This is a reprint from ACTRIMS-ECTRIMS 2020 virtual congress; the references to “Merck” or “Merck KGaA” within refer to (1) Merck KGaA, Darmstadt, Germany; (2) an affiliate of Merck KGaA, Darmstadt, Germany; or (3) one of the businesses of Merck KGaA, Darmstadt, Germany, which operate as EMD Serono in the healthcare, MilliporeSigma in the life science and EMD Electronics in the electronics business in the U.S. and Canada.

There are two different, unaffiliated companies that use the name “Merck”. Merck KGaA, Darmstadt, Germany, which is providing this reprint for the educational, scientific information contained therein, uses the firm name “Merck KGaA, Darmstadt, Germany” and the business names EMD Serono in the healthcare, MilliporeSigma in the life science and EMD Electronics in the electronics business in the U.S. and Canada. The other company, Merck & Co., Inc. holds the rights in the trademark “Merck” in the U.S. and Canada. Merck & Co., Inc. is not affiliated with or related to Merck KGaA, Darmstadt, Germany, which owns the “Merck” trademark in all other countries of the world.

Evaluation of Disability Improvement in Patients with Relapsing-Remitting Multiple Sclerosis Receiving Cladribine Tablets as Measured by the Expanded Disability Status Scale Score

M.P. Sormani[1,2], A. Signori[1], G. Giovannoni[3], N. Alexandri[4]

[1]Department of Health Sciences, University of Genoa, Genoa Italy; [2]Ospedale Policlinico San Martino IRCCS, Genoa, Italy; [1]Department of Health Sciences, University of Genoa, Genoa, Italy; [3]Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK; [4]Merck KGaA, Darmstadt, Germany

ACTRIMS-ECTRIMS 2020 Virtual Congress | 11 – 13 September

Disclosures

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

- **M.P. Sormani** has received consulting fees from Biogen, GeNeuro, Genzyme, MedDay, Merck KGaA (Darmstadt, Germany), Novartis, Roche, and Teva.
- **A. Signori** received personal compensation from Novartis for teaching activities outside of this work.
- **G. Giovannoni** 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.
- **N. Alexandri** is an employee of Merck KGaA, Darmstadt, Germany.

Medical writing assistance was provided by Joe Ward of inScience Communications, Springer Healthcare Ltd, UK, and was funded by Merck KGaA, Darmstadt, Germany.

The CLARITY study: NCT00213135; the CLARITY Extension study

INTRODUCTION

- The incidence of EDSS improvement in MS has previously been studied using KM curves, the same methodology used to assess the incidence of progression.[1,2]
  - However, in a chronic progressive disease improvement can revert. The cumulative incidence curves just indicate whether there was an improvement event, but they do not show the duration of improvement
  - A key question is to evaluate whether and for how long cladribine tablets can improve EDSS scores, by estimating the **prevalence** of disability improvement over time, considering both occurrence and duration of improvement.

CT, cladribine tablets; **CT3.5,** cladribine tablets 10 mg (cumulative dose 3.5 mg/kg over 2 years); **EDSS,** Expanded Disability Status Scale; **KM,** Kaplan-Meier; **MS,** multiple sclerosis

