Real-World Comparative Effectiveness and Persistence of Cladribine Tablets and Other Oral Disease-Modifying Treatments for Multiple Sclerosis from GLIMPSE: Results from the MSBase Registry

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ACKNOWLEDGMENTS

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

DISCLOSURES

HB has served on scientific advisory boards for Biogen, Novartis, and Sanofi; and has received conference travel support from Biogen, Novartis, and Sanofi. He has served on steering committees for trials conducted by Biogen and Novartis, and has received research support from Biogen, the healthcare business of Merck KGaA (Darmstadt, Germany), and Novartis. **TS** has received compensation for serving on scientific advisory boards, honoraria for consultancy, and funding for travel from Biogen; and speaker honoraria from Novartis. **SO** declares no conflicts of interest. **RA** has received honoraria as a speaker and scientific advisory board participant, and research grants from Bayer, Biogen, Biologix, Genpharm, GlaxoSmithKline, Lundbeck, the healthcare business of Merck KGaA (Darmstadt, Germany), Novartis, Roche, and Sanofi. **MT** has received travel grants from Bayer, the healthcare business of Merck KGaA (Darmstadt, Germany), Novartis, and Teva; and has participated in clinical trials by Novartis, Roche, and Sanofi. **SH** serves on advisory boards for Bayer, Biogen, the healthcare business of Merck KGaA (Darmstadt, Germany), Novartis, Roche, and Sanofi. 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H. Butzkueven[1,2], T. Spelman[2], S. Ozakbas[3], R. Alroughani[4], M. Terzi[5], S. Hodgkinson[6], G. Laureys[7], T. Kalincik[8,9], A. Van der Walt[1], B. Yamout[10], J. Lechner-Scott[11,12], A. Soysal[13], J. Kuhle[14], J.L. Sanchez-Menoyo[15], Y. Blanco[16], D.L.A. Spitaleri[17], V. Van Pesch[18], D. Horakova[19], R. Ampapa[20], F. Patti[21], R. Macdonell[22], A. Al-Asmi[23], O. Gerlach[24,25], J. Oh[26], A. Altintas[27], N.L. Tundia[28], S.L. Wong[28]

[1]Department of Neuroscience, Central Clinical School, Monash University, Melbourne, VIC, Australia; [2]MSBase Foundation, Alfred Centre, Melbourne, VIC, Australia; [3]Dokuz Eylul University, Izmir, Turkey; [4]Amiri Hospital, Sharq, Kuwait; [5]Department of Neurology, Medical Faculty, 19 Mayis University, Samsun, Turkey; [6]Liverpool Hospital, Sydney, NSW, Australia; [7]University Hospital Ghent, Ghent, Belgium; [8]MS Centre, Department of Neurology, Royal Melbourne Hospital, Melbourne, VIC, Australia; [9]CORe, Department of Medicine, University of Melbourne, Melbourne, VIC, Australia; [10]Harley Street Medical Center, Abu Dhabi, United Arab Emirates; [11]School of Medicine and Public Health, University of Newcastle, Newcastle, NSW, Australia; [12]Department of Neurology, John Hunter Hospital, Hunter New England Health, Newcastle, NSW, Australia; [13]Bakirkoy Education and Research Hospital for Psychiatric and Neurological Diseases, Istanbul, Turkey; [14]Universitatsspital Basel, Basel, Switzerland; [15]Department of Neurology, Galdakao-Usansolo University Hospital, Osakidetza-Basque Health Service, Biocruces-Bizkaia Health Research Institute, Galdakao, Spain; [16]Center of Neuroimmunology, Service of Neurology, Hospital Clinic de Barcelona, Barcelona, Spain; [17]Azienda Ospedaliera di Rilievo Nazionale San Giuseppe Moscati Avellino, Avellino, Italy; [18]Cliniques Universitaires Saint-Luc, UCLouvain, Brussels, Belgium; [19]Department of Neurology and Center of Clinical Neuroscience, First Faculty of Medicine, Charles University in Prague and General University Hospital, Prague, Czech Republic; [20]Nemocnice Jihlava, Jihlava, Czech Republic; [21]Department of Medical and Surgical Sciences and Advanced Technologies, GF Ingrassia, Catania, Italy; [22]Austin Health, Melbourne, VIC, Australia; [23]Neurology Unit, Department of Medicine, College of Medicine and Health Sciences and Sultan Qaboos University Hospital, SQU, Al Khodh, Oman; [24]Academic MS Center Zuyderland, Department of Neurology, Zuyderland Medical Center, Sittard-Geleen, The Netherlands; [25]School for Mental Health and Neuroscience, Maastricht University, Maastricht, The Netherlands; [26]St Michael's Hospital, Toronto, ON, Canada; [27]Koc University School of Medicine and Koc University Research Center for Translational Medicine (KUTTAM), Istanbul, Turkey; [28]EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, on behalf of the MBase Study Group

