

A plain language summary on the effectiveness of cladribine tablets compared with other oral treatments for multiple sclerosis: results from the MSBase registry

Tim Spelman¹, Serkan Ozakbas², Raed Alroughani³, Murat Terzi⁴, Suzanne Hodgkinson⁵, Guy Laureys⁶, Tomas Kalincik^{7,8}, Anneke Van Der Walt⁹, Bassem Yamout^{10,11}, Jeannette Lechner-Scott^{12,13}, Aysun Soysal¹⁴, Jens Kuhle^{15,16}, Jose Luis Sanchez-Menoyo¹⁷, Yolanda Blanco Morgado¹⁸, Daniele LA Spitaleri¹⁹, Vincent van Pesch²⁰, Dana Horakova²¹, Radek Ampapa²², Francesco Patti²³, Richard Macdonell²⁴, Abdullah Al-Asmi²⁵, Oliver Gerlach^{26,27}, Jiwon Oh²⁸, Ayse Altintas²⁹, Namita Tundia³⁰, Schiffron L Wong³⁰ & Helmut Butzkueven^{1,9}; MSBase Study Group

¹MSBase Foundation, Melbourne, Australia; ²Dokuz Eylul University, Izmir, Turkey; ³Amiri Hospital, Sharq, Kuwait; ⁴Department of Neurology, 19 Mayıs University, Samsun, Turkey; ⁵Liverpool Hospital, Sydney, Australia; ⁶University Hospital Ghent, Ghent, Belgium; ⁷MS Centre, Department of Neurology, Royal Melbourne Hospital, Melbourne, Australia; ⁸CORE, Department of Medicine, University of Melbourne, Melbourne, Australia; ⁹Department of Neuroscience, Central Clinical School, Monash University, Melbourne, Australia; ¹⁰Neurology Institute, Harley Street Medical Center, Abu Dhabi, United Arab Emirates; ¹¹American University of Beirut Medical Center, Beirut, Lebanon; ¹²School of Medicine and Public Health, University of Newcastle, Newcastle, Australia; ¹³Department of Neurology, John Hunter Hospital, Hunter New England Health, Newcastle, Australia; ¹⁴Bakirkoy Education and Research Hospital for Psychiatric and Neurological Diseases, Istanbul, Turkey; ¹⁵Multiple Sclerosis Centre, Neurology, Departments of Head, Spine and Neuromedicine, Biomedicine and Clinical Research, University Hospital Basel and University of Basel, Basel, Switzerland; ¹⁶Research Center for Clinical Neuroimmunology and Neuroscience (RC2NB), University Hospital and University of Basel, Switzerland; ¹⁷Department of Neurology, Galdakao-Usansolo University Hospital, Osakidetza-Basque Health Service, Biocruces-Bizkaia Health Research Institute, Galdakao, Spain; ¹⁸Center of Neuroimmunology, Service of Neurology, Hospital Clinic de Barcelona, Barcelona, Spain; ¹⁹Azienda Ospedaliera di Rilievo Nazionale San Giuseppe Moscati Avellino, Avellino, Italy; ²⁰Cliniques Universitaires Saint-Luc, UCLouvain, Brussels, Belgium; ²¹Department of Neurology and Center of Clinical Neuroscience, First Faculty of Medicine, Charles University in Prague and General University Hospital, Prague, Czech Republic; ²²Nemocnice Jihlava, Jihlava, Czech Republic; ²³Department of Medical and Surgical Sciences and Advanced Technologies, GF Ingrassia, Catania, Italy; ²⁴Department of Neurology, Austin Health, Melbourne, Australia; ²⁵Neurology Unit, Department of Medicine, College of Medicine & Health Sciences and Sultan Qaboos University Hospital, SQU, Al Khodh, Oman; ²⁶Academic MS Center Zuyderland, Department of Neurology, Zuyderland Medical Center, Sittard-Geleen, The Netherlands; ²⁷School for Mental Health and Neuroscience, Maastricht University, Maastricht, The Netherlands; ²⁸Division of Neurology, St Michael's Hospital, University of Toronto, Toronto, Canada; ²⁹Koc University School of Medicine and Koc University Research Center for Translational Medicine (KUTTAM) Istanbul, Turkey; ³⁰EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA

First draft submitted: 24 February 2023; Accepted for publication: 22 May 2023; Published online: TBC

Summary

What is this summary about?

