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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

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This study was sponsored by Merck KGaA, Darmstadt, Germany.

Disclosures: This study was sponsored by Merck (CrossRef Funder ID: 10.13039/100009945). Medical writing support was provided by Claire Mwape of inScience Communications, Springer Healthcare Ltd, UK, and was funded by Merck Healthcare KGaA, Darmstadt, Germany.
GG has received speaker honoraria and consulting fees from AbbVie, Actelion (Janssen/J&J), Atara Bio,Almirall, Bayer, Biogen, Celgene (BMS), FivePrime, GlaxoSmithKline, GW Pharma, Ironwood, Merck & Co., Novartis, Merck, Pfizer Inc., Protein Discovery Laboratories, Roche, Sanofi-Genzyme, Teva Pharmaceutical Industries Ltd, UCB, and Vertex Pharmaceuticals; and has received research support unrelated to this study from Biogen, Ironwood, Merck & Co., Novartis, Merck and Takeda.
TL has received consultancy fees or clinical research grants from Acorda, Bayer, Biogen, Daiichi, EMD Serono, Inc. (an affiliate of Merck KGaA), Novartis, ONO, Pfizer, and Teva Neuroscience.
AA and **EVDC** are employees of EMD Serono Research & Development Institute, Inc., Billerica, MA, USA (an affiliate of Merck KGaA).

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]

OBJECTIVES

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

Primary: long-term mobility (no wheelchair use/ bedridden; i.e., Expanded Disability Status Scale [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)

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.

METHODS

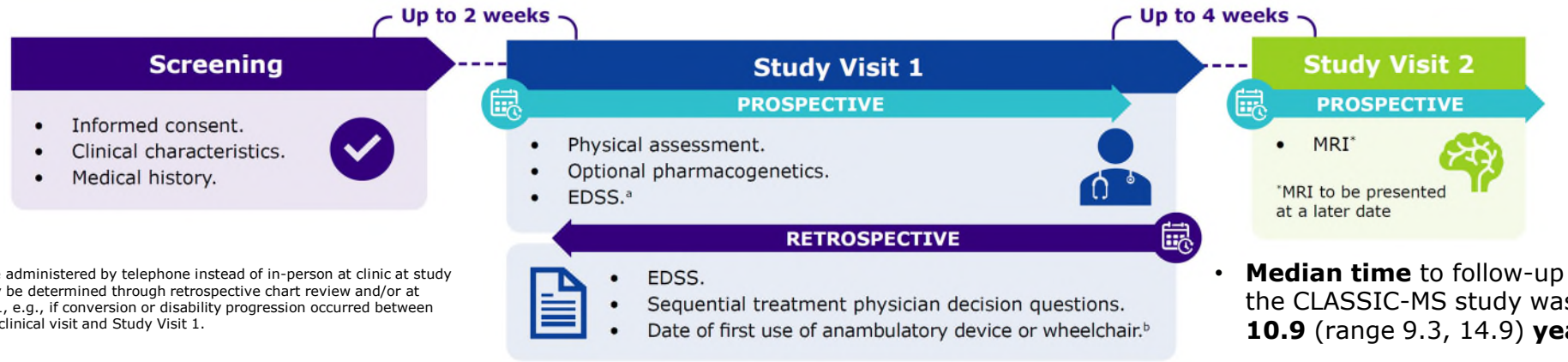
- Patients with relapsing multiple sclerosis (MS) who participated in CLARITY,[1] with or without subsequent enrolment to CLARITY Extension,[2] were evaluated.
- All patients must have received ≥1 course of cladribine tablets or placebo during the parent study.

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**.

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.

EDSS, Expanded Disability Status Scale; **MRI**, magnetic resonance imaging.

RESULTS

- 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

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)

	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 (%)	296 (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)

*Data for 365 ORACLE-MS patients are not included in the non-CLASSIC-MS cohort. [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.

DMT, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **HDA**, high disease activity; **SD**, standard deviation.

RESULTS

- 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.

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

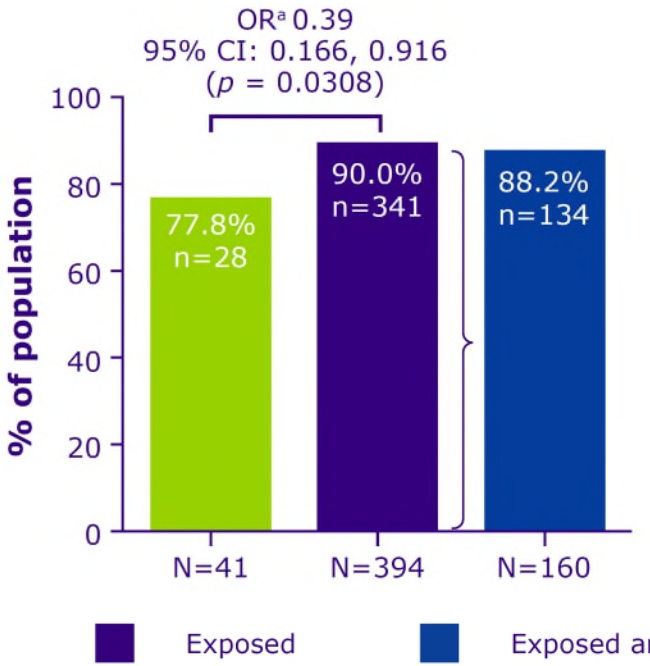
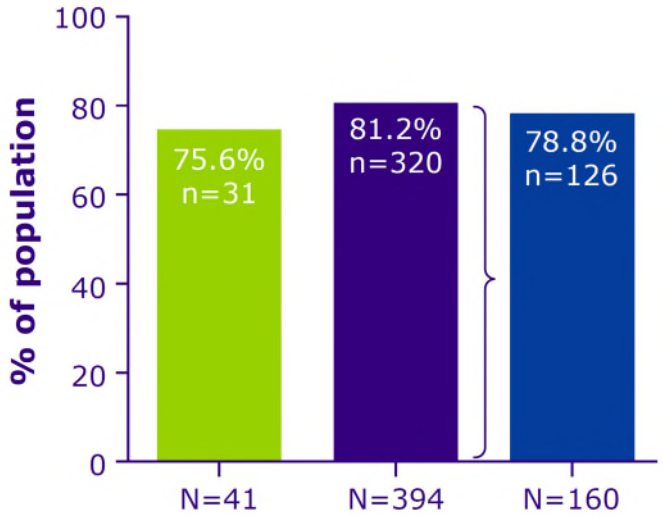


