Clinical trial results:
A 2-year extension study to evaluate long-term effectiveness of Mavenclad® in participants who have completed Trial MS700568_0022 (MAGNIFY MS) (Magnify MS Extension)

Summary

EudraCT number	2020-003995-42
Trial protocol	DE CZ HU FI AT PL IT
Global end of trial date	21 September 2023

Results information

Result version number	v1 (current)
This version publication date	06 October 2024
First version publication date	06 October 2024

Trial information

Trial identification

Sponsor protocol code	MS700568_0157

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04783935
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Healthcare KGaA, Darmstadt, Germany
Sponsor organisation address	Frankfurter Strasse 250, Darmstadt, Germany, 64293
Public contact	Communication Centre, Merck Healthcare KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.com
Scientific contact	Communication Center, Merck Healthcare KGaA, Darmstadt, Germany, an affiliate of Merck KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 September 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary purpose of this study was to evaluate the long-term effectiveness of Mavenclad® tablets, in terms of disease activity and safety, in subjects with highly active relapsing multiple sclerosis (RMS) previously participating in the MAGNIFY MS trial MS700568_0022 (NCT03364036).

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	Czechia: 78
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	Israel: 10
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	Australia: 7
Worldwide total number of subjects	219
EEA total number of subjects	173

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	219
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The primary purpose of this study was to evaluate the long-term effectiveness of Mavenclad® tablets, in terms of disease activity and safety, in subjects with highly active relapsing multiple sclerosis (RMS) previously participating in the MAGNIFY MS trial MS700568_0022 (NCT03364036).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Cladribine

Arm description:

Subjects received oral Cladribine (tradename MavencladÂ®) over 2 years, administered as 1 treatment course of 1.75 mg/kg body weight per year in MAGNIFY MS study. The treatment course consists of 2 treatment weeks, one at the beginning of the first month and one at the beginning of the second month of the respective treatment year. Each treatment week consists of 4 or 5 days on which a patient receives 10 mg or 20 mg (one or two tablets) as a single daily dose, depending on body weight.

Arm type	Experimental
Investigational medicinal product name	Mavenclad
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Oral tablets

Number of subjects in period 1	Cladribine
Started	219
Completed	206
Not completed	13
Consent withdrawn by subject	6
PROGRESSIVE DISEASE	2
PATIENT HAS MOVED AND GOES TO ANOTHER HOSPITAL	1
Lost to follow-up	3
PROTOCOL NON-COMPLIANCE	1

Baseline characteristics

Reporting groups	
Reporting group title	Cladribine
Reporting group description:	
Subjects received oral Cladribine (tradename MavencladÂ®) over 2 years, administered as 1 treatment course of 1.75 mg/kg body weight per year in MAGNIFY MS study. The treatment course consists of 2 treatment weeks, one at the beginning of the first month and one at the beginning of the second month of the respective treatment year. Each treatment week consists of 4 or 5 days on which a patient receives 10 mg or 20 mg (one or two tablets) as a single daily dose, depending on body weight.	

Reporting group values	Cladribine	Total	
Number of subjects	219	219	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	219	219	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	40		
standard deviation	± 9.5	-	
Sex: Female, Male Units: subjects			
Female	142	142	
Male	77	77	
Race Units: Subjects			
Race-Asian	2	2	
Race-Black or African American	1	1	
Race-Other	6	6	
Race-Unknown or Not Reported	26	26	
Race-White	184	184	

End points

End points reporting groups

Reporting group title	Cladribine

Reporting group description:

Subjects received oral Cladribine (tradename MavencladÂ®) over 2 years, administered as 1 treatment course of 1.75 mg/kg body weight per year in MAGNIFY MS study. The treatment course consists of 2 treatment weeks, one at the beginning of the first month and one at the beginning of the second month of the respective treatment year. Each treatment week consists of 4 or 5 days on which a patient receives 10 mg or 20 mg (one or two tablets) as a single daily dose, depending on body weight.

Primary: Percentage of Participants with No Evidence of Disease Activity (Three Parameter [NEDA-3]) During Year 3 to 4

End point title	Percentage of Participants with No Evidence of Disease Activity (Three Parameter [NEDA-3]) During Year 3 to 4[1]

End point description:

The definition of NEDA-3 encompasses a combination of the following 3 related measures of disease activity: No relapses, no confirmed disability progression sustained for 12 weeks as measured on EDSS, and no magnetic resonance imaging (MRI) disease activity, defined as no gadolinium-enhancing (GdE) lesions and no new or enlarging T2 lesions. NEDA-3 was analyzed with the Kaplan-Meier (KM) time-to-event method to reduce the impact of unknown/missing information. The Full Analysis Set included all enrolled, eligible subjects.

End point type	Primary

End point timeframe:

Year 3 to 4 after the initial dose of Mavenclad® tablets in parent study

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical and comparison analysis were performed in single arm for this endpoint.