Patient registries contain anonymous data from people who share the same medical condition. The MSBase registry contains information from over 80,000 people living with multiple sclerosis (MS) across 41 countries.

Using information from the MSBase registry, the GLIMPSE (Generating Learnings In MultiPle Sclerosis) study looked at **real-life outcomes** in 3475 people living with MS who were treated with cladribine tablets (Mavenclad®) compared with other oral treatments.

What were the results?

Results showed that people treated with cladribine tablets stayed on treatment for longer than other treatments given by mouth. They also had fewer relapses (also called flare ups of symptoms) than people who received a different oral treatment for their MS.

What do the results mean?

The results provide evidence that, compared with other oral treatments for MS, cladribine tablets are an effective medicine for people living with MS.

How to say (double click sound icon to play sound)...

- **Cladribine:** CLAD-ree-BEEN
- **Dimethyl fumarate:** DIE-me-thigh-el FU-mur-ate
- **Fingolimod:** FING-oh-lee-MOD
- **Multiple sclerosis:** MUHL-tuh-pl sklr-OW-suhs
- **Myelin:** Mai-UH-lin
- **Ocrelizumab:** Ock-ree-LEE-zoo-mab
- **Teriflunomide:** TEH-ree-FLEW-no-mide

Real-life outcomes: Real-life outcomes means that these people were not participating in a clinical trial and were receiving treatment as part of their usual care.

Who sponsored this summary?

Financial support for this summary was provided entirely by a contract with EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA (CrossRef Funder ID: 10.13039/100004755).

Who should read this article?

The authors of the original publication developed this summary to help people living with MS, their caregivers, healthcare professionals, and patient advocates to understand the results of their study.

What is multiple sclerosis?

- Multiple sclerosis (also known as MS) is a potentially disabling disease where the body's own immune cells (the body's own defence cells) attack the **central nervous system** (CNS). The reasons why this happens are not yet understood.
- Specifically, immune cells damage the CNS by attacking the nerves and the fatty covering (known as myelin) that protect the nerves. This means it is more difficult for nerve signals to travel through the body in someone with MS, resulting in a range of possible symptoms.
- For example, people living with MS may experience problems with movement, fatigue (lack of energy), eyesight, or cognition (thinking, learning, and planning). These are just some of the examples of the possible symptoms of MS.

Central nervous system: The central nervous system (CNS) is made up of the brain and spinal cord. The CNS controls most functions of the body through nerves.



Movement



Fatigue



Eyesight



Cognition

- There is currently no cure for MS. However, drug treatments have been proven to help modify the disease course and manage symptoms.
- There are different **types of MS**. The most common is called relapsing-remitting MS, which affects around 85% of people first diagnosed with the disease. People living with relapsing-remitting MS have relapses (also called a flare up of symptoms) followed by a period of full or partial recovery.

Types of MS

There are several types of MS that people initially present with or develop over time:

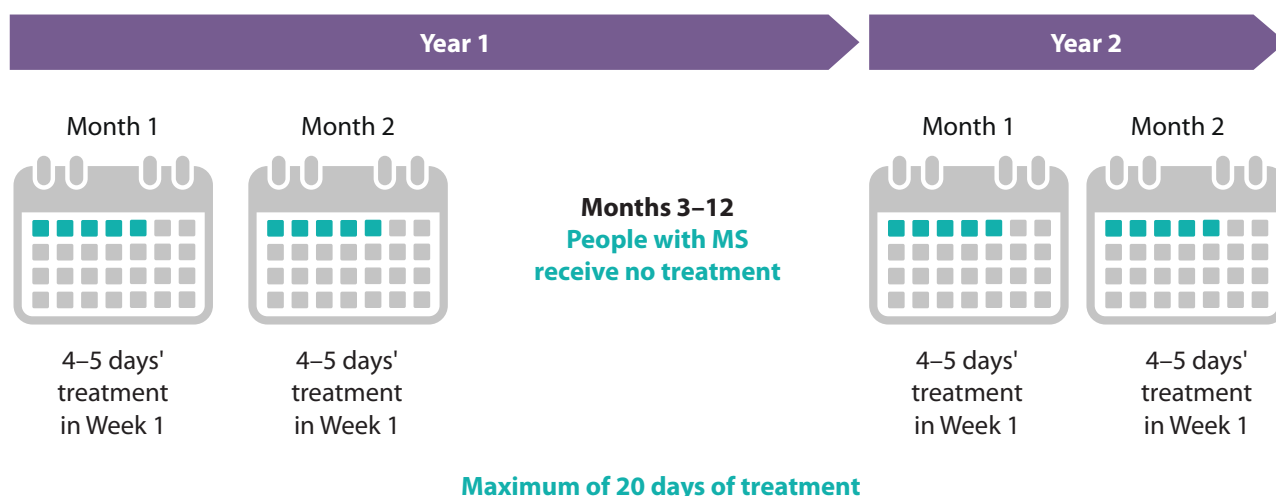
- *Clinically isolated syndrome* is where a person has symptoms relating to the nervous system but has not yet met the full criteria for a diagnosis of MS.
- *Relapsing-remitting MS* is the most common course of MS, where people have relapses of symptoms then a period of full or partial recovery.
- *Secondary-progressive MS* can follow on from relapsing-remitting MS, where disability will increasingly get worse over time with or without relapses.
- *Primary-progressive MS* is a type of MS in which people have worsening disability from the onset of symptoms, without early relapses.