CONCLUSIONS

For all three pairwise comparisons, relapse and discontinuation outcomes significantly favored cladribine tablets over other oral DMTs.

Future analyses with longer follow-up comparing disability progression events are warranted.

INTRODUCTION

- There are few clinical trials or real-world studies comparing effectiveness of cladribine tablets to other oral disease-modifying therapies (DMTs).
- The brief treatment schedule of cladribine tablets (a maximum of 20 days over a 2-year period with no treatment required in Years 3 and 4) could improve adherence compared to daily or twice-daily use of other approved oral DMTs, including fingolimod, dimethyl fumarate, and teriflunomide.[1]
- The MSBase registry records demographics, DMT use, Expanded Disability Status Scale (EDSS) scores, and relapses in over 74,000 multiple sclerosis (MS) patients globally.

OBJECTIVES

Compare treatment patterns and clinical outcomes in MS patients newly treated with cladribine tablets versus fingolimod, dimethyl fumarate, and teriflunomide in the real world.

METHODS

- Baseline demographics and outcomes were described for all adult (aged >18 years) relapsing MS patients newly initiating cladribine tablets or oral comparators starting from January 2018 in the MSBase registry.
- Propensity-score matching (PSM, 1:1) for three pairwise comparisons (cladribine tablets versus oral DMTs) included age, sex, EDSS score, pre-baseline relapses, prior DMT initiation, and country.
- Outcomes included time-to-treatment discontinuation (for cladribine tablets this was taken as switch to alternate DMT), annualized relapse rate (ARR), time-to-first relapse, and time-to-treatment switch.
- Time-to-event analyses used marginal Cox models with hazard ratio (HR) and 95% confidence intervals (CI). ARRs were compared with a weighted negative binomial model with a cluster term for matched patient sets. *P*-values were not adjusted for multiple testing and should be considered nominal.

RESULTS

Table 1. Patient Characteristics at Index Date

Characteristic	Cladribine tablets (n=633)	Fingolimod (n=1195)	Dimethyl fumarate (n=912)	Teriflunomide (n=735)
Age (years), mean (SD)	44.10 (12.27)	37.99 (10.72)	36.88 (11.35)	43.76 (12.61)
Female, n (%)	482 (76.1)	867 (72.6)	655 (71.8)	525 (71.4)
Disease duration (years), mean (SD)	12.48 (9.56)	8.97 (7.16)	6.77 (7.68)	10.33 (9.54)
EDSS score, median (IQR)	2.5 (1.5, 4.5)	1.5 (1, 2.5)	1.5 (1, 2)	1.5 (1, 2.5)
No. of relapses in 12 months pre-index, mean (SD)	0.55 (0.93)	0.58 (0.76)	0.73 (0.84)	0.50 (0.74)
No. of relapses in 24 months pre-index, mean (SD)	0.83 (1.40)	0.89 (1.04)	0.99 (1.12)	0.70 (0.95)
No. of prior DMTs, mean (SD)	2.20 (2.77)	1.69 (2.17)	1.06 (1.66)	1.36 (2.09)
Treatment naïve, n (%)	137 (21.6)	166 (13.9)	422 (46.3)	253 (34.4)
MS classification, n (%)				
Relapsing-remitting MS	551 (87.0)	1126 (94.2)	845 (92.7)	668 (90.9)
Secondary progressive MS	55 (8.7)	37 (3.1)	11 (1.2)	22 (3.0)
Primary progressive MS	1 (0.2)	4 (0.3)	2 (0.2)	8 (1.1)
Progressive-relapsing MS	4 (0.6)	7 (0.6)	3 (0.3)	1 (0.1)
Clinically isolated syndrome	5 (0.8)	16 (1.3)	30 (3.3)	22 (3.0)
Not reported	17 (2.7)	5 (0.4)	21 (2.3)	14 (1.9)

