standard deviation.

Figure 1. MSQoL-54 Physical and Mental Health Component Scores: Change From Baseline to Month 12 by Subgroup

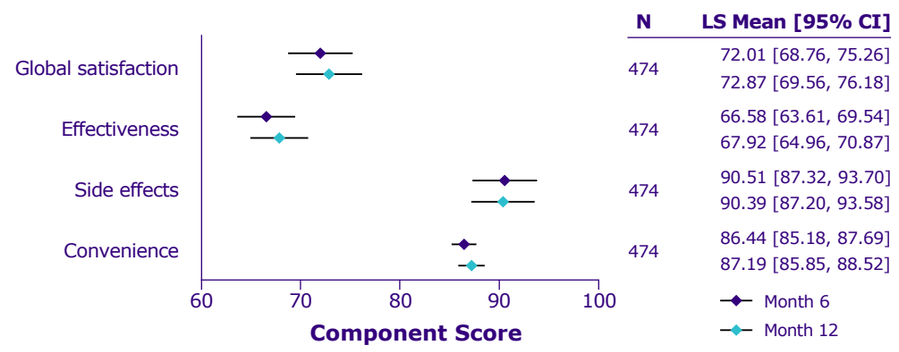


	N	LS Mean [95% CI]	p-value
Total	426	4.51 [3.24, 5.77]	< 0.0001
		4.53 [3.00, 6.05]	< 0.0001
Pre-treatment naïve	121	4.44 [1.93, 6.94]	0.0006
		5.25 [1.46, 9.05]	0.0128
DMT pre-treated	305	4.55 [3.08, 6.02]	< 0.0001
		4.20 [2.37, 6.03]	< 0.0001
Before start of COVID-19 pandemic	259	4.37 [1.99, 6.75]	0.0037
		4.80 [2.80, 6.80]	< 0.0001
After start of COVID-19 pandemic	167	4.90 [2.95, 6.85]	< 0.0001
		4.26 [1.93, 6.60]	0.0004

*Before and after the COVID-19 pandemic denotes the time at which the 12-month assessment was conducted.
LS Mean was determined using a repeated mixed effects linear model, adjusted for age (years), EDSS at Baseline (>3 vs 3 [reference], Visit (Month 6 visit vs. Month 12 Visit [reference]), within-pooled-center correlation and within-subject correlation. p-values are nominal and not adjusted for multiple testing.

CI, confidence interval; **DMT,** disease-modifying therapy; **LS Mean**, least squares mean; **MSQoL-54**, Multiple Sclerosis Quality of Life-54 questionnaire; **N**, total number of patients.

Figure 2. TSQM (v1.4) Component Scores at Months 6 and 12



LS Mean was determined using a repeated mixed-effects linear model , adjusted for age (years), EDSS at Baseline (>3 vs 3 [reference], Visit (Month 6 visit vs. Month 12 Visit [reference]), within-pooled-center correlation and within-subject correlation.
CI, confidence interval; **LS Mean**, least squares mean; **N**, total number of patients; **TSQM**, Treatment Satisfaction Questionnaire for Medication.

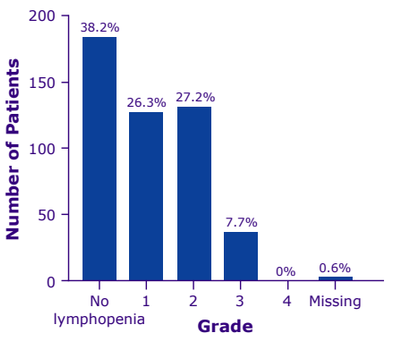
Table 2. Relapses and AEs up to 12 Months After Initiating Treatment with Cladribine Tablets

Patients, n (%)	Treatment naïve N=135	Prior DMT N=347	Total N=482
Any qualifying relapse	16 (11.9)	46 (13.3)	62 (12.9)
Treated with steroids	14 (10.4)	41 (11.8)	55 (11.4)
Leading to hospitalization	5 (3.7)	11 (3.2)	16 (3.3)
Any treatment-emergent AE*	94 (69.6)	228 (65.7)	322 (66.8)
Mild	56 (41.5)	132 (38.0)	188 (39.0)
Moderate	34 (25.2)	91 (26.2)	125 (25.9)
Severe	4 (3.0)	5 (1.4)	9 (1.9)
Any serious treatment-emergent AE	3 (2.2)	10 (2.9)	13 (2.7)

*Worst severity reported for each patient.
AE, adverse event; **DMT**, disease-modifying therapy; **N**, number of patients; **n**, number of occurrences.

Figure 3. Lymphopenia – Highest Post-Baseline Grade to Month 12

- Most post-baseline lymphopenias were of grade 1–2 (NCI-CTCAE version 5.0).
- Incidence of grade 3 lymphopenia was low:
  - 7.7% (37/482) of the study overall population.
  - 2.2% (3/135) of treatment naïve and 9.8% (34/347) of prior DMT subgroups, respectively.
- No grade 4 lymphopenia was observed.



DMT, disease-modifying therapy; **NCI-CTCAE**, National Cancer Institute-Common Terminology Criteria for Adverse Events.

REFERENCE
1. Afolabi D, et al. *Mult Scler*. 2018;24:1461–1468.

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