CLASSIC-MS: Long-Term Efficacy and Real-World Treatment Patterns for Patients who Received Cladribine Tablets in Phase III Parent Trials

G. Giovannoni, A. Aydemir, E. Verdun Di Cantogno, T. Leist, on behalf of the CLASSIC-MS Steering Committee

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[1]Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK; [2]EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, a business of Merck KGaA, Darmstadt, Germany; [3]Merck KGaA, Darmstadt, Germany; [4]Division of Clinical Neuroimmunology, Jefferson University, Comprehensive MS Center, Philadelphia, PA, USA

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CONCLUSIONS

This interim analysis from a small sample of patients with RRMS (CLARITY/CLARITY Extension), and a median follow-up of 10.4 years after last dose in the parent study,[a] suggests sustained efficacy of cladribine tablets.

Over the median 10.4 years follow-up there was minimal increase in disability.

The majority (83%) of patients did not receive further DMT treatment for at least 4 years after last dose in the parent study.[a]

The CLASSIC-MS study is ongoing.

[a]CLARITY with or without subsequent participation in CLARITY Extension.
DMT, disease-modifying therapy; **RRMS**, relapsing-remitting multiple sclerosis.

INTRODUCTION

- CLARITY[1] and CLARITY Extension[2] 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 studies.

OBJECTIVES

To present interim data* on long-term outcomes for patients with relapsing-remitting multiple sclerosis originally enrolled to CLARITY with or without subsequent enrolment to CLARITY Extension, as part of the CLASSIC-MS study.

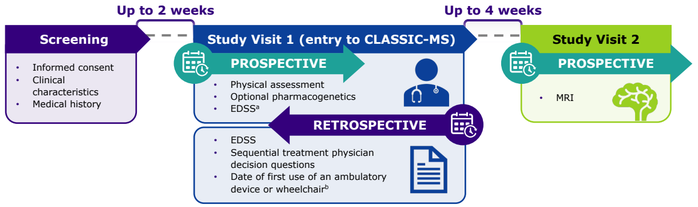
*As per protocol, the analysis was conducted when data were available from a minimum of 100 patients in the full analysis set.

METHODS

- Patients with RRMS who participated in CLARITY[1] with or without subsequent participation in CLARITY Extension[2] were eligible for inclusion.
- All patients must have received ≥1 course of cladribine tablets or placebo during the parent study.
- The objective was the evaluation of long-term responder rates and subsequent DMT use after the last dose in the parent study.

Analysis Set*
CLARITY n = 93
CLARITY Extension n = 79

Figure 1. Median time to follow-up: 10.4 years (range 9.5, 14.2)



*In the analysis set, 93.5% (87/93) of patients had been exposed to cladribine tablets in the parent studies. [a]Can also be administered by telephone instead of in-person at clinic at entry to CLASSIC-MS; [b]May be determined through retrospective chart review and/or at entry to CLASSIC-MS, e.g. if conversion or disability progression occurred between last regular clinical visit and entry to CLASSIC-MS. **DMT**, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **MRI**, magnetic resonance imaging; **RRMS**, relapsing-remitting multiple sclerosis.

RESULTS

Table 1. Patient Characteristics

Parameter	Total (n = 93)
Exposed to cladribine tablets in the parent study,[a] n (%)	**87 (93.5)**
Female, n (%)	57 (61.3)
Mean (± SD) age at entry to CLASSIC-MS, years	51.8 ± 10.0
Mean (± SD) disease duration,[b] years	21.3 ± 7.4
Median (range) time since first dose in the parent study[a] to entry to CLASSIC-MS, years	13.9 (13.0, 14.6)
Median (range) time since last dose in the parent study[a] to screening visit, years	**10.4 (9.5, 14.2)**
Mean (± SD) EDSS score	
At baseline of parent study[a]	3.05 ± 1.15
At entry to CLASSIC-MS	4.06 ± 2.00

Figure 2. Employment Status at Entry to CLASSIC-MS (on or before March 02, 2020)

Total = 93 patients
Mean age, 51.8 years

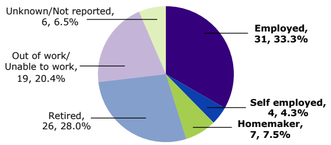
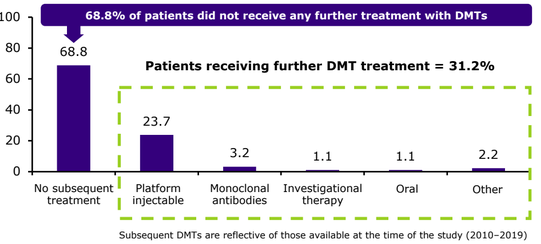