Figure 3. Secondary Endpoint: Long-term Disability Status (EDSS <6)

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



Exposed | Exposed and received approved dose | Never exposed

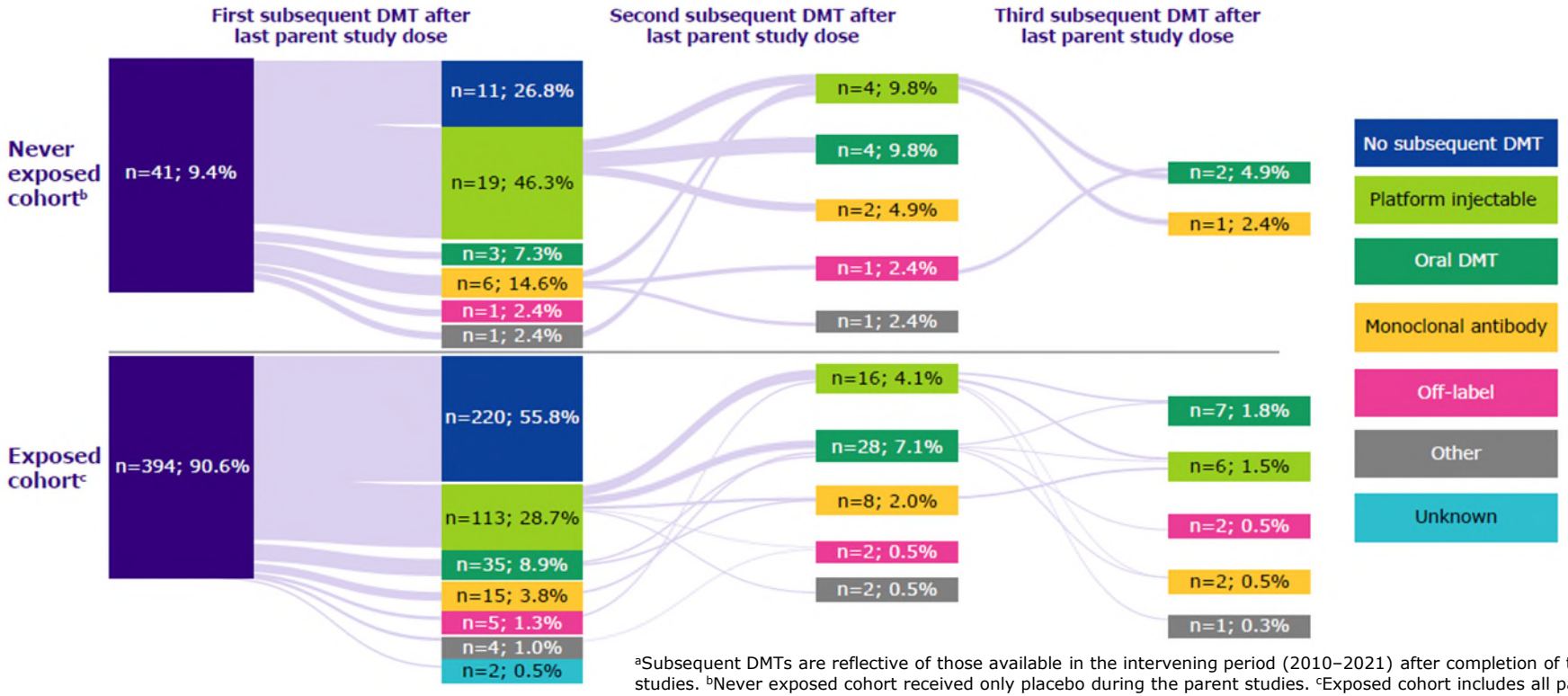
[a]From a logistic regression model with fixed effects for treatment group. Missing data were not included in the analysis.

CI, confidence interval; **EDSS**, Expanded Disability Status Scale; **OR**, odds ratio.

RESULTS

- 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.

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.

DMT, disease-modifying therapy.

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.

MS, multiple sclerosis.