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219			
Units: percentage of subjects				
number (confidence interval 95%)	54.23 (47.26 to 60.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with No Evidence of Disease Activity (Three Parameter [NEDA-3]) at Year 3 and 4

End point title	Percentage of Participants with No Evidence of Disease Activity (Three Parameter [NEDA-3]) at Year 3 and 4

End point description:

The definition of NEDA-3 encompasses a combination of the following 3 related measures of disease activity: No relapses, no confirmed disability progression sustained for 12 weeks as measured on EDSS, and no magnetic resonance imaging (MRI) disease activity, defined as no gadolinium-enhancing (GdE) lesions and no new or enlarging T2 lesions. NEDA-3 was analyzed with the Kaplan-Meier (KM) time-to-event method to reduce the impact of unknown/missing information.

End point type	Secondary

End point timeframe:

At Year 3 and 4 after the initial dose of Mavenclad® tablets in parent study

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219			
Units: percentage of participants				
number (confidence interval 95%)				
At Year 3	81.63 (75.71 to 86.23)			
At Year 4	79.20 (72.30 to 84.56)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with No Evidence of Disease Activity (Three Parameter [NEDA-3]) After the Start of Study Treatment During the Parent Study until the End of Year 3 and 4

End point title	Percentage of Participants with No Evidence of Disease Activity (Three Parameter [NEDA-3]) After the Start of Study Treatment During the Parent Study until the End of Year 3 and 4

End point description:

The definition of NEDA-3 encompasses a combination of the following 3 related measures of disease activity: No relapses, no confirmed disability progression sustained for 12 weeks as measured on EDSS, and no magnetic resonance imaging (MRI) disease activity, defined as no gadolinium-enhancing (GdE) lesions and no new or enlarging T2 lesions. NEDA-3 was analyzed with the Kaplan-Meier (KM) time-to-event method to reduce the impact of unknown/missing information.

End point type	Secondary

End point timeframe:

After the initial dose of Mavenclad® tablets in parent study until the end of Year 3 and 4

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219			
Units: percentage of participants				
number (confidence interval 95%)				
Up to Year 3	31.89 (25.81 to 38.11)			
Up to Year 4	26.72 (21.03 to 32.74)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Remaining Three Parameter No Evidence of Disease Activity (NEDA-3) During Year 3 or 4 among those with NEDA-3 During Year 1 or 2

End point title	Percentage of Participants Remaining Three Parameter No Evidence of Disease Activity (NEDA-3) During Year 3 or 4 among those with NEDA-3 During Year 1 or 2

End point description:

The definition of NEDA-3 encompasses a combination of the following 3 related measures of disease activity: No relapses, no confirmed disability progression sustained for 12 weeks as measured on EDSS, and no magnetic resonance imaging (MRI) disease activity, defined as no gadolinium-enhancing (GdE) lesions and no new or enlarging T2 lesions. NEDA-3 was analyzed with the Kaplan-Meier (KM) time-to-event method to reduce the impact of unknown/missing information.

End point type	Secondary

End point timeframe:

At Year 3 and 4 after the initial dose of Mavenclad® tablets in parent study

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219			
Units: percentage of participants				
number (confidence interval 95%)				
NEDA During Year 1	92.93 (83.82 to 97.00)			
NEDA During Year 2	81.92 (72.95 to 88.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Second Qualifying Relapse During Parent and Extension Study Period

End point title	Time to Second Qualifying Relapse During Parent and Extension Study Period

End point description:

A qualifying relapse is defined as new, worsening or recurrent neurological symptoms attributed to Multiple Sclerosis (MS) that last for at least 24 hours without fever or infection, or adverse reaction to prescribed medication, preceded by a stable or improving neurological status of at least 30 days.

End point type	Secondary

End point timeframe:

From the initial dose of Mavenclad® tablets in parent study until the end of extension study (approximately 4 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219[2]			
Units: months				
median (confidence interval 95%)	9.99999 (9.99999 to 9.99999)			

Notes:

[2] - 9.99999 denotes values not calculable as fewer than 50% of participants experienced an event.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Qualifying Relapse During Parent and Extension Study Period

End point title	Time to First Qualifying Relapse During Parent and Extension Study Period

End point description:

A qualifying relapse is defined as new, worsening or recurrent neurological symptoms attributed to Multiple Sclerosis (MS) that last for at least 24 hours without fever or infection, or adverse reaction to prescribed medication, preceded by a stable or improving neurological status of at least 30 days.

End point type	Secondary

End point timeframe:

From the initial dose of Mavenclad® tablets in parent study until the end of extension study (approximately 4 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219[3]			
Units: Months				
median (confidence interval 95%)	9.99999 (9.99999 to 9.99999)			

Notes:

[3] - 9.99999 denotes values not calculable as fewer than 50% of participants experienced an event.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Disease Activity During up to Parent and Extension study Period (4 Years)

End point title	Time to First Disease Activity During up to Parent and Extension study Period (4 Years)

End point description:

Time to first disease activity is defined as the time to first occurrence of either qualifying relapse, or 6MCDP, or new or enlarging T2-hyperintense lesions (active T2 lesions), or new T1 Gd+ lesions.