DMT, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **IQR**, interquartile range; **MS**, multiple sclerosis; **SD**, standard deviation

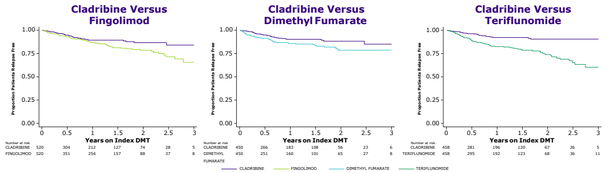
- With PSM, cohorts were found to be well balanced regarding demographic and clinical characteristics. Median follow-up times were between 11–13 months.

Table 2. Annualized Relapse Rate: Treatment Cohort Pairwise Comparisons

Characteristic	Number of relapses	DMT follow-up (years)	ARR (95% CI)	*P*-value
Cladribine tablets (n=520)	47	498.28	0.0943 (0.069, 0.1254)	0.0156
Fingolimod (n=520)	89	612.27	0.1454 (0.1167, 0.1789)	
Cladribine tablets (n=450)	41	426.22	0.0962 (0.069, 0.1305)	0.0307
Dimethyl fumarate (n=450)	64	433.19	0.1477 (0.1138, 0.1887)	
Cladribine tablets (n=458)	40	451.46	0.0886 (0.0633, 0.1207)	0.0005
Teriflunomide (n=458)	88	514.78	0.1709 (0.1371, 0.2106)	

ARR, annualized relapse rate; **CI**, confidence interval; **DMT**, disease-modifying therapy

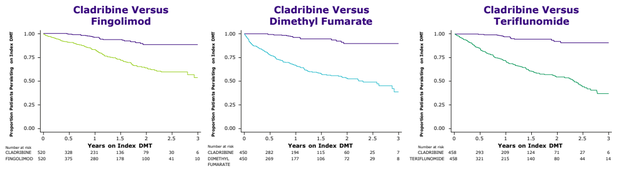
Figure 1. Time to First Relapse



	Cladribine versus fingolimod (n=520)	Cladribine versus dimethyl fumarate (n=450)	Cladribine versus teriflunomide (n=458)
HR (95% CI)	0.60 (0.41, 0.88)	0.58 (0.37, 0.90)	0.33 (0.21, 0.52)
P-value	0.010	0.016	<0.001

CI, confidence interval; **DMT**, disease-modifying therapy; **HR**, hazard ratio

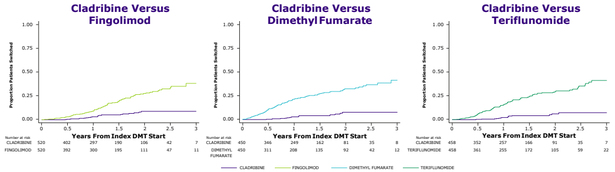
Figure 2. Time-to-Treatment Discontinuation



	Cladribine versus fingolimod (n=520)	Cladribine versus dimethyl fumarate (n=450)	Cladribine versus teriflunomide (n=458)
HR (95% CI)	0.22 (0.14, 0.34)	0.10 (0.06, 0.17)	0.10 (0.06, 0.17)
P-value	<0.001	<0.001	<0.001