Table 2. Long-term Responders

- **Definition A** – Did not receive further DMT treatment until ≥ 4 years after last dose in the parent study[a]
- **Definition B** – No evidence of disease reactivation (based on investigator assessment of clinical outcomes) in the 4 years after last dose in the parent study[a]

Variable	Definition A	Definition B
Met definition, n (%)	77 (82.8)	34 (36.6)
Did not meet definition, n (%)	15 (16.1)	54 (58.1)
Missing, n (%)	1 (1.1)	5 (5.4)

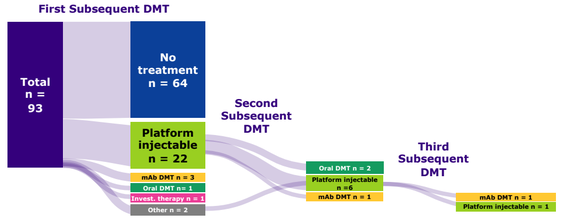
Figure 3. First Subsequent DMT After Last Dose in the Parent Study[a] (median 10.4 years' follow up)



Subsequent DMTs are reflective of those available at the time of the study (2010–2019)

Figure 4. Types of Subsequent DMT After Last Dose in the Parent Study[a] (median 10.4 years' follow up)

- Of the 31.2% of patients receiving further treatment:
  - 21.5% received one subsequent DMT;
  - 7.5% received two subsequent DMTs, and;
  - 2.2% received three subsequent DMTs.
- Majority of patients (22/29, 75.9%) with subsequent treatment received a platform injectable as the first subsequent DMT.



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[a]CLARITY with or without subsequent participation in CLARITY Extension; [b]Disease duration = (Date of entry to CLASSIC-MS – date of MS diagnosis +1) / 365.25.

EDSS, Expanded Disability Status Scale; **DMT**, disease-modifying therapy; **Invest.**, investigational; **mAb**, monoclonal antibody; **SD**, standard deviation.

1. Giovannoni G, et al. *N Engl J Med.* 2010; 362:416–426. 2. Giovannoni G, et al. *Mult Scler.* 2018; 24:1594–1604.

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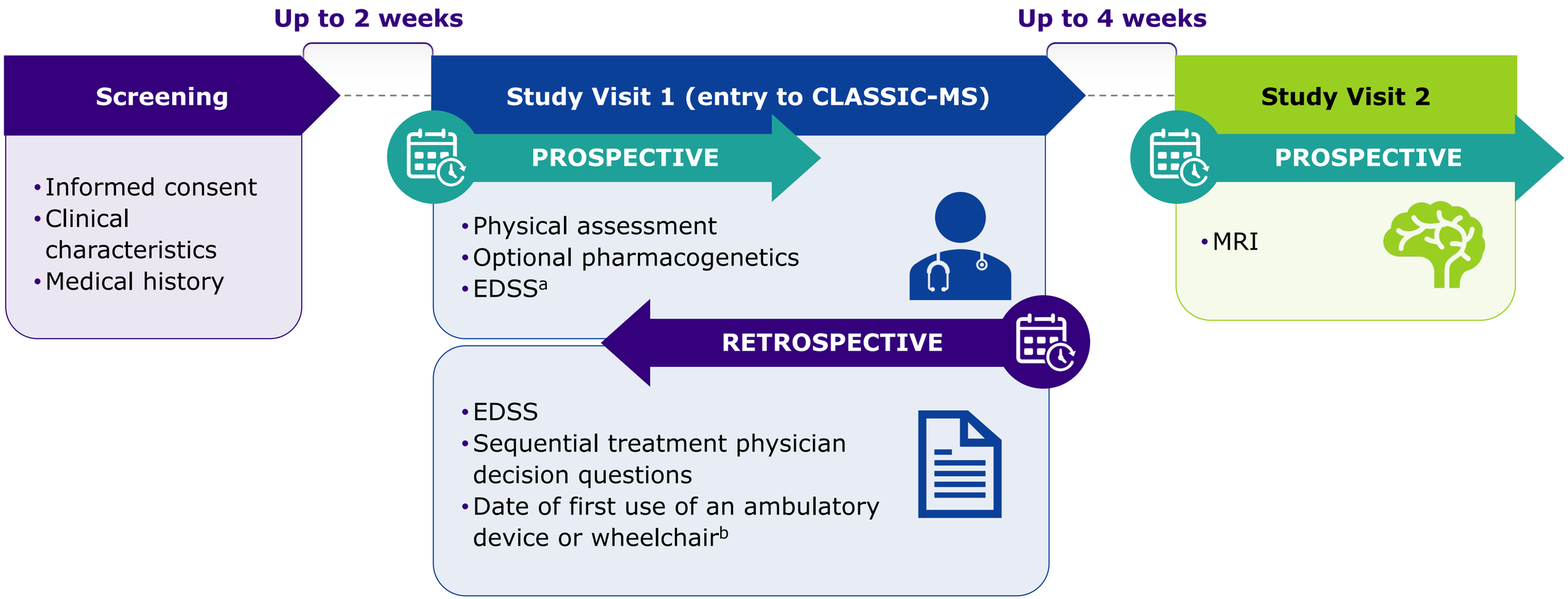
METHODS

