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Improvements in quality of life of people with relapsing multiple sclerosis treated with cladribine tablets during the 2-year CLARIFY-MS study: a plain language summary

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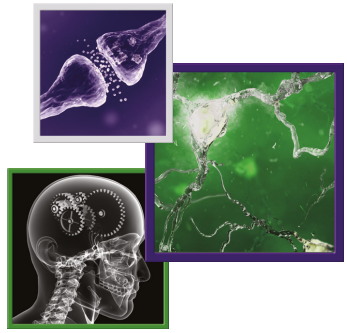
Neurodegenerative Disease Management

Improvements in quality of life of people with relapsing multiple sclerosis treated with cladribine tablets during the 2-year CLARIFY-MS study: a plain language summary



Bruno Brochet[a*], Alessandra Solari[b], Jeannette Lechner-Scott[c,d], Fredrik Piehl[e], Dawn Langdon[f], Raymond Hupperts[g], Krzysztof Selmaj[h,i], Francesco Patti[j], Luis Brieva[k], Eva Maria Maida[l], Nektaria Alexandri[m], Andrzej Smyk[m], Axel Nolting[m], Xavier Montalban[n] and Eva Kubala Havrdova[o] on behalf of the CLARIFY-MS Investigators
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Where can I find the original article on which this summary is based?

The original article is called 'Improvements in quality of life over 2 years with cladribine tablets in people with relapsing multiple sclerosis: The CLARIFY-MS study'. You can read the original article published in the *Multiple Sclerosis Journal* for free at: https://doi.org/10.1177/13524585231205962

Summary

What is this summary about?
This article summarises the findings from the CLARIFY-MS study. Cladribine tablets are an oral medication for the treatment of **relapsing multiple sclerosis (MS)**. The exact number of tablets and number of days depends on the person's body weight. In the CLARIFY-MS study, researchers investigated whether treatment with cladribine tablets improved the health-related quality of life of people with highly active relapsing MS over a 2-year period. Most of the participants (348/482, 72%) were previously treated with other MS disease-modifying treatments (DMTs) before starting treatment with cladribine tablets in this study.

What were the results?
Treatment with cladribine tablets significantly improved the health-related quality of life of the participants over the 2-year study period. Similar level of improvement in health-related quality of life was seen in participants who had previously been treated with other MS DMTs and in those who had not. Safety findings were also similar to previously reported data for cladribine tablets. No cases of the most severe grade of reduction in lymphocyte counts (grade 4; severely compromised immune system) were recorded.

What do the results mean?
Treatment with cladribine tablets improves the health-related quality of life of people with highly active relapsing MS regardless of whether they received or did not receive DMTs for MS before cladribine tablets treatment.

How to say (download PDF and double click sound icon to play sound)...

- **Cladribine:** CLAD-ree-BEEN
- **Multiple sclerosis:** MUHL-tuh-puhl sklr-OW-suhs
- **Relapse:** RE-lapse
- **Lymphocyte:** Lim-foh-site
- **Interferon:** In-ter-feer-on
- **Dimethyl fumarate:** DIE-me-thigh-el FU-mur-ate
- **Glatiramer acetate:** gluh-TEER-uh-mer as-uh-tayt
- **Teriflunomide:** TEH-ree-FLEW-no-mide
- **Fingolimod:** FING-oh-lee-MOD

Relapsing MS: A chronic disease that is caused by the immune system when it attacks healthy cells in the brain and spinal cord by mistake. People with MS can experience a 'relapse'. These are new MS symptoms or existing symptoms that worsen over 24 hours or longer.

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What is the purpose of this plain language summary?

The purpose of this plain language summary is to help you to understand the findings from recent research. The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence, and not on the results of a single study.

Who is this article for?

The authors of the original publication created this summary to help people with MS, caregivers, patient advocates, healthcare professionals, policy makers, and insurance providers understand the results of this study.

Who sponsored this study?

The CLARIFY-MS study was **sponsored** by Merck (CrossRef Funder ID: 10.13039/100009945).

Sponsor: A company or organisation that oversees and pays for a clinical research study. The sponsor also collects and analyses the information from the study.

What is multiple sclerosis (MS)?