1. Giovannoni G, et al. *Mult Scler*. 2018;24:1594–1604. 2. Kalinick T, et al. *Lancet Neurol*. 2017;16:271–281.

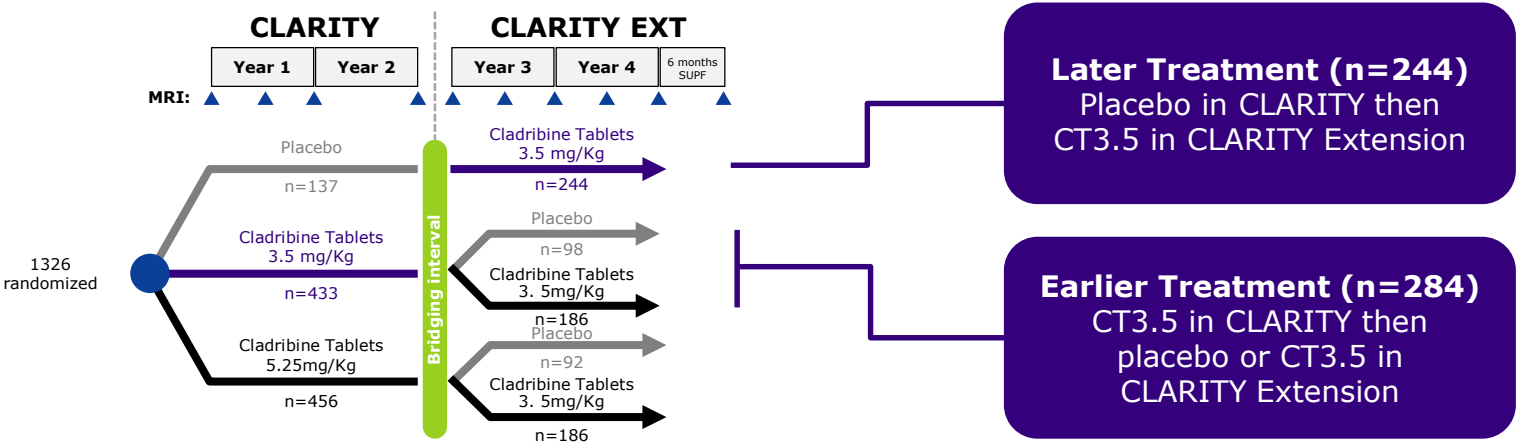
OBJECTIVES

To evaluate *post hoc* long-term prevalence of disability improvement assessed by EDSS score in RRMS patients treated with cladribine tablets enrolled into CLARITY Extension.

EDSS, Expanded Disability Status Scale; **RRMS,** relapsing-remitting multiple sclerosis

METHODS

Patient Population



- After completing CLARITY there was a variable bridging interval before patients entered CLARITY Extension (0.1 – 118.0 weeks)
  - Median bridging interval duration for the overall population was 40.3 weeks

CT3.5, cladribine tablets 10 mg (cumulative dose 3.5 mg/kg over 2 years); **MRI,** magnetic resonance imaging; **SUPF**, supplementary follow-up

1. Giovannoni G, et al. *Mult Scler.* 2018;24:1594–1604.

METHODS

Disability Improvement

Disability improvement

Improvement: A decrease in EDSS from baseline, confirmed at 6 months, of:

- ≥1 point for baseline EDSS <5.5, or
- ≥0.5 points for baseline EDSS ≥5.5

Improvement lost: When EDSS returned to ≥ baseline (regression of improvement confirmed at 6 months)

Improvement start and stop

Start: The visit at which improvement was registered

Stop: The time when the definition of improvement was lost, when EDSS returned to the baseline value (or to a value non qualifying for the improvement definition)

- The regression of improvement has to be confirmed at 6 months to be defined as an improvement stop

Statistical Analysis

- Prevalence was estimated as the difference between the KM estimators for the probability of having an improvement before time t and the probability of returning to baseline before time t.
  - *P* values were estimated using a bootstrap technique on the area under the modified KM curve.

EDSS, Expanded Disability Status Scale; **KM,** Kaplan-Meier

RESULTS

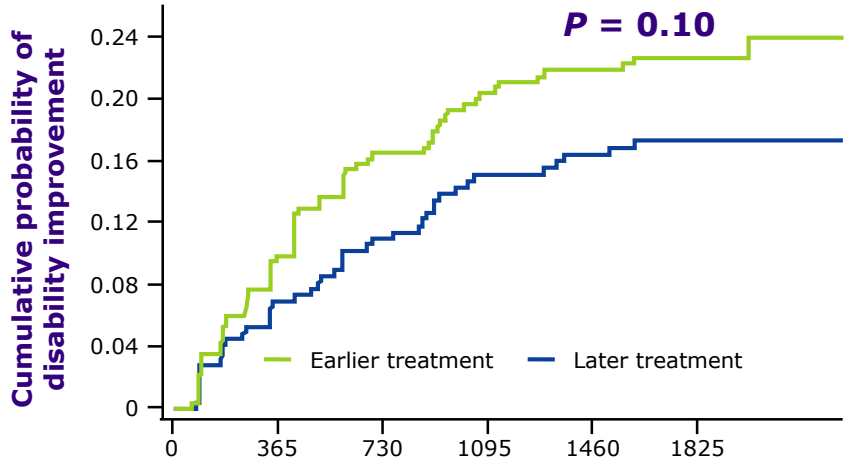
Patient Characteristics

	Earlier Treatment (n=284)	Later Treatment (n=244)
Median age, years	38.0	38.0
Female, n (%)	191 (67.3)	156 (63.9)
Median baseline EDSS	2.5	2.5
Median disease duration, years	2.56	3.36
Received prior DMD treatment, n (%)	61 (21.5)	71 (29.1)
Mean number of baseline T1 Gd+ lesions	1.07	0.85
Mean number of relapses in previous year	1.35	1.31

DMD, disease-modifying drug; **EDSS**, Expanded Disability Status Scale; **Gd**+, gadolinium enhancing

RESULTS

Cumulative Incidence of Disability Improvement



Patients at risk

Earlier treatment	284	256	237	221	205	110
Later treatment	244	227	217	208	187	110

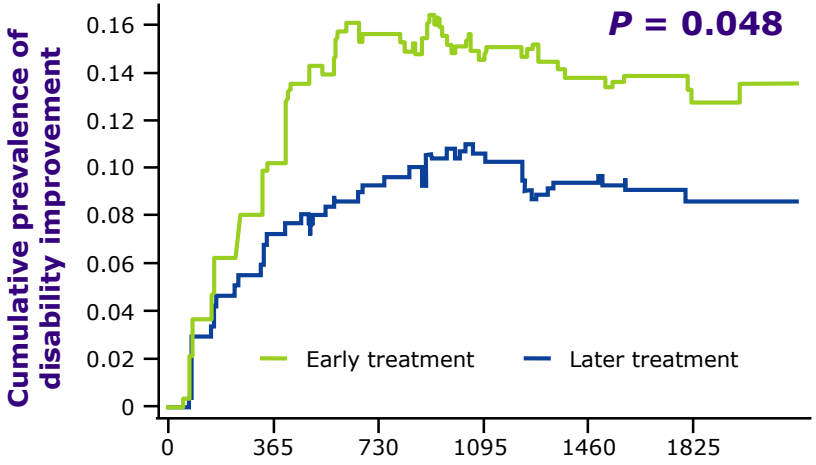
In the **Earlier Treatment** group the cumulative probability of disability improvement was 16.6% (95% CI:12.7–21.4) at Year 2 and 22.7% (95% CI: 18.2– 28.1) at Year 5

For the **Later Treatment** group the cumulative probability of disability improvement was 11.1% (95% CI: 7.7–15.7) at Year 2 and 17.4% (95% CI: 13.2–22.8) at Year 5 (*P* = 0.10)

Purple arrow represents the time point where the Later Treatment group were switched from placebo to cladribine tablets
CI, confidence interval;

RESULTS

Cumulative Prevalence of Disability Improvement



Patients at risk

Early treatment	284	256	237	221	205	110
Later treatment	244	227	217	208	187	110

The prevalence of disability improvement (KM estimate) for the Earlier vs Later Treatment groups at 2-years post-CLARITY baseline was 15.6% (95% CI:11.9–19.3) vs 9.3% (95% CI:6.1–12.4), respectively

At 5-years: 12.7% (95% CI: 8.8–16.6) vs 8.6% (95% CI: 4.8–12.4), respectively (Earlier vs Later Treatment group: *P* = 0.048 for 5-years difference)

Purple arrow represents the time point where the Later Treatment group were switched from placebo to cladribine tablets
CI, confidence interval; **KM**, Kaplan-Meier

CONCLUSIONS

At 2 years after starting cladribine tablets treatment, 15% of patients had experienced a sustained EDSS improvement which was maintained for up to 5 years after starting treatment.

A delay of 2 or more years in taking cladribine tablets reduced the prevalence of patients who improved and maintained improvement over time.

EDSS, Expanded Disability Status Scale