Figure 1. Median time to follow-up: 10.4 years (range 9.5, 14.2)



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0.0	1.0	2.0	3.0	4.0	5.0	6.0	7.0
Normal neurological function	No disability with only minimal signs	Minimal disability	Moderate disability	Relatively severe disability	Disability affect full daily activities	Assistance required to walk & work	Essentially restricted to wheelchair

[a]CLARITY with or without subsequent participation in CLARITY Extension; [b]Disease duration = (Date of entry to CLASSIC-MS – date of MS diagnosis +1) / 365.25. **EDSS**, Expanded Disability Status Scale; **SD**, standard deviation.

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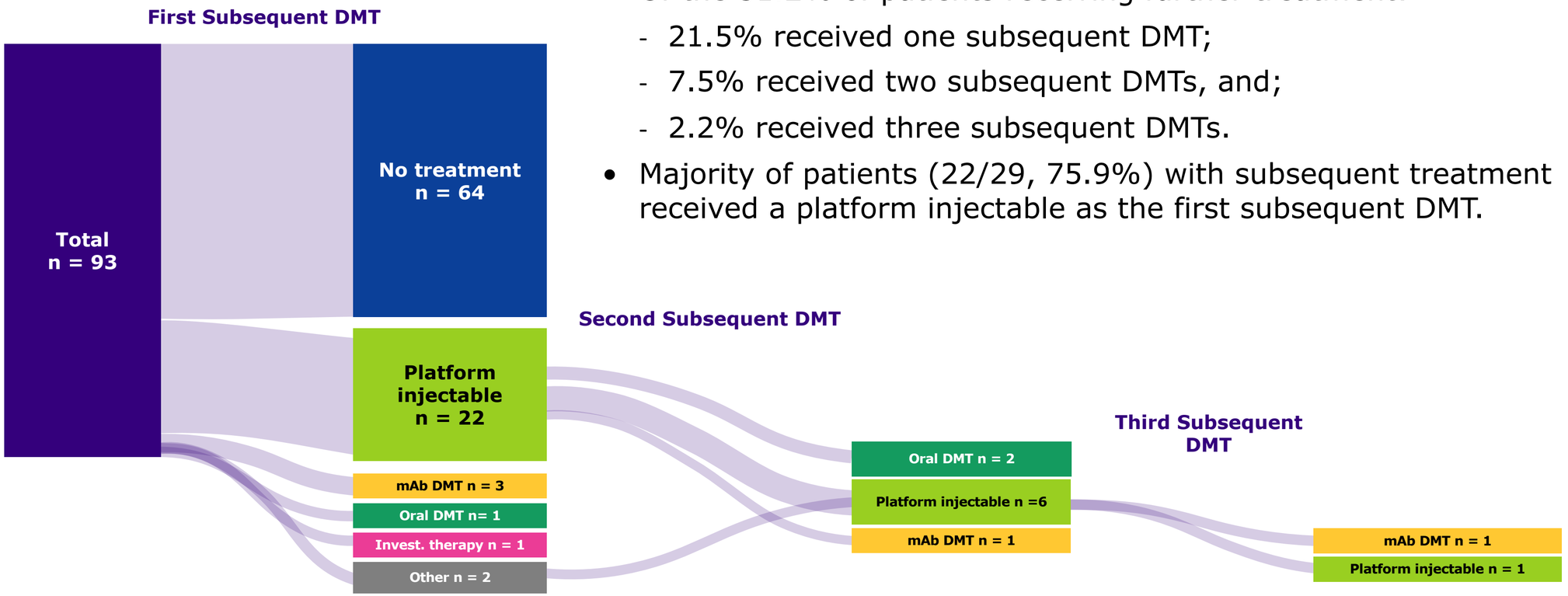

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