CI, confidence interval; **DMT**, disease-modifying therapy; **HR**, hazard ratio

Figure 3. Time-to-Treatment Switch



	Cladribine versus fingolimod (n=520)	Cladribine versus dimethyl fumarate (n=450)	Cladribine versus teriflunomide (n=458)
HR (95% CI)	4.00 (2.54, 6.32)	7.04 (4.16, 11.93)	6.52 (3.79, 11.22)
P-value	<0.001	<0.001	<0.001

CI, confidence interval; **DMT**, disease-modifying therapy; **HR**, hazard ratio

REFERENCE
1. Nicholas JA, et al. *BMC Neurol*. 2020;20:281.

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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This poster was previously presented at ACTRIMS 2022 Forum (24–26 February). Medical writing assistance was provided by Ruth Butler-Ryan of inScience Communications, Springer Healthcare Ltd, UK, and was funded by the healthcare business of Merck KGaA, Darmstadt, Germany.

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)

INTRODUCTION

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- The brief treatment schedule of cladribine tablets (a maximum of 20 days over a 2-year period with no treatment required in Years 3 and 4) could improve adherence compared to daily or twice-daily use of other approved oral DMTs, including fingolimod, dimethyl fumarate, and teriflunomide.[1]
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OBJECTIVE

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DMT, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **MS**, multiple sclerosis

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RESULTS

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MS classification, n (%)				
Relapsing-remitting MS	551 (87.0)	1126 (94.2)	845 (92.7)	668 (90.9)
Secondary progressive MS	55 (8.7)	37 (3.1)	11 (1.2)	22 (3.0)
Primary progressive MS	1 (0.2)	4 (0.3)	2 (0.2)	8 (1.1)
Progressive-relapsing MS	4 (0.6)	7 (0.6)	3 (0.3)	1 (0.1)
Clinically isolated syndrome	5 (0.8)	16 (1.3)	30 (3.3)	22 (3.0)
Not reported	17 (2.7)	5 (0.4)	21 (2.3)	14 (1.9)

- With PSM, cohorts were found to be well balanced regarding demographic and clinical characteristics. Median follow-up times were between 11-13 months.

DMT, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **IQR**, interquartile range; **MS**, multiple sclerosis; **PSM**, propensity-score matching; **SD**, standard deviation

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

RESULTS

Table 2. Annualized Relapse Rate: Treatment Cohort Pairwise Comparisons

Characteristic	Number of relapses	DMT follow-up (years)	ARR (95% CI)	*P*-value
Cladribine tablets (n=520)	47	498.28	0.0943 (0.069, 0.1254)	0.0156
Fingolimod (n=520)	89	612.27	0.1454 (0.1167, 0.1789)	
Cladribine tablets (n=450)	41	426.22	0.0962 (0.069, 0.1305)	0.0307
Dimethyl fumarate (n=450)	64	433.19	0.1477 (0.1138, 0.1887)	
Cladribine tablets (n=458)	40	451.46	0.0886 (0.0633, 0.1207)	0.0005
Teriflunomide (n=458)	88	514.78	0.1709 (0.1371, 0.2106)	

ARR, annualized relapse rate; **CI**, confidence interval; **DMT**, disease-modifying therapy

