Improvements in Quality of Life Over 2 Years in Patients Treated With Cladribine Tablets for Highly Active Relapsing Multiple Sclerosis: Final Analysis of CLARIFY-MS

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CONCLUSIONS

Treatment with CladT significantly improved mean MSQoL-54 physical and mental health composite scores over 2 years

No new safety signals impacting the established benefit:risk profile of CladT in patients with highly active RMS emerged from the CLARIFY-MS study

INTRODUCTION

- The symptoms, burden of disability and comorbidities experienced by patients with multiple sclerosis (MS) have a detrimental effect on their quality of life (QoL), including physical and mental health[1]
- By including the patients' perspective, health–related QoL (HRQoL) assessments contribute to a comprehensive clinical evaluation and may be helpful during shared decision making and treatment selection[2]
- The CLARIFY-MS study (NCT03369665) assessed the effect of cladribine tablets (CladT) on the physical and mental health of patients with highly active relapsing MS (RMS) using the Multiple Sclerosis Quality of Life (MSQoL)-54 instrument

OBJECTIVE

To evaluate HRQoL through the MSQoL-54 instrument in patients with highly active RMS treated with CladT (3.5 mg/kg cumulative dose for 2 years)

METHODS

- CLARIFY-MS is a 2-year, prospective, open-label, single-arm, multi-centre, phase IV study (**Supplementary Figure 1**)
- Patients were recruited as per the European label of CladT, and eligible patients received CladT 3.5 mg/kg cumulative dose over 2 years
- Changes in MSQoL-54 composite scores were analysed using a repeated mixed-effects linear model adjusted for Baseline MSQoL-54 composite score, Expanded Disability Status Scale (EDSS) score at Baseline, age, within-pooled center correlation and within-participant correlation
- Patients were grouped into 2 subgroups: those who did not receive any disease-modifying therapies (DMTs) before CladT treatment (pre-treatment naïve subgroup) and those who received DMTs at any time prior to start of treatment (prior DMT subgroup)

Selected Endpoints

- **Changes in MSQoL-54 composite scores at 24 months from Baseline**
- **ARR and EDSS scores**
- **TEAEs, serious AEs, and lymphocyte counts**

AE, adverse event; **ARR,** annualised relapse rate; **EDSS,** Expanded Disability Status Scale; **MSQoL-54**, Multiple Sclerosis Quality of Life-54 instrument; **TEAE,** treatment-emergent AE.

RESULTS

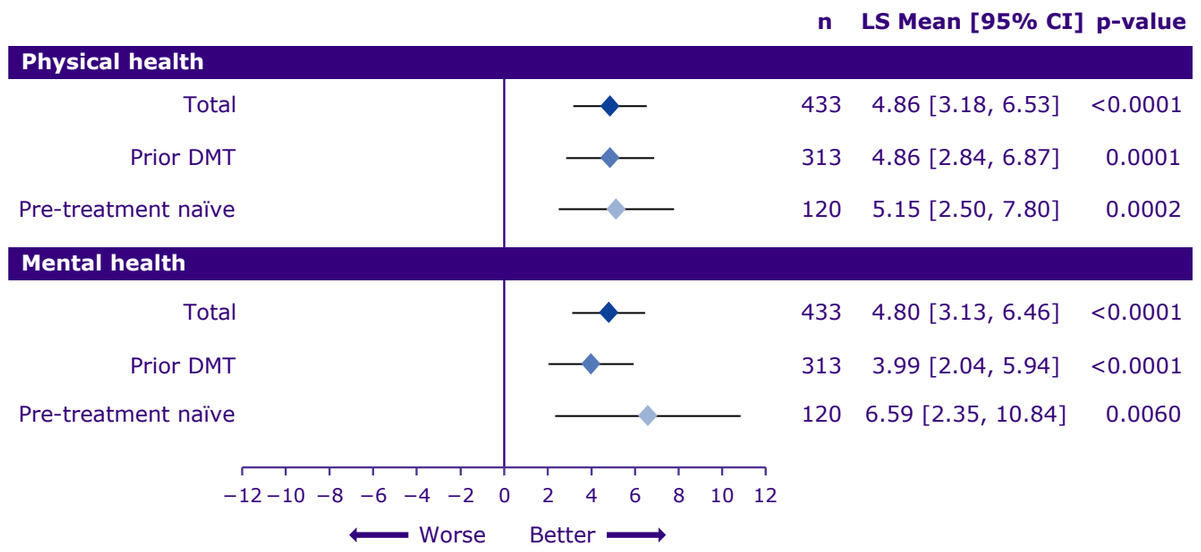
Table 1: Patient Baseline Characteristics

