Long-term Efficacy for Patients Receiving Cladribine Tablets in CLARITY/CLARITY Extension: Primary Results from 9–15 Years of Follow-up in the CLASSIC-MS Study

Gavin Giovannoni,[1] Thomas Leist,[2] Aida Aydemir,[3] Elisabetta Verdun Di Cantogno,[3] on behalf of the CLASSIC-MS Steering Committee

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Disclosures:

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CONCLUSIONS

Reported findings for CLASSIC-MS, with a median of 10.9 years' follow-up after CLARITY/CLARITY Extension, suggests sustained efficacy of cladribine tablets in terms of long-term mobility and disability status in patients with relapsing MS

INTRODUCTION

- CLASSIC-MS (NCT03961204) was an exploratory, ambispective Phase IV study designed to evaluate the long-term efficacy of cladribine tablets in the real-world setting, for patients who were previously enrolled to Phase III (parent) trials: CLARITY,[1] CLARITY Extension,[2] and ORACLE-MS[3]

OBJECTIVE

Report results for long-term mobility and disability from CLARITY/CLARITY Extension

Primary: long-term mobility (no wheelchair use/bedridden; i.e. EDSS <7 in the 3 months prior to first visit in CLASSIC-MS)

Secondary: long-term disability status (no requirement for an ambulatory device; i.e. EDSS <6 any time since last parent study dose)

METHODS

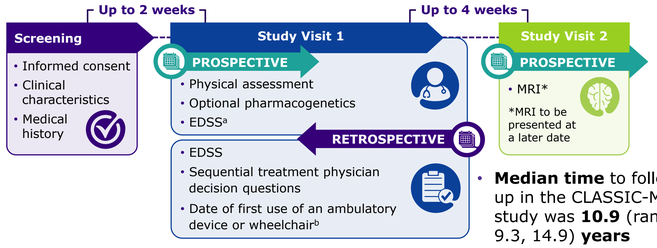
- Patients with relapsing MS who participated in CLARITY,[1] with or without subsequent enrollment to CLARITY Extension,[2] were evaluated
- All patients must have received ≥1 course of cladribine tablets or placebo during the parent study

CLARITY n=435

Patients also enrolled to CLARITY Extension n=345

- A total of 394 patients (90.6%) were exposed to cladribine tablets during the CLARITY/CLARITY Extension parent trials
  - 160 patients received the approved cumulative dose of 3.5 mg/kg over 2 years
- A total of 41 patients (9.4%) were never exposed

Figure 1. CLASSIC-MS Study Design



[a]Can also be administered by telephone instead of in-person at clinic at study visit 1; [b]May be 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.

- **Median time** to follow-up in the CLASSIC-MS study was **10.9** (range 9.3, 14.9) **years**

RESULTS

Table 1. Characteristics of CLASSIC-MS Patients From CLARITY/CLARITY Extension Compared With Non-CLASSIC-MS Patients From the Parent Studies (CLARITY, CLARITY Extension, and ORACLE MS)

Variable	CLASSIC-MS patients from CLARITY/CLARITY Extension n=435	Non-CLASSIC-MS patients n=1232
Age at parent study baseline, years (mean ± SD)	38.5 ± 9.66	37.5 ± 10.25
Female, n (%)	295 (67.8)	815 (66.2)
EDSS score at parent study baseline (mean ± SD)	2.82 ± 1.29	2.56 ± 1.38
No. of relapses during last year before enrolment to parent study (mean ± SD)	1.3 ± 0.62	1.4 ± 0.6
Prior use of DMT at parent study baseline, n (%)	94 (21.6)	293 (33.8)
HDA[a] status at parent study baseline, n (%)	128 (29.4)	303 (34.9)

[a]HDA defined as patients with ≥2 relapses during the year prior to Parent Study entry, regardless of prior DMT use, OR patients with ≥1 relapse in the previous year and ≥1 T1 gadolinium enhancing lesion or ≥9 T2 lesions while on therapy with other DMTs.