MS is an autoimmune condition, in which the body's immune system mistakenly causes damage to the nerve cells in the brain and spinal cord. The possible symptoms of MS include: difficulty in walking, fatigue (feeling tired), vision problems, problems controlling the bladder, numbness or tingling in different parts of the body, muscle stiffness and spasms, problems with balance and coordination, problems with thinking, learning, and planning.

The challenges faced by people with MS due to their disease, such as aggravating symptoms, development and worsening of disability, and other coexisting conditions (such as depression, anxiety and high blood pressure), may have detrimental effects on their health-related quality of life, gradually impacting their family, social, and work life.

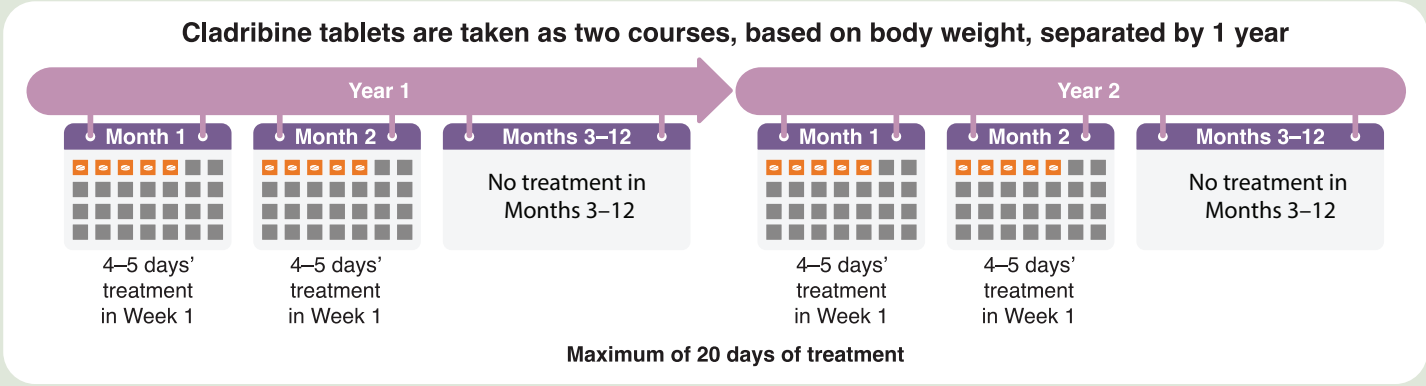
What are cladribine tablets?

There are many treatments available for MS to manage disease activity, some of which are taken orally while others are taken by injection or as **infusions**.

Infusion: A type of treatment that delivers the medication in a liquid form directly into a person's bloodstream via a small tube or needle placed in a vein.

Cladribine tablets are a type of medication taken orally for the treatment of relapsing MS. The recommended total dose of cladribine tablets is 3.5mg/kg body weight over 2 years, taken as 1 treatment course of 1.75mg/kg per year. Each treatment course consists of 2 treatment weeks, 1 at the beginning of the first month and 1 at the beginning of the second month. During each treatment week, people with MS take tablets for 4 or 5 days. The exact number of tablets and number of days depends on the person's body weight.

Overall, people with MS take the tablets for up to 20 days over 2 years.



Treatment with cladribine tablets is associated with improvements in mobility, activity, pain and anxiety reduction, and the ability of people with MS to look after themselves.

Why was the study carried out?

Health-related quality of life is the patient's perception of the effect of illness and treatment on the physical, psychological, and social aspects of life. Such assessments provide additional information about the benefits and risks of medications.

CLARIFY-MS was a 2-year, **single-arm, phase IV**, multicentre study that looked at improvements in the health-related quality of life of people with highly active relapsing MS treated with cladribine tablets.

In addition to clinical responses and **magnetic resonance imaging (MRI)** measurements, improvement in health-related quality of life can be considered an important factor when assessing how efficient and safe a medicine is for the treatment of people with MS. The findings of this study may help people with MS and doctors make the right decisions together and identify the most appropriate treatment option to manage MS.

Single-arm study: A clinical study in which all participants receive the same medication. In CLARIFY-MS, all participants received cladribine tablets for their MS.
Phase IV study: A clinical study that takes place after an investigational medicine is approved by regulatory bodies and can be prescribed to patients.
MRI: A medical imaging method that uses magnetic fields and radio waves to show detailed pictures of the body's internal organs and tissues, including the brain.

