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CLASSIC-MS: Long-term Efficacy and Real-World Treatment Patterns for Patients Receiving Cladribine Tablets - Interim Data with 8–14 Years' Follow-up

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Disclosures

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- **GG** has received speaker honoraria and consulting fees from AbbVie, Actelion, Atara Bio, Almirall, Bayer Schering Pharma, Biogen, Celgene, FivePrime, GlaxoSmithKline, GW Pharma, Ironwood, Merck & Co., Merck KGaA (Darmstadt, Germany), Novartis, 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, and Takeda.
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INTRODUCTION

- CLARITY[1], CLARITY Extension[2], and ORACLE-MS[3] have previously demonstrated the efficacy of cladribine tablets (cumulative dose 3.5 mg/kg over 2 years).
- CLASSIC-MS seeks to explore the long-term efficacy and durability of effect of cladribine tablets beyond the 2 annual treatment courses in patients enrolled to these parent trials.

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.

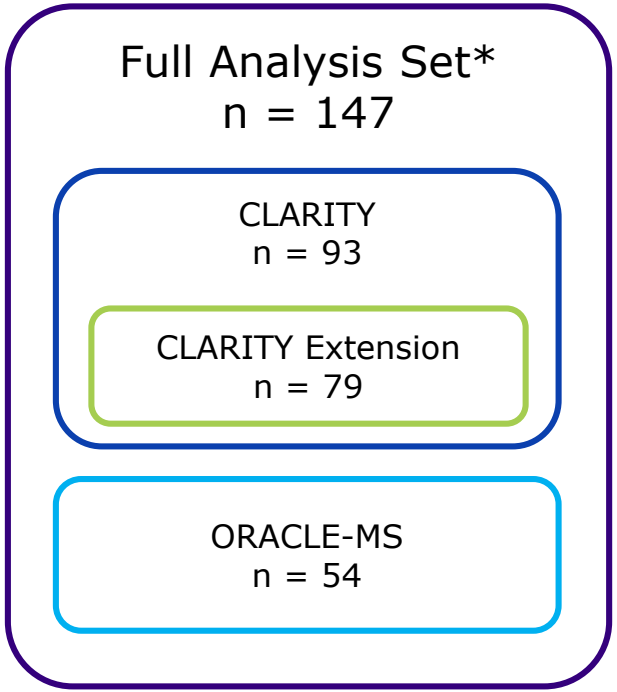
OBJECTIVES

To present interim data* on long-term efficacy and durability of effect of cladribine tablets and real-world treatment patterns in CLASSIC-MS.

*As per protocol, the analysis was conducted when data were available from a minimum of 100 patients in the full analysis set.

METHODS

- Patients with MS who participated in CLARITY[1], CLARITY Extension[2], and those with a first clinical demyelinating event in ORACLE-MS[3], were eligible for inclusion.
- All patients must have received ≥1 course of cladribine tablets or placebo during the parent study.
- The primary objective was the evaluation of long-term mobility; secondary / tertiary objectives were long-term disability status.