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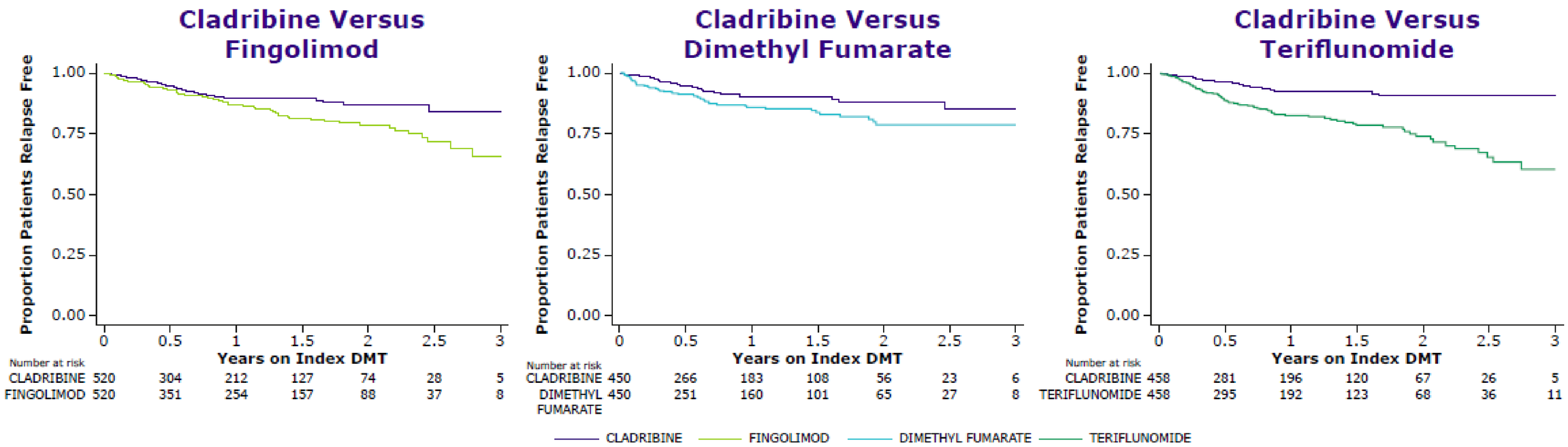
RESULTS

Figure 1. Time to First Relapse



	Cladribine versus fingolimod (n=520)	Cladribine versus dimethyl fumarate (n=450)	Cladribine versus teriflunomide (n=458)
HR (95% CI)	0.60 (0.41, 0.88)	0.58 (0.37, 0.90)	0.33 (0.21, 0.52)
P-value	0.010	0.016	<0.001

CI, confidence interval; **DMT**, disease-modifying therapy; **HR**, hazard ratio

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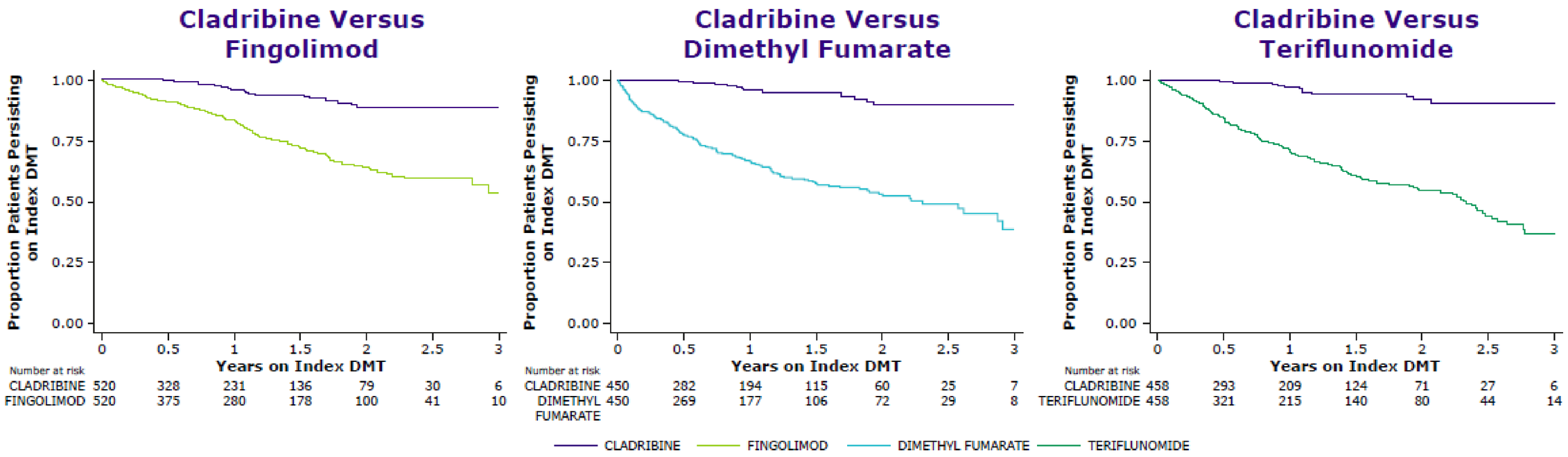
RESULTS