Who took part in the study and how was the analysis carried out?

A total of 482 people with highly active relapsing MS participated in the CLARIFY-MS study.

Highly active relapsing MS:
For the purpose of this study, people were considered to have highly active relapsing MS if they had experienced either of the following:

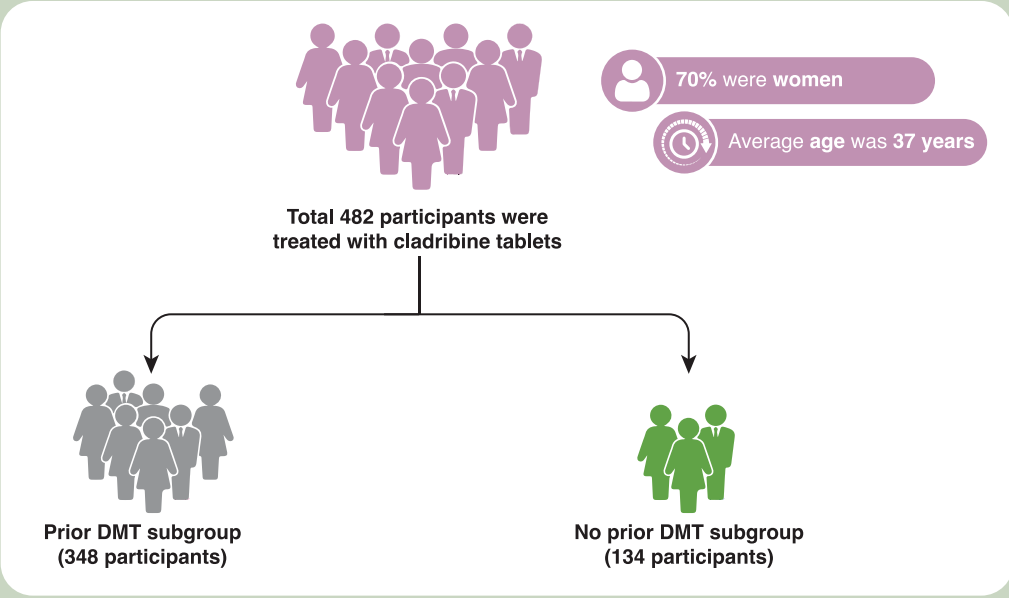
- Two or more relapses during the previous year whether taking any DMTs for MS or not; OR
- One relapse in the previous year, with brain lesions on MRI (areas of abnormality or damage to brain tissue as seen on MRI scans), while taking a DMT for MS

CLARIFY-MS study participant subgroups (based on previous DMT status):

- Prior DMT: Participants who had previously taken a DMT for their MS treatment before entering the CLARIFY-MS study
- No prior DMT: Participants who had never taken a DMT for their MS treatment before entering the study

The 'prior DMT' subgroup included 348 participants, and the 'no prior DMT' subgroup included 134 participants. Most common DMTs taken by the participants before taking cladribine tablets were interferons (injection; 24.1% [84/348 participants]), dimethyl fumarate (tablet; 18.1% [63/348 participants]), glatiramer acetate (injection; 11.8% [41/348 participants]), teriflunomide (tablet; 11.2% [39/348 participants]) and fingolimod (capsule; 10.9% [38/348 participants]).

To understand how well cladribine tablets worked in people with MS to improve their health-related quality of life, the researchers compared the responses of participants in the total population, prior DMT subgroup, and no prior DMT subgroup.



What did the researchers want to find out and what were the findings?

Did the participants experience any benefits with cladribine tablets with respect to their physical and mental health-related quality of life?

Health-related quality of life was assessed using the MS-specific Multiple Sclerosis Quality of Life (MSQoL)-54 questionnaire, which contains 54 items grouped into 14 scales and 2 composite (summary) scores: the Physical Health Composite and the Mental Health Composite. MSQoL-54 scale, and summary scores can range between 0–100, with higher scores indicating higher health-related quality of life.

Findings: The mean MSQoL-54 physical and mental health summary scores for participants significantly improved with cladribine tablets treatment by approximately 4.8 points at Month 24 (end of study) compared with the scores recorded at the start of the study (Baseline). This change was observed in 433 participants whose data were available for this assessment.