What are cladribine tablets?

- Cladribine tablets (Mavenclad®) are an oral medicine (given by mouth) for treating relapsing types of MS.
- The treatment works by reducing the levels of certain immune cells, called B and T **lymphocytes**.
 - These lymphocytes are thought to be the main immune cells involved in MS, and so MS treatments often target them
- Cladribine tablets are given for a short amount of time followed by a long treatment break. The full course is given as 8–10 days of treatment a year, for two years.
- Studies on cladribine tablets have shown that the treatment is effective at reducing relapses in people living with MS and slows the worsening of their disease.

Lymphocytes: Lymphocytes are types of white blood cells that are part of the immune system. Lymphocytes include B cells, T cells, and natural killer cells. B and T cells work together to fight infections.

Cladribine tablets are administered as two courses, based on the patient's weight, separated by 1 year



Why was the study carried out?



- Several oral treatments have been approved for people living with MS.
- A lot of clinical trials have been performed with treatments for MS. However, it is also important to check how effective they are in real life, for people living with MS.
- In this real-life study, which included patients from January 2018 to August 2021, researchers looked at the effectiveness of cladribine tablets in people living with MS compared with other oral treatments: dimethyl fumarate (Tecfidera®), fingolimod (Gilenya®), and teriflunomide (Aubagio®).
 - Dimethyl fumarate, fingolimod, and teriflunomide are often prescribed for people living with MS who are in the same stage of their disease as those treated with cladribine tablets.

How was the study carried out and who took part in the study?

- The GLIMPSE (Generating Learnings In MultiPle SclErosis) study was based on information from the **MSBase registry**.
- The people who took part in the study were:
 - Around 40 years old
 - Mostly women
 - Typically had relapsing-remitting MS and had experienced MS for around 7 to 12.5 years
- To compare results in groups of people who received different treatments, the researchers used a method called **propensity score matching** (also shortened to PSM). The number of people in each comparison group differed, but within each PSM pair group the numbers were the same.

MSBase registry: The MSBase registry includes 80,000 people living from MS, across 41 countries.

The registry includes anonymous information on people's age and sex, how long they have had MS, what treatment they are using and have tried, and how effective it has been (in terms of relapses and their disability).

Summary of statistical terms

What is propensity score matching?

Propensity score matching (PSM) is a statistical method used by researchers to compare treatment groups. PSM attempts to make comparisons fairer between groups by matching people based on things like age, sex, and disability status. This tries to make sure any comparisons between groups of people are based on the treatment they received, rather than something not related to the drug.

What is meant by median?

The median is the middle number in a list of numbers, sorted from smallest to largest.

What is the hazard ratio?

The hazard ratio compares how often a particular event – such as relapses – happened in one group compared with another group, over time. When the hazard ratio is one it means no difference between the two groups. But a hazard ratio of less than one means that fewer relapses (events) happened in one group compared with another group, over time.

What did the researchers measure?

- How many people remained on their treatment?
 - The proportion of people that stayed on their current MS treatment
- Possibility of having to switch to another treatment from the one they were already taking
 - The likelihood that a person started taking a different medicine for their MS
 - What treatment was switched to, for those that changed their MS treatment
- Annualised relapse rate (ARR) and time to first relapse
 - ARR is the average number of relapses (flare ups of symptoms) a group of people living with MS have in one year
 - Researchers were also interested in the time to first relapse, after starting treatment

What were the results from the study?