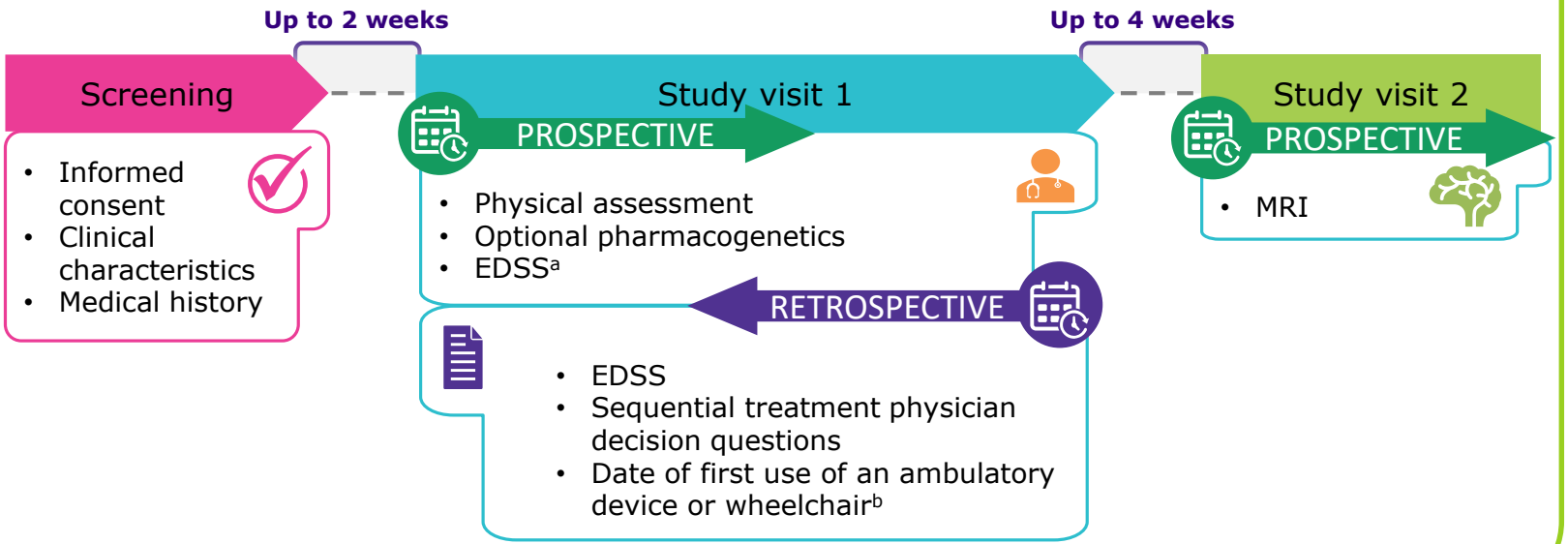


*In the full analysis set, 88.4% (130/147) of patients had been exposed to cladribine tablets in the parent studies, comprising exposure in: CLARITY, 93.5% (87/93); CLARITY Extension, 100% (79/79); or ORACLE-MS, 79.6% (43/54).

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

Median time to follow-up: 10 years (range 8.3, 14.2)



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

RESULTS

Patient Characteristics

Parameter	Total (n = 147)
Exposed to cladribine tablets in parent study, n (%)	**130 (88.4)**
Female, n (%)	89 (60.5)
Age in years at study visit 1[†], mean ± SD	48.1 ± 10.4
Disease duration[‡] (years), mean ± SD	14.78 ± 10.69
Time since last parent study dose to screening visit,	
Mean ± SD	**10.23 ± 1.33**
Median (range)	**10.03 (8.3, 14.2)**

[†]Study visit 1 was conducted either on the phone or in the clinic. [‡]Disease duration = (study visit 1 – date of MS diagnosis +1) / 365.25.
SD, standard deviation

RESULTS

Patient Characteristics

Parameter	Total (n = 147)
EDSS score	
At parent study baseline, mean ± SD	2.61 ± 1.19
At study visit 1[†], mean ± SD	3.25 ± 2.07

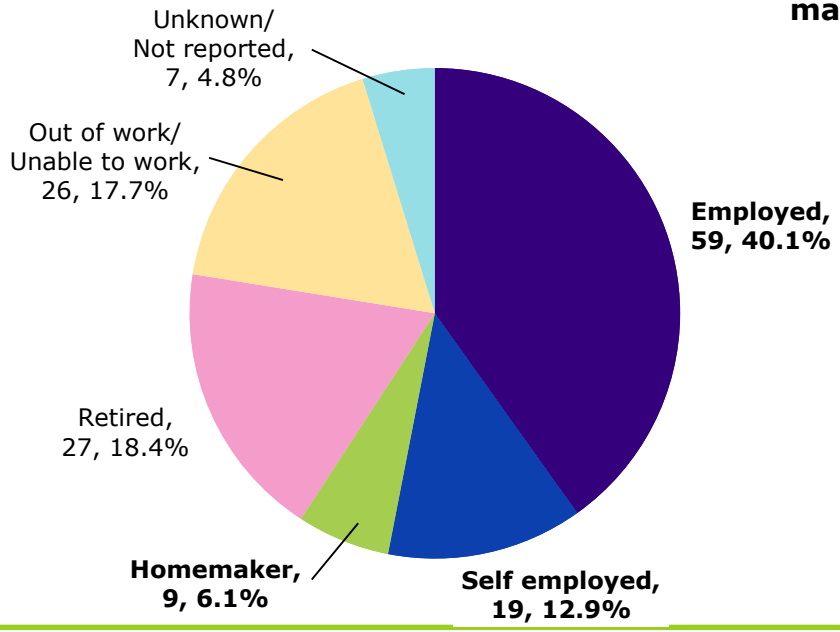
[†]Study visit 1 was conducted either on the phone or in the clinic.
EDSS, Expanded Disability Status Scale; **SD**, standard deviation

RESULTS

Employment Status at Study Visit 1

Total = 147 patients

Active employment maintained by 59.2%



NB. The mean (± SD) age of participants in the CLASSIC-MS study was 48.1 ± 10.4 years.