End point type	Secondary

End point timeframe:

From the initial dose of Mavenclad® tablets in parent study until the end of extension study (approximately 4 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219			
Units: months				
median (confidence interval 95%)	6.14 (6.05 to 11.70)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Disease Activity During Extension Study Period (Year 3 and 4)

End point title	Time to First Disease Activity During Extension Study Period (Year 3 and 4)

End point description:

Time to first disease activity is defined as the time to first occurrence of either qualifying relapse, or 6-month confirmed disability progression (6mCDP), or new or enlarging T2-hyperintense lesions (active T2 lesions), or new T1 Gd+ lesions.

End point type	Secondary

End point timeframe:

From Month 24 after the initial dose of Mavenclad tablets in parent study until the end of extension study (approximately 2 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219			
Units: months				
median (confidence interval 95%)	24.05 (19.91 to 24.41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Treatment Start with Other Disease Modifying Drugs (DMDs) During Parent and Extension Study Period

End point title	Time to Treatment Start with Other Disease Modifying Drugs (DMDs) During Parent and Extension Study Period

End point description:

End point type	Secondary

End point timeframe:

From the initial dose of Mavenclad® tablets in parent study until the end of extension study (approximately 4 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219[4]			
Units: months				
median (confidence interval 95%)	9.99999 (9.99999 to 9.99999)			

Notes:

[4] - 9.99999 denotes values not calculable as fewer than 50% of participants experienced an event.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First New T1 Gadolinium Enhancing (Gd+) Lesion During Parent and Extension Study Period

End point title	Time to First New T1 Gadolinium Enhancing (Gd+) Lesion During Parent and Extension Study Period

End point description:

Time taken for newly enlarging T1 Gadolinium Enhancing (Gd+) Lesion to show up is measured by follow-up MRI.

End point type	Secondary

End point timeframe:

From the initial dose of Mavenclad® tablets in parent study until the end of extension study (approximately 4 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219[5]			
Units: months				
median (confidence interval 95%)	99999 (50.73 to 99999)			

Notes:

[5] - 99999 denotes values not calculable as fewer than 50% of participants experienced an event.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Confirmed Disability Progression (CDP) as measured by Expanded Disability Status Scale (EDSS) During Parent and Extension Study Period

End point title	Time to First Confirmed Disability Progression (CDP) as measured by Expanded Disability Status Scale (EDSS) During Parent and Extension Study Period

End point description:

The EDSS is an ordinal clinical rating scale in half-point increments. It assesses the following eight functional systems, areas of the central nervous system that control bodily functions: Pyramidal (ability to walk), Cerebellar (coordination), Brain stem (speech and swallowing), Sensory (touch and pain), Bowel and bladder functions, Visual, Mental, Other (includes any other neurological findings due to Multiple Sclerosis [MS]). EDSS overall score ranging from 0 (normal) to 10 (death due to MS). The 6MCDP during Extension Study Period is defined as sustained increase in EDSS score that started during the Period. Six-month CDP was considered.

End point type	Secondary

End point timeframe:

From the initial dose of Mavenclad® tablets in parent study until the end of extension study (approximately 4 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219[6]			
Units: months				
median (confidence interval 95%)	9.99999 (9.99999 to 9.99999)			

Notes:

[6] - 9.99999 denotes values not calculable as fewer than 50% of participants experienced an event.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First New or Enlarging T2 Lesion During Extension Study Period

End point title	Time to First New or Enlarging T2 Lesion During Extension Study Period

End point description:

Time taken for newly enlarging T2 lesions to show up is measured by follow-up MRI.

End point type	Secondary

End point timeframe:

From the initial dose of Mavenclad® tablets in parent study until the end of extension study (approximately 4 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219			
Units: months				
median (confidence interval 95%)	6.41 (6.05 to 19.32)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First New T1 Gadolinium Enhancing (Gd+) Lesion During Extension Study Period

End point title	Time to First New T1 Gadolinium Enhancing (Gd+) Lesion During Extension Study Period

End point description:

Time taken for newly enlarging T1 Gadolinium Enhancing (Gd+) Lesion to show up is measured by follow-up MRI.

End point type	Secondary

End point timeframe:

From Month 24 after the initial dose of Mavenclad® tablets in parent study until the end of extension study (approximately 2 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219[7]			
Units: months				
median (confidence interval 95%)	9.99999 (9.99999 to 9.99999)			

Notes:

[7] - 9.99999 denotes values not calculable as fewer than 50% of participants experienced an event.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant. An AE was any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease

temporally associated with use of a study intervention. A serious adverse event (SAE) was any untoward medical occurrence that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial or prolonged inpatient hospitalization; congenital anomaly/birth defect or was otherwise considered medically important.

End point type	Secondary

End point timeframe:

From Month 24 after the initial dose of Mavenclad tablets in parent study until the end of extension study (approximately 4 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219			
Units: participants				
AEs	142			
Serious AEs	13			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Qualifying Relapse During Extension Study Period

End point title	Time to First Qualifying Relapse During Extension Study Period

End point description:

A qualifying relapse is defined as new, worsening or recurrent neurological symptoms attributed to Multiple Sclerosis (MS) that last for at least 24 hours without fever or infection, or adverse reaction to prescribed medication, preceded by a