3475 people with MS were included in the study



PSM pair populations

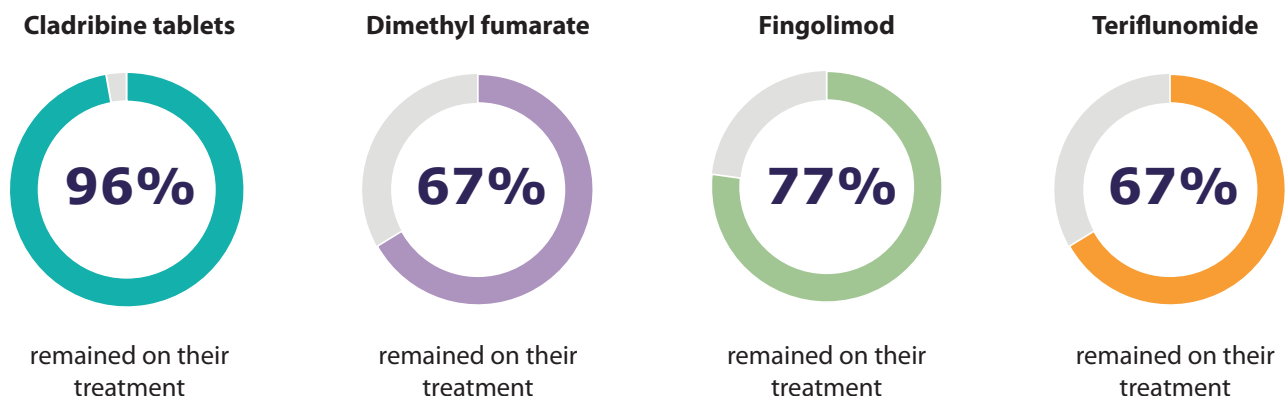


Median length of time that people were studied

Cladribine tablets, 11 months (0.91 years)	Cladribine tablets, 11 months (0.90 years)	Cladribine tablets, 11 months (0.94 years)
Fingolimod, 13 months (1.07 years)	Dimethyl fumarate, 8.5 months (0.71 years)	Teriflunomide, 11 months (0.94 years)

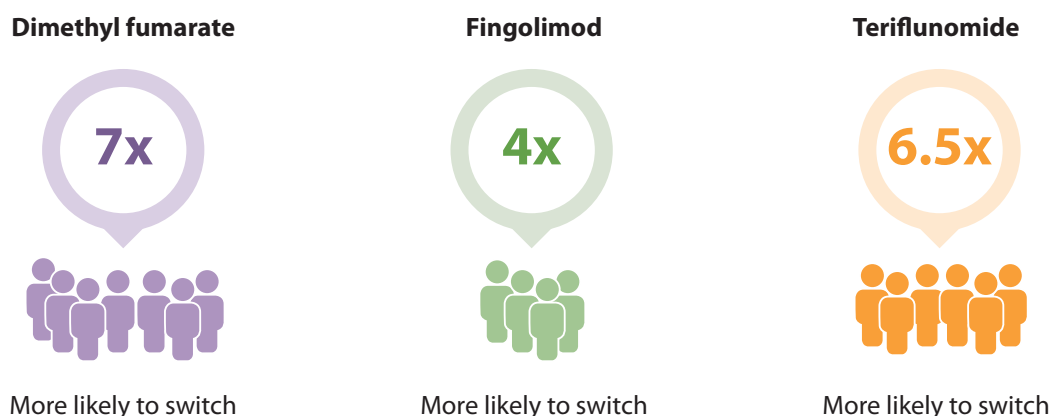
How many people remained on their treatment?

In total, 96% of people who started taking cladribine tablets remained on this treatment for their MS. This was higher than for people taking fingolimod (77%), dimethyl fumarate (67%), or teriflunomide (67%).



