Long-Term Efficacy for Patients Receiving Cladribine Tablets (3.5 mg/kg Over 2 Years) in CLARITY/CLARITY Extension: A *Post hoc* Analysis of CLASSIC-MS

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CONCLUSION

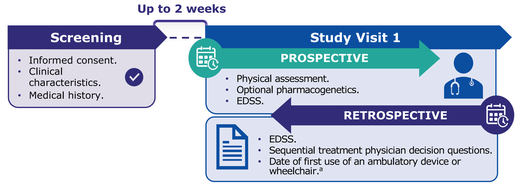
With 9.5–14.5 years' follow-up since last dose, findings suggest a numerical improvement in mobility and disability outcomes for patients who received cladribine tablets 3.5 mg/kg over 2 years compared with placebo.

Additionally, 58.1% of patients who received cladribine tablets 3.5 mg/kg over 2 years used no subsequent DMTs, compared with 26.8% of patients in the placebo group.

INTRODUCTION

- CLASSIC-MS (NCT03961204) was a Phase IV study evaluating the long-term efficacy of cladribine tablets in patients enrolled in the Phase III (parent) trials CLARITY,[1] CLARITY Extension,[2] and ORACLE-MS.[3]

Figure 1. CLASSIC-MS Study Design



[a]Was determined through retrospective chart review and/or at Study Visit 1, e.g. if conversion or disability progression occurred between last regular clinical visit and Study Visit 1.
EDSS, Expanded Disability Status Scale.

OBJECTIVES

To report on long-term efficacy findings for patients who participated in CLARITY/ CLARITY Extension, in terms of:

Mobility
(no wheelchair use in the previous 3 months and not bedridden at any time prior to first visit in CLASSIC-MS; i.e. Expanded Disability Status Scale [EDSS] score <7)

Disability status
(no use of an ambulatory device at any time since last parent study dose [LPSD]; i.e. EDSS score <6)

Relapses and **subsequent disease-modifying therapy (DMT) use**

METHODS

- CLASSIC-MS was an exploratory, low-interventional, multicenter, ambispective*, Phase IV study of patients with MS (**Figure 1**).
- This *post hoc* analysis focused on the sub-group of patients from CLASSIC-MS who received cladribine tablets 3.5 mg/kg over 2 years, compared with placebo.
- A total of 201 patients were included in the analysis, with 160 (79.6%) patients having received cladribine tablets 3.5 mg/kg over 2 years during the parent trials. The remaining 41 patients (20.4%) received placebo.
- The follow-up period since LPSD was 9.5–14.5 years.

*Ambispective: having both retrospective and prospective components.

RESULTS

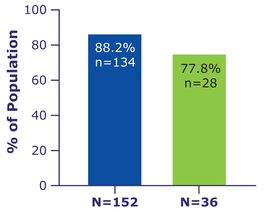
Table 1. Patient Demographics at Parent Study Baseline and Study Visit 1 of CLASSIC-MS

	Cladribine tablets 3.5 mg/kg over 2 years (N=160)	Placebo (N=41)
Age at Study Visit 1 (years), mean ± SD	51.7 ± 9.76	51.6 ± 10.25
Female, n (%)	103 (64.4)	31 (75.6)
Disease duration at Study Visit 1 (years), mean ± SD	21.32 ± 6.21	22.38 ± 6.85
Time since LPSD to Study Visit 1 (years), median (min–max)	10.65 (9.47–14.39)	13.40 (12.37–14.52)
EDSS score at parent study baseline, mean ± SD	2.74 ± 1.31	2.74 ± 1.33
EDSS score at Study Visit 1, mean ± SD	3.78 ± 2.07	4.50 ± 2.59
No. of relapses in the 12 months before enrollment to parent study, mean ± SD	1.3 ± 0.62	1.6 ± 0.78
Employment status at Study Visit 1, n (%)		
Employed for wages	60 (37.5)	8 (19.5)
Self-employed	10 (6.3)	0 (0)
Homemaker	16 (10.0)	3 (7.3)
Not in active employment[a]	60 (37.5)	21 (51.2)
Unknown[b]	14 (8.6)	9 (22.0)

[a]Not in active employment includes retired and out of work/unable to work. [b]Unknown includes those with missing/not reported data or information not collected at study site.
EDSS, Expanded Disability Status Scale; **LPSD**, last parent study dose; **SD**, standard deviation.