Figure 2. Primary Endpoint: Long-term Mobility (EDSS <7)

Patients who were not using a wheelchair or bedridden in the 3 months prior to CLASSIC-MS

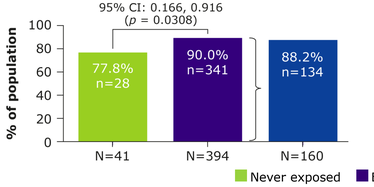
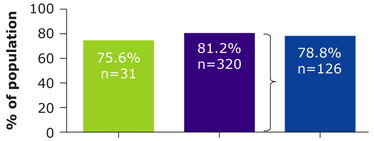


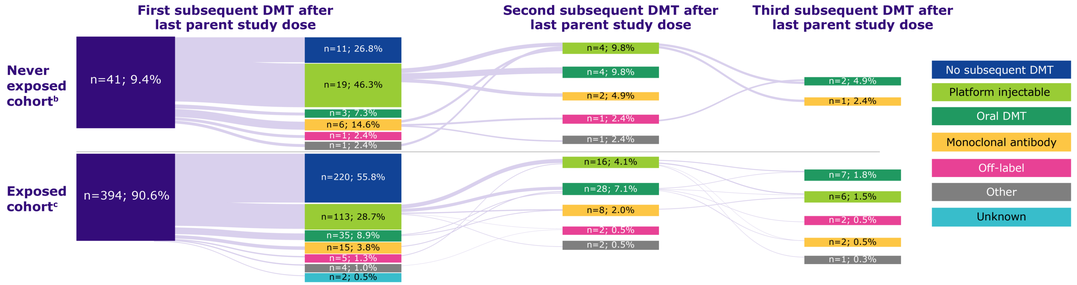
Figure 3. Secondary Endpoint: Long-term Disability Status (EDSS <6)

Patients who did not require an ambulatory device at any time since the last parent study dose



[a]From a logistic regression model with fixed effects for treatment group. Missing data were not included in the analysis.

Figure 4. Patterns of DMT[a] Use in the CLASSIC-MS Population at Any Time After Last Parent Study Dose (N=435)



[a]Subsequent DMTs are reflective of those available in the intervening period (2010–2021) after completion of the parent studies. [b]Never exposed cohort received only placebo during the parent studies. [c]Exposed cohort includes all patients who received ≥1 dose of cladribine tablets during the parent studies.

- Baseline patient characteristics suggest that patients enrolled to CLASSIC-MS from CLARITY/CLARITY Extension were a representative sample of patients included in the parent studies (**Table 1**)
- The mean disease duration for this cohort of patients in CLASSIC-MS was 22.36 ± 6.972 years, where disease duration = (Study Visit 1 - date of MS diagnosis +1) / 365.25
- For patients exposed to ≥1 dose of cladribine tablets in CLARITY/CLARITY Extension (**Figures 2 and 3**):
  - 90.0% did not require wheelchair use/not bedridden
  - 81.2% did not require an ambulatory device
- Patients exposed to cladribine tablets during the parent studies were less likely to receive further treatment with DMTs (**Figure 4**)
- 55.8% of the exposed cohort did not receive further treatment with DMTs versus 26.8% in the never exposed cohort

Abbreviations: **CI**, confidence interval; **DMT**, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **HDA**, high disease activity; **MRI**, magnetic resonance imaging; **MS**, multiple sclerosis; **OR**, odds ratio; **SD**, standard deviation | **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.| **Acknowledgments**: This study was previously presented at ECTRIMS 2021 Virtual Congress | 13–15 October. Medical writing assistance was provided by Claire Mwape of inScience Communications, Springer Healthcare Ltd, UK, and was funded by the healthcare business of Merck KGaA, Darmstadt, Germany (CrossRef Funder ID: 10.13039/100009945). ClinicalTrials.gov identifier: NCT03961204

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