RESULTS

Primary and Other Endpoints

Primary Endpoint: Patients Using a Wheelchair or Bedridden (EDSS ≥ 7)

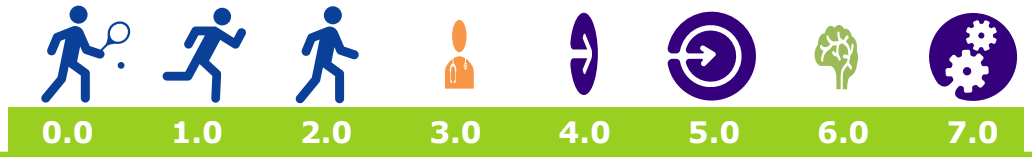
- **94.6%** of patients were **not using a wheelchair or bedridden** in the 3 months prior to CLASSIC-MS.

Secondary Endpoint: Proportion of Patients with EDSS ≥ 6 Since Last Parent Study Dose

- **83.7%** of patients **did not require an ambulatory device** at any time since the last parent study dose.

Tertiary Endpoint: Time to First use of an Ambulatory Device Since Last Parent Study Dose

- Estimated **time to 25% of patients using a first ambulatory device was 10.9 years** since last parent study dose.



EDSS, Expanded Disability Status Scale

RESULTS

Long-term Responders

Definition A - Not requiring further DMD treatment until ≥ 4 years after last parent study dose

Definition B - No evidence of disease reactivation based on investigator assessment of clinical outcomes in the 4 years following last parent study dose

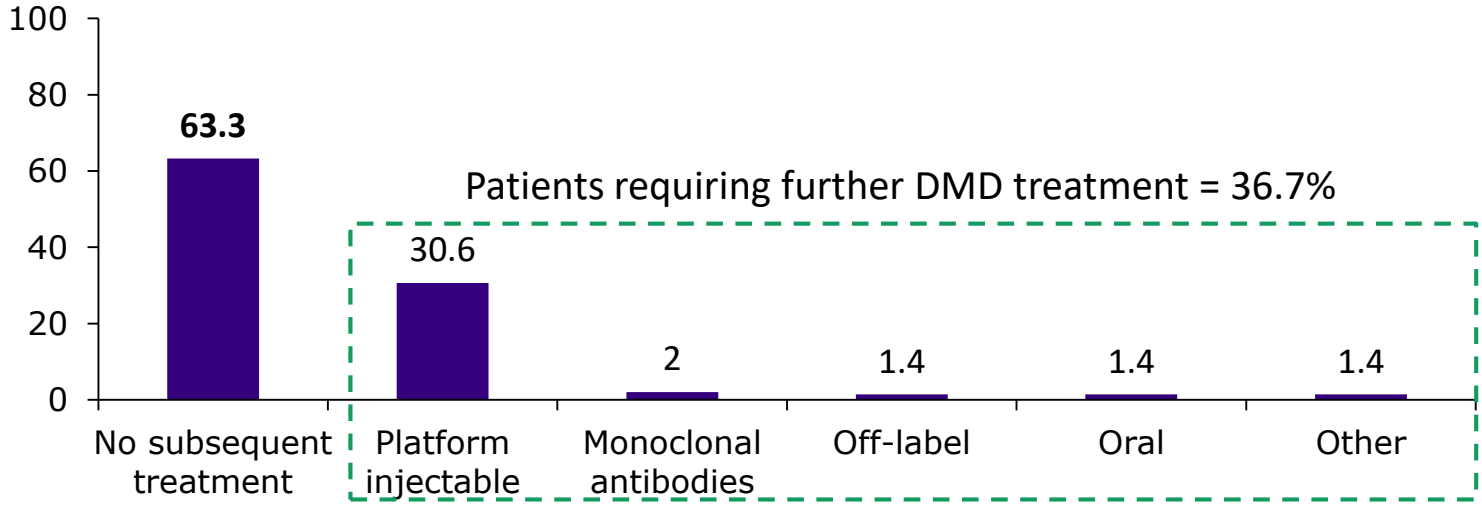
	Definition A	Definition B
Met definition, n (%)	108 (73.5)	67 (45.6)
Did not meet definition, n (%)	33 (22.4)	74 (50.3)
Missing, n (%)	6 (4.1)	6 (4.1)