MSQoL Item 20 on Social Function:

Question: "During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?"

Answer: Participants to select any one option which describes their condition best:

1. Not at all
2. Slightly
3. Moderately
4. Quite a bit
5. Extremely

The improvements in MSQoL-54 physical and mental health summary scores were considered clinically relevant for more than 40% of the participants. Similar trends were observed in the prior DMT and no prior DMT subgroups.

Clinical relevance was determined by assessing the minimal clinically important difference (MCID).

MCID: The smallest difference in an outcome that would be considered worthwhile by clinicians and patients. In this study, the MCID was considered an improvement of at least 5 points in the MSQoL-54 summary scores.
Mean: The sum of all values in a dataset divided by the number of values. Example: for the data set 3, 5, 7 and 9, the sum of all values is 24 divided by the number of values that is 4 would give a mean value of 6.

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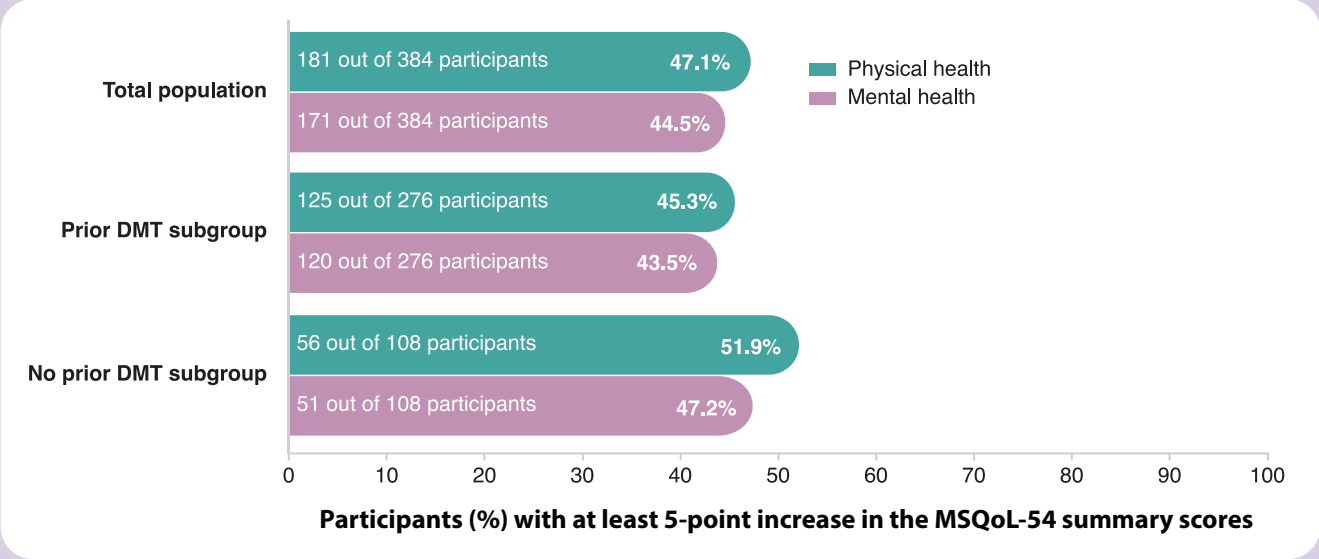
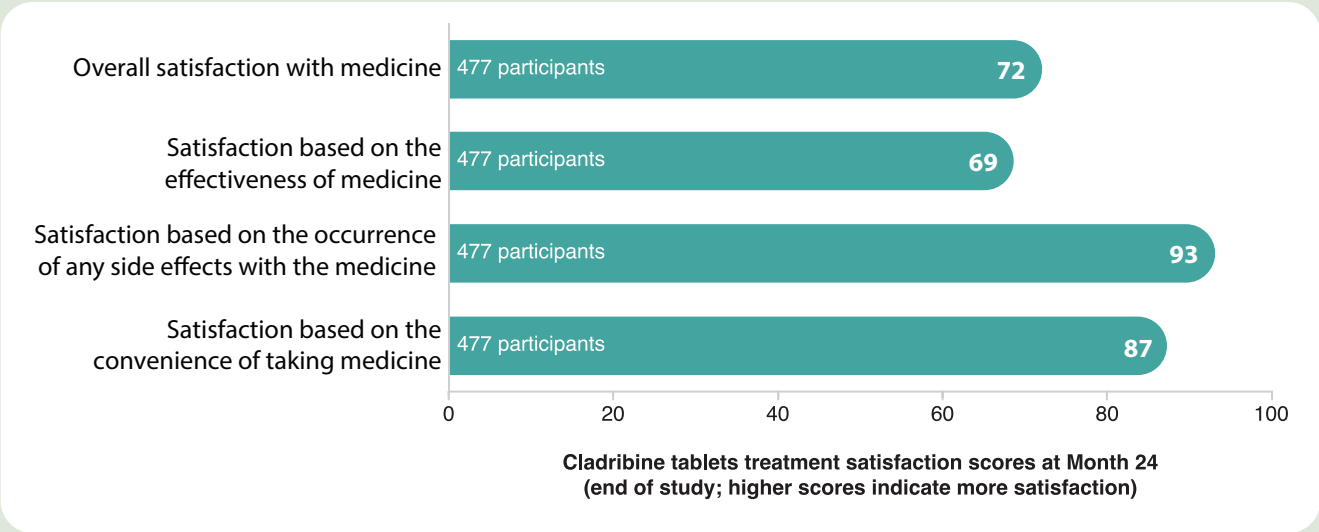


