Comparative Effectiveness of Cladribine Versus Fingolimod in the Treatment of Highly Active Relapsing Multiple Sclerosis: The MavEnclad Real worLd comparative efficacY non-iNterventional (MERLYN) study

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ACKNOWLEDGMENTS

Medical writing assistance was provided by Ruth Butler-Ryan and Joseph Ward of inScience Communications, Springer Healthcare Ltd, UK, and was funded by the healthcare business of Merck KGaA, Darmstadt, Germany.

DISCLOSURES

WB has participated in advisory board consulting for Biogen, Celgene (BMS), EMD Serono, Mylan, Novartis, Roche, and Sanofi; and has received speaker honoraria for educational activities for Biogen, the healthcare business of Merck KGaA (Darmstadt, Germany), Mylan, Novartis, Roche, and Sanofi.
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[1]Queen Square MS Center, UCL Institute of Neurology, London, UK; [2]Department of Neurology, Otto-von-Guericke University, Magdeburg, Germany; [3]EMD Serono, Inc., Rockland, MA, USA; [4]ICON plc, Burlington, ON, Canada; [5]ICON plc, Marlow, UK; [6]ICON plc, North Wales, PA, USA; [7]the healthcare business of Merck KGaA, Darmstadt, Germany

CONCLUSIONS

In the first 12 months of treatment, with only half of the recommended 2-year course, cladribine tablets demonstrated comparable effectiveness to fingolimod.

Treatment switching / discontinuation was more common in the fingolimod group.

The full dose of cladribine tablets is reached in the second year. Future studies should therefore investigate effectiveness and treatment persistence beyond the first 12 months of treatment.

INTRODUCTION

- In the EU, cladribine tablets and fingolimod are both approved for the treatment of patients with highly active relapsing multiple sclerosis (MS).[1,2]
- However, limited published data are available concerning real-world comparative effectiveness of these disease-modifying therapies (DMTs).[3–5]

OBJECTIVE

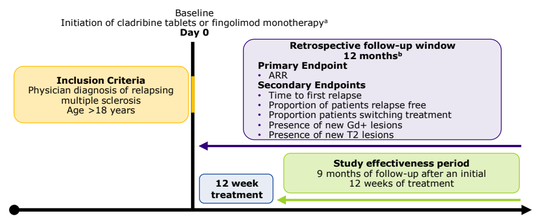
- **Primary:** to compare relapse rates between patients who received either cladribine tablets or fingolimod for treatment of highly active relapsing MS.
- **Secondary:** to compare additional relapse outcomes, treatment switching, and discontinuation.

METHODS

- The MERLYN study was a multicenter, non-interventional, retrospective chart review study to assess the non-inferiority in relapse rate of cladribine tablets versus fingolimod in highly active relapsing MS patients over 12 months.
- The study design of MERLYN and inclusion criteria can be seen in **Figure 1**.
- The primary analytic time period for relapse outcomes was the study effectiveness period, after patients had completed 12 weeks of treatment.
- In order to reduce the impact of confounders, propensity score analysis was applied based on the inverse probability of treatment weighting approach. Non-inferiority was established if the upper limit of the two-sided 95% confidence interval (CI) of the annualized relapse rate (ARR) ratio was less than the non-inferiority margin of 1.2.

Note: Patients in the cladribine tablets cohort only received year one of treatment (1.75 mg/kg cumulative dose). Results therefore reflect those achieved with half of the recommended 2-year course.

Figure 1. Study Design



[a]Treatment initiation on or after August 22, 2017. [b]Patients were censored at discontinuation of treatment, commencement of another disease-modifying therapy, death, loss to follow-up, or after 12 months post-baseline.