Possibility of having to switch to another treatment from the one they were already taking

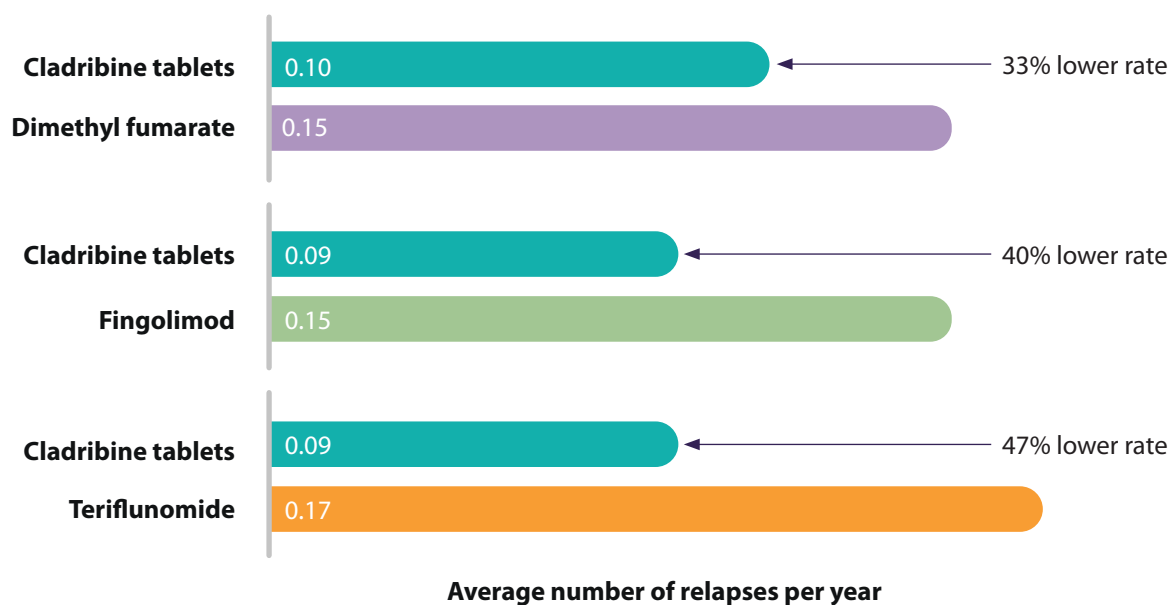
People taking dimethyl fumarate, fingolimod, or teriflunomide were much more likely to have to switch to another medicine than people taking cladribine tablets for their MS.



- In each treatment group, most people who switched treatment started taking ocrelizumab (Ocrevus®; another treatment option for MS that is given by intravenous infusion every 6 months).
- For people taking dimethyl fumarate, fingolimod, or teriflunomide, the most common reasons for switching treatment were adverse events (side effects of the medication) or that their MS symptoms did not improve.

ARR and time to first relapse

People taking cladribine tablets were less likely to have a relapse than people taking other oral treatments for their MS.



- Based on hazard ratios, people taking cladribine tablets also had a higher likelihood of staying relapse free over time than people taking other oral treatments for MS. The time to first relapse when taking cladribine tablets was longer compared with taking:
 - Dimethyl fumarate (hazard ratio, 0.58)
 - Fingolimod (hazard ratio, 0.60)
 - Teriflunomide (hazard ratio, 0.33)

What do the results of this study mean for people with MS?

The findings provide evidence that, compared with other oral treatments for MS, cladribine tablets are an effective medicine for people living with MS. This is based on the following findings for real-life outcomes:



- People taking cladribine tablets were less likely to either switch to another medicine for their MS or stop taking their medicine than people taking other oral treatments for their MS.
- People taking cladribine tablets were less likely to have a relapse, and took longer to have their next relapse, than people taking other oral treatments for their MS.

Where can readers find more information on this study?

- This is a summary of an article called “Comparative effectiveness of cladribine tablets versus other oral disease-modifying treatments for multiple sclerosis: results from MSBase registry”, originally published in *Multiple Sclerosis Journal*. You can read the full article [here](#).
- The original publication citation is: Spelman T, Ozakbas S, Alroughani R *et al*. Comparative effectiveness of cladribine tablets versus other oral disease-modifying treatments for multiple sclerosis: results from MSBase registry. *Mult. Scleros. J.* 29(2), 221–235 (2023); doi: 10.1177/13524585221137502.

Educational resources

- Read more about multiple sclerosis, including symptoms and criteria for diagnosis, treatment options, and general support for those living with multiple sclerosis, at these websites:
 - National Multiple Sclerosis Society available at: <https://www.nationalmssociety.org>
 - Multiple Sclerosis Trust available at: <https://mstrust.org.uk/>

Financial & competing interests disclosure

Full author disclosure and ethical information can be found in the original article. The authors had full control of this summary and provided their final approval of all content.

Plain language summary writing and editorial support was provided by Joseph Ward and Steve Winter of inScience Communications, Springer Healthcare Ltd, UK, and was funded by Merck.