DMD, disease-modifying drug

RESULTS

Secondary Endpoint: First Subsequent DMD* After Last Parent Study Dose (median 10 years' follow up)

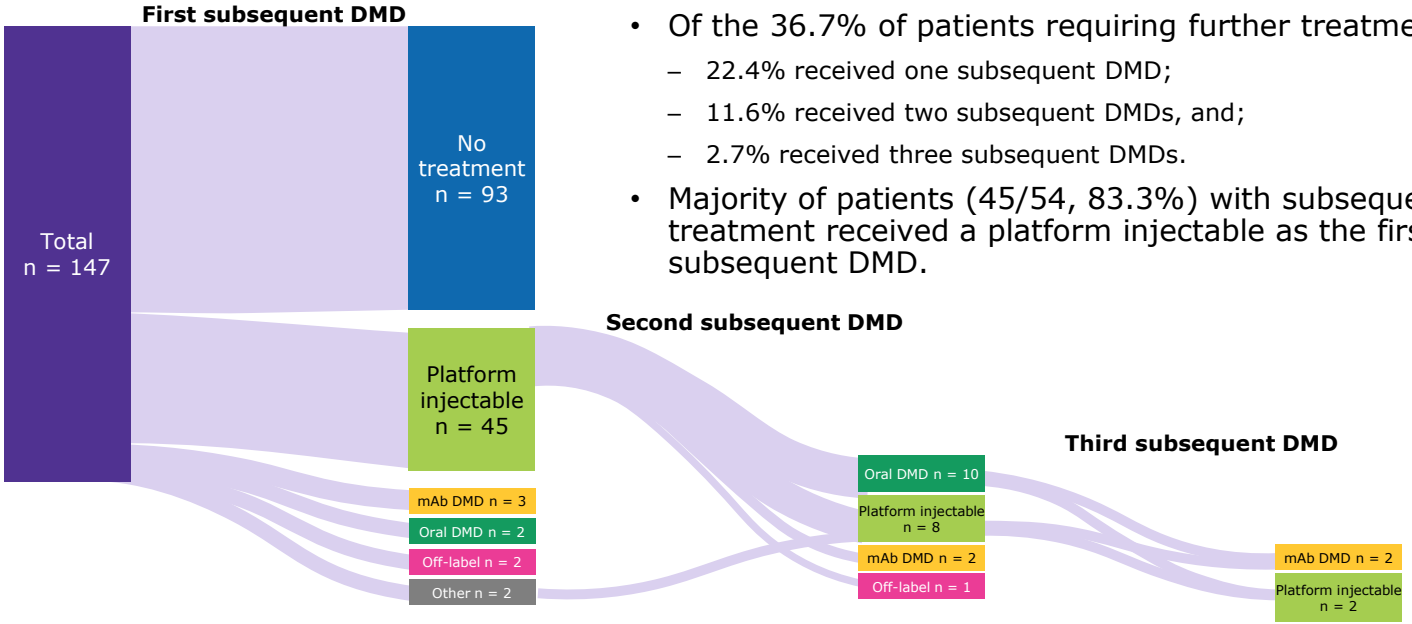
63.3% of patients did not require any further treatment with DMDs following last parent study dose.



*Subsequent DMDs are reflective of those available at the time of the study (2010–2019).
DMD, disease-modifying drug

RESULTS

Secondary Endpoint: Types of Subsequent DMD* After Last Parent Study Dose (median 10 years' follow up)



- Of the 36.7% of patients requiring further treatment:
  - 22.4% received one subsequent DMD;
  - 11.6% received two subsequent DMDs, and;
  - 2.7% received three subsequent DMDs.
- Majority of patients (45/54, 83.3%) with subsequent treatment received a platform injectable as the first subsequent DMD.

*Subsequent DMDs are reflective of those available at the time of the study (2010-2019).
DMD, disease-modifying drug; **mAb**, monoclonal antibody

CONCLUSIONS

Interim data from a small sample of CLASSIC-MS, with a **median of 10 years'** follow-up, suggests **sustained efficacy of cladribine tablets**.

- The study is ongoing and participating centers have enrolled >30% of the intended population

Over the median 10 years' follow-up:

- **94.6% did not require wheelchair use/not bedridden.**
- **83.7% did not require an ambulatory device.**
- **66.3% did not require further treatment with DMDs.**
- **Active employment was maintained by 59.2%.**

DMD, disease-modifying drug