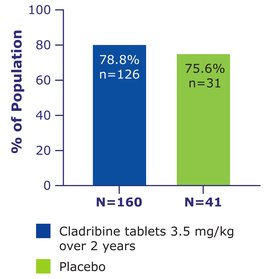
- Patient characteristics are shown in **Table 1**.
  - Of the patients who received cladribine tablets 3.5 mg/kg over 2 years, 53.8% (n=86) were **actively employed** at inclusion in CLASSIC-MS compared with 26.8% (n=11) of the placebo group.

Figure 2. Long-Term Mobility



Missing data were not included in the **long-term mobility** analysis (n=8 and n=5 for cladribine and placebo cohorts, respectively). **Long-term disability** concerns no use of an ambulatory device at any time since LPSD.

Figure 3. Long-Term Disability

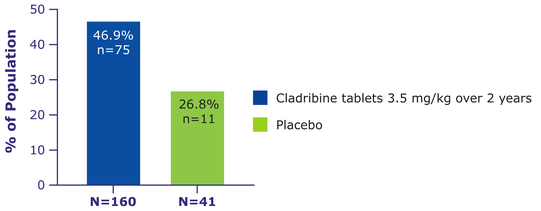


Long-Term Mobility and Disability Status

- For patients who received cladribine tablets 3.5 mg/kg over 2 years vs patients who received placebo:
  - 88.2% vs 77.8% did not use a wheelchair in the previous 3 months and were not bedridden at any time prior to first visit in CLASSIC-MS (odds ratio* 0.47; 95% confidence interval: 0.186–1.188; **Figure 2**).
  - 78.8% vs 75.6% did not use an ambulatory device at any time since LPSD (**Figure 3**).

*Adjusted odds ratio from a logistic regression model with fixed effects for treatment group and disease duration.

Figure 4. Long-Term Relapse-Free Status



- The proportion of patients remaining relapse-free since LPSD was 46.9% in those who received cladribine tablets 3.5 mg/kg over 2 years and 26.8% in the placebo group (**Figure 4**).

Table 2. Subsequent DMT Use

	Cladribine tablets 3.5 mg/kg over 2 years (N=160)	Placebo (N=41)
Any subsequent DMT after LPSD, n (%)	67 (41.9)	30 (73.2)
Platform injectable therapy	47 (29.4)	21 (51.2)
Oral DMT	31 (19.4)	9 (22.0)
mAbs	11 (6.9)	9 (22.0)
Off-label treatment	3 (1.9)	2 (4.9)
Other	2 (1.3)	3 (7.3)
Unknown	1 (0.6)	0 (0)

Subsequent DMTs are reflective of those available at the time of the study (2010–2019). The same DMT can have multiple ATC codes, as determined by WHO-DD Version September 2020.
ATC, Anatomical Therapeutic Chemical; **DMT**, disease-modifying therapy; **LPSD**, last parent study dose; **mAbs**, monoclonal antibodies; **WHO-DD**, World Health Organization Drug Dictionary.

- In all, 58.1% of patients who received cladribine tablets did not use subsequent DMTs compared with 26.8% of the placebo group (**Table 2**).
- Time to subsequent DMT use was 3.9 years and 1.0 year, respectively, at the 25th percentile.

REFERENCES
1. Giovannoni G, et al. *N Engl J Med*. 2010;362:416–426. 2. Giovannoni G, et al. *Mult Scler*. 2018;24:1594–1604. 3. Leist T, et al. *Lancet Neurol*. 2014;13:257–267.

Cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years) are indicated for the treatment of patients with MS in the United States (relapsing forms of MS, including relapsing-remitting disease and active secondary progressive disease, in adults). The CLASSIC-MS study: NCT03961204.

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