Figure 2. Time-to-Treatment Discontinuation



	Cladribine versus fingolimod (n=520)	Cladribine versus dimethyl fumarate (n=450)	Cladribine versus teriflunomide (n=458)
HR (95% CI)	0.22 (0.14, 0.34)	0.10 (0.06, 0.17)	0.10 (0.06, 0.17)
P-value	<0.001	<0.001	<0.001

CI, confidence interval; **DMT**, disease-modifying therapy; **HR**, hazard ratio

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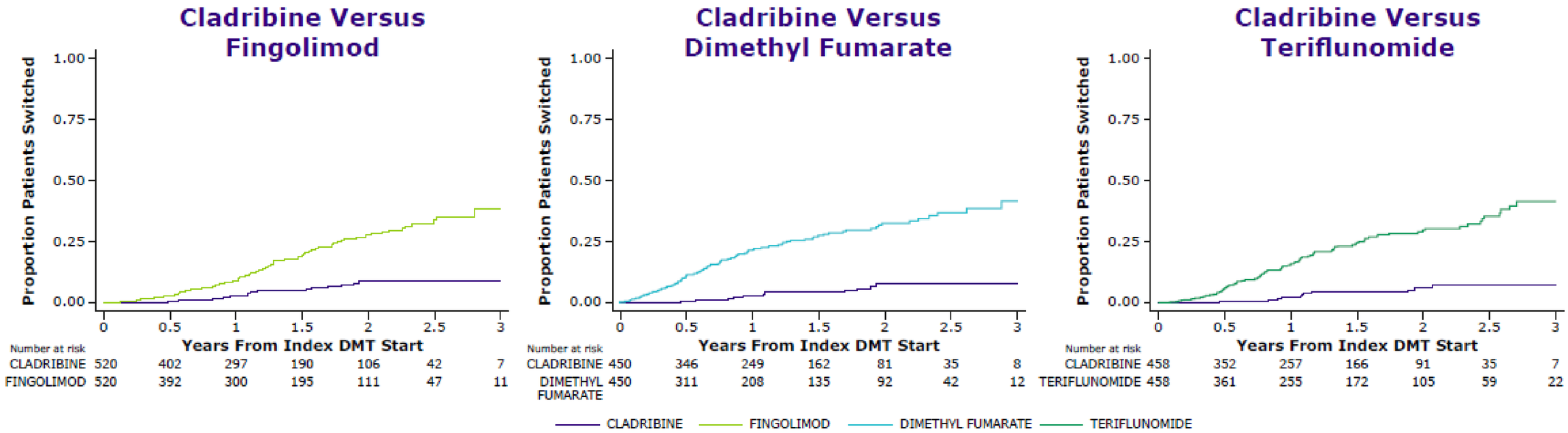
RESULTS

Figure 3. Time-to-Treatment Switch



	Cladribine versus fingolimod (n=520)	Cladribine versus dimethyl fumarate (n=450)	Cladribine versus teriflunomide (n=458)
HR (95% CI)	4.00 (2.54, 6.32)	7.04 (4.16, 11.93)	6.52 (3.79, 11.22)
P-value	<0.001	<0.001	<0.001

CI, confidence interval; **DMT**, disease-modifying therapy; **HR**, hazard ratio

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CONCLUSIONS

- **For all three pairwise comparisons, relapse and discontinuation outcomes significantly favoured cladribine tablets over other oral DMTs.**
- **Future analyses with longer follow-up comparing disability progression events are warranted.**

DMT, disease-modifying therapy

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