Were the participants satisfied with their cladribine tablets treatment?

To assess satisfaction with treatment, participants completed a questionnaire called the 'Treatment Satisfaction Questionnaire for Medication'. They were asked to score their experience with cladribine tablets in terms of overall satisfaction, effectiveness, side effects (unwanted effects of the medicine on the body), and convenience, on a scale of 0–100, with higher scores indicating better performance.

Findings: Overall, participants were satisfied with the treatment with cladribine tablets. The mean overall satisfaction, effectiveness, side effects and convenience scores also remained similar across different time points in the study.



How many participants experienced a relapse during the study? What were the estimated relapse rates?

The proportion of participants experiencing a **qualifying relapse** was recorded during the study period. To compare between participant groups, the number of relapses during the study period was calculated per person per year (also known as annualised relapse rate, or **ARR**).

Findings: In the total population, 91 out of 482 of the participants (19% of total participants in the study) experienced a qualifying relapse during the study. The rate of qualifying relapses per person per year was low. An ARR of 0.13 overall means that people with MS treated with cladribine tablets in this study could expect 1.3 relapses per person over a 10-year period.

Qualifying relapse: New MS symptoms or existing symptoms that worsen over 24 hours or longer. For symptoms to qualify as a relapse in this study, they must have negatively impacted the participant's disability.
ARR: Is calculated by dividing the total number of relapses by the total number of person-years of follow-up. For example, if 100 people with MS are followed up for one year and experience 50 relapses, the ARR would be 0.5.

Did the participants experience any deterioration in their disability levels during the study?

Disability was examined by looking at changes in disability during the study using the Expanded Disability Status Scale (**EDSS** [score range: 0–10]); higher scores indicate more disability.

EDSS: The EDSS helps measure a person's disability due to MS in terms of walking and moving, muscle strength, balance, speech, swallowing, sensory functions, bowel and bladder functions, eyesight, and memory and thinking.

Findings: The EDSS scores remained stable over time for at least half of the participants in this study, indicating no deterioration in disability levels during the study. An EDSS score of 2.5 indicates that people with MS may experience mild disability in one bodily function or very small disability in two functions.