	Pre-treatment naïve N=134	Prior DMT N=348	Total N=482
Age (years), mean ± SD	35.2 ± 11.3	38.3 ± 9.9	37.4 ± 10.4
Female, n (%)	89 (66.4)	249 (71.6)	338 (70.1)
Time since onset of MS (months), mean ± SD	42.6 ± 58.7	120.9 ± 90.3	99.1 ± 89.8
DMT in prior 6 months, n (%)	0 (0.0)	287 (82.5)	287 (59.5)
Relapses within 12 Month prior to Baseline visit, n (%)			
0	0 (0.0)	4 (1.1)	4 (0.8)
1	35 (26.1)	225 (64.7)	260 (53.9)
≥2	99 (73.9)	119 (34.2)	218 (45.2)
EDSS score, median (min; max)	2.0 (0.0; 5.0)	2.5 (0.0; 5.0)	2.5 (0.0; 5.0)
MSQoL-54 composite scores[a], mean ± SD			
Physical health	62.5 ± 19.7	59.3 ± 19.6	60.2 ± 19.7
Mental health	61.8 ± 21.8	61.0 ± 21.7	61.2 ± 21.7

[a]Pre-treatment naïve, n=124; Prior DMT, n=326; Total, n=450.

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

Figure 1: MSQoL-54 Physical and Mental Health Composite Scores: Change From Baseline to Month 24, by Subgroup



CI, confidence interval; **DMT,** disease-modifying therapy; **LS,** least squares; **MSQoL-54**, Multiple Sclerosis Quality of Life-54 instrument.

MSQoL-54 Composite Scores

- Statistically significant ($p \leq 0.0001$) improvements from Baseline were observed for mean MSQoL-54 physical and mental health composite scores (**Figure 1**)
- Changes in mean MSQoL-54 composite scores were consistent across pre-treatment naïve and prior DMT subgroups (**Figure 1**)

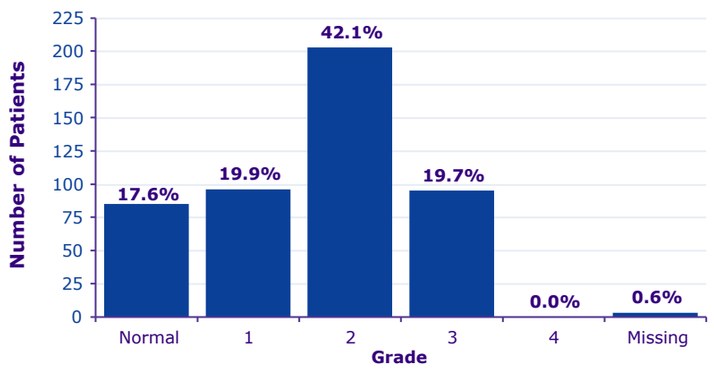
ARR and EDSS Scores

- Annualised relapse rate (ARR) of qualifying relapses was 0.13 (95% CI: 0.11, 0.16) (**Supplementary Figure 2; Supplementary Table 1**)
- EDSS scores remained stable over time for the majority of patients in the overall population and in both subgroups (**Supplementary Figure 3**)

Safety

- At least one treatment-emergent adverse event (TEAE) was experienced by 78% of patients (n=376) (**Supplementary Table 2**)
- The most common TEAEs were headache, lymphopenia, and nasopharyngitis
- No new severe or opportunistic infections were observed
- As per the laboratory assessments, most post-Baseline lymphopenias were of Grade 1–2 in severity. Grade 3 lymphopenia was observed in 19.7% of patients (**Figure 2**)
- No grade 4 lymphopenia was observed (**Figure 2**)

Figure 2: Lymphopenia – Highest Post-Baseline Grade[a]



[a]Absolute lymphocyte count grading was based on NCI-CTCAE V5.0.

NCI-CTCAE, National Cancer Institute-Common Terminology Criteria for Adverse Events.

Supplementary material available here:

References: 1. Berrigan LI, et al. *Neurology*. 2016;86(15):1417–1424; 2. Jongen PJ. *CNS Drugs*. 2017.31:585–602.

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