ARR, annualized relapse rate; **Gd+**, gadolinium enhancing

RESULTS

Table 1. Patient Characteristics

Characteristic	Cladribine tablets (n=610)	Fingolimod (n=485)
Age (years) at baseline, mean (SD)	40.2 (11.52)	39.4 (10.94)
Female, n (%)	443 (72.6)	324 (66.8)
Disease duration (years) from diagnosis to baseline, median (IQR)	5.1 (1.7, 10.9)	5.3 (2.4, 10.1)
Two or more physician-confirmed relapses in the 12 months prior to baseline, n (%)	127 (20.8)	60 (12.4)
No. of DMTs received at any time prior to baseline, n (%)[a]		
0 (treatment naïve)	128 (21.0)	37 (7.6)
1	196 (32.1)	261 (53.8)
2	148 (24.3)	126 (26.0)
≥3	135 (22.1)	60 (12.4)
Unknown	3 (0.5)	1 (0.2)
EDSS score at baseline, median (IQR)[b]	2.5 (1.5, 4.0)	2.0 (1.5, 3.5)
Presence of new Gd+ lesions, n (%)[c]	138 (22.6)	86 (17.7)
Presence of new T2 lesions, n (%)[c]	236 (38.7)	196 (40.4)

[a]The most common DMTs received in the 12 months prior to baseline were glatiramer acetate, dimethyl fumarate, and interferon beta-1a. [b]Based on latest available score taken on or within 12 months prior to treatment initiation. [c]Lesions in the most recent magnetic resonance imaging data prior to baseline.

DMT, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **Gd+**, gadolinium enhancing; **IQR**, interquartile range; **SD**, standard deviation

- A total of 1,098 patients met eligibility criteria and were enrolled. Of these, 1,095 patients completed 12 weeks of treatment and entered the study effectiveness period (**Table 1**).
- ARR findings are shown in **Table 2**.
  - The adjusted ARR ratio of 0.68 (95% CI: 0.42, 1.11) was numerically favorable to cladribine tablets, and the 95% CI upper bound was within the non-inferiority margin.

Table 2. Relapse Rates

	Relapses during study effectiveness period, n (%)	Adjusted ARR (95% CI)	Relapses during 12-month follow-up, n (%)	Adjusted ARR including 12-month follow-up (95% CI)
Cladribine tablets (n=610)	42 (6.9)	0.10 (0.07, 0.14)	65 (10.7)	0.11 (0.09, 0.15)
Fingolimod (n=485)	41 (8.5)	0.14 (0.10, 0.20)	51 (10.5)	0.13 (0.10, 0.18)

ARR, annualized relapse rate; **CI**, confidence interval

- Time to first relapse and proportion of patients relapse-free were similar between groups.
- During the 12-month period following treatment initiation, one patient (0.2%) who initiated cladribine tablets discontinued and switched to another DMT, whereas 17 patients (3.5%) discontinued treatment with fingolimod (including 10 patients who switched to another DMT).

Table 3. New MRI Lesions in the 12 Months after Treatment Initiation

Patients, n (%)	Presence of new Gd+ lesions (of patients with Gd+ MRI data)	Presence of ≥1 new T2 lesion (of patients with MRI data)
Cladribine tablets (n=610)	13/162 (8.0)	78/370 (21.1)
Fingolimod (n=485)	9/122 (7.4)	54/315 (17.1)

Gd+, gadolinium enhancing; **MRI**, magnetic resonance imaging

- A total of 370 (60.7%) patients treated with cladribine tablets and 315 (64.9%) patients treated with fingolimod had interpretable magnetic resonance imaging (MRI) data during the 12-month period after treatment initiation (**Table 3**).
  - There were no statistically significant differences in MRI outcomes between treatment groups.

REFERENCES
1. MAVENCLAD 10 mg tablets. Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/mavenclad-epar-product-information_en.pdf (accessed February 2022). 2. Gilenya 0.25 mg/0.5 mg hard capsules. Summary of Product Characteristics. https://www.ema.europa.eu/en/documents/product-information/gilenya-epar-product-information_en.pdf (accessed February 2022). 3. Siddiqui MK, et al. *Curr Med Res Opin*. 2018;34:1361–1371. 4. Kalincik T, et al. *Mult Scler*. 2018;24:1617–1626. 5. Signori A, et al. *Neurol Neuroimmunol Neuroinflamm*. 2020;7:e878.

Cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years) are indicated for the treatment of patients with MS in the United States (relapsing forms of MS, including relapsing-remitting disease and active secondary progressive disease, in adults).

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Presented at AAN 2022 | April 2–7 | Seattle, Washington, USA

Data collection and analysis was sponsored by the healthcare business of Merck KGaA, Darmstadt, Germany (CrossRef Funder ID: 10.13039/100009945)

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EU, European Union; **DMT**, disease-modifying therapy; **MS**, multiple sclerosis

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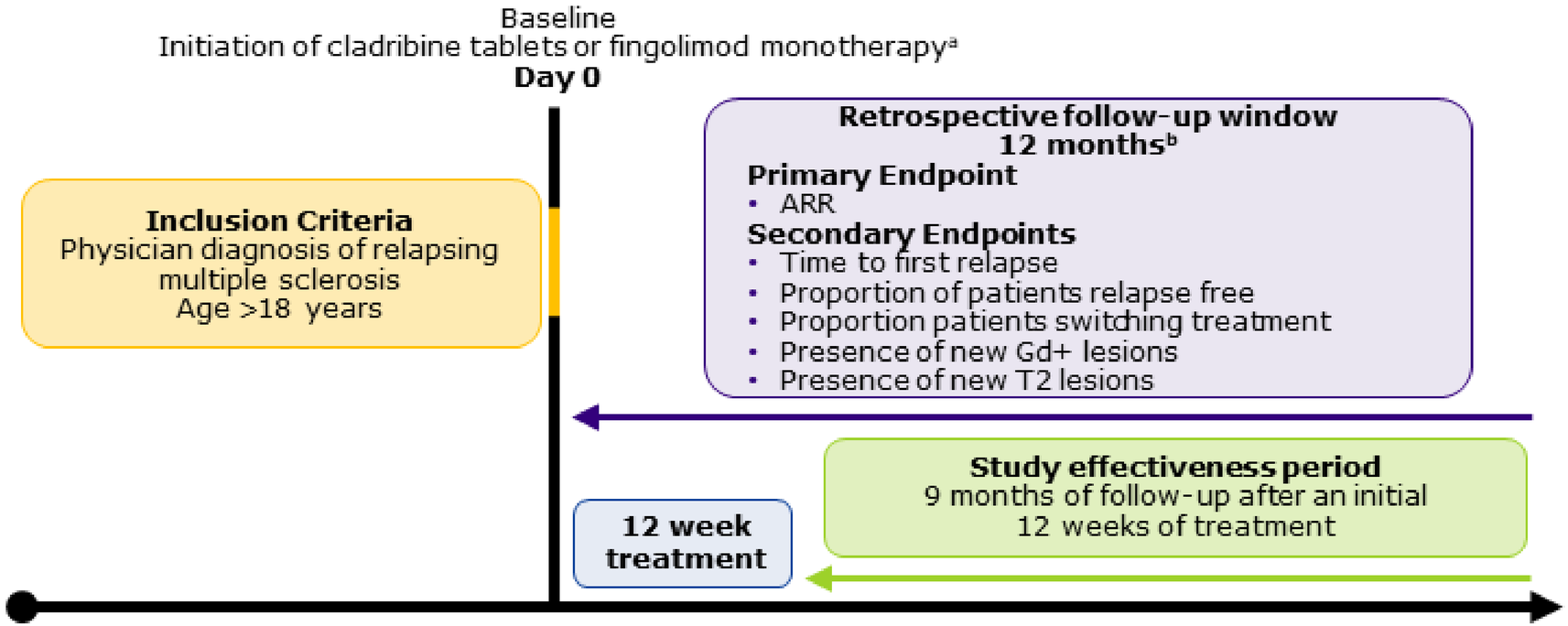

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- **Treatment switching / discontinuation was more common in the fingolimod group.**
- **The full dose of cladribine tablets is reached in the second year. Future studies should therefore investigate effectiveness and treatment persistence beyond the first 12 months of treatment.**

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