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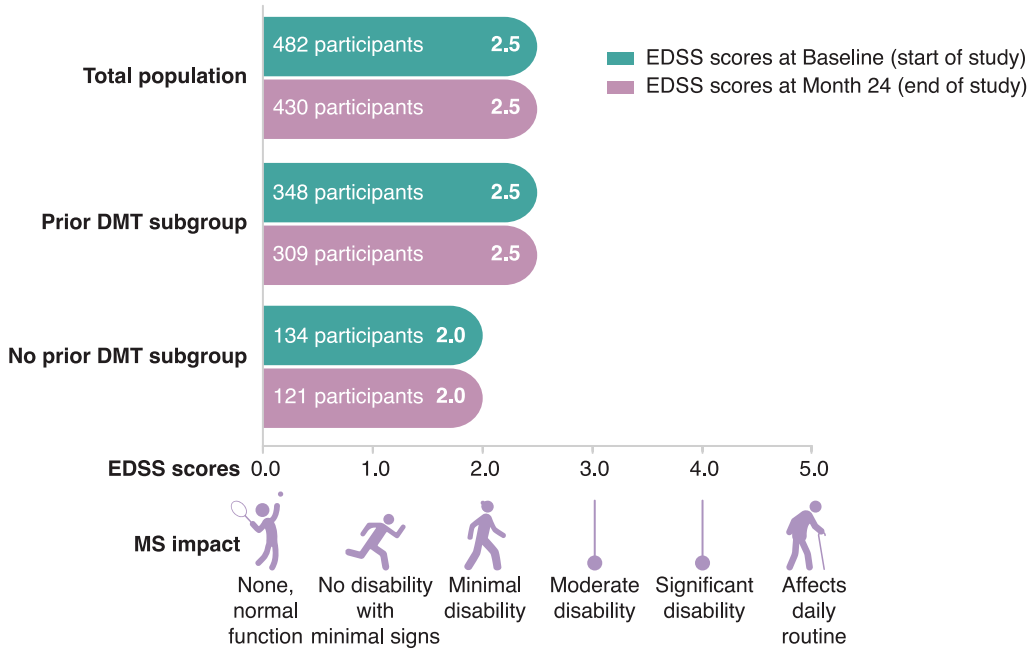

Were there any adverse events associated with the use of cladribine tablets?

The safety profile of cladribine tablets among participants was assessed by recording, reporting, and analysing medical conditions, **adverse events**, and physical examination and blood test findings, including the assessment of **lymphocyte** counts.

Lymphocyte: The body's immune system is made up of different types of cells that protect a person from and help fight off infections. A lymphocyte is a type of white blood cell, which forms a part of the immune system.
Adverse event: Any harmful or negative reaction to medical care or medicines.

Of the 482 participants in the study, 137 (39%) experienced at least one adverse event associated with the use of cladribine tablets. The most common adverse events related to the use of cladribine tablets were headache (21.8% [105/482 participants]), low lymphocyte counts (15.1% [73/482 participants]) and inflammation of nose or throat (13.5% [65/482 participants]). Most of the treatment-related adverse events were mild-to-moderate in nature. None of the participants experienced the most severe grade of reductions in lymphocyte count (grade 4).

What do the results of this study mean?

The results of this study show that treatment with cladribine tablets significantly improved the health-related quality of life of the CLARIFY-MS study participants over the 2-year study period, with similar trends being observed in the prior DMT and no prior DMT subgroups. Safety findings were similar to previously reported data for cladribine tablets. No cases of the most severe grade of reduction in lymphocyte counts were recorded.

These findings suggest that treatment with cladribine tablets may help to improve the health-related quality of life of people with highly active relapsing MS regardless of whether they received or did not receive any DMTs for MS in the past.

Where can readers find more information on this study?

The CLARIFY-MS study was conducted between June 2018 and August 2021. CLARIFY-MS Extension (NCT04776213), a separate follow-up study to the CLARIFY-MS study, was designed to assess the effects of cladribine tablets on cognition and health-related quality of life in people with relapsing MS up to 4 years after the initial dose of cladribine tablets.

This article is a plain language summary of the article titled 'Improvements in quality of life over 2 years with cladribine tablets in people with relapsing multiple sclerosis: The CLARIFY-MS study' which is published in the *Multiple Sclerosis Journal*. To read the original article being summarised, for free, please visit: https://doi.org/10.1177/13524585231205962

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For more information on MS please visit the sites mentioned below:
National Multiple Sclerosis Society: https://www.nationalmssociety.org/
Multiple Sclerosis Trust: https://mstrust.org.uk/about-ms/what-ms/types-ms
For more information on cladribine tablets (trade name MAVENCLAD®) please visit: https://www.mavenclad.com/en
You can read more about the CLARIFY-MS study described here at the following study registration website: CLARIFY-MS study - https://clinicaltrials.gov/ct2/show/NCT03369665
To read the first article on the CLARIFY-MS study, for free, please visit: https://www.sciencedirect.com/science/article/pii/S2211034821006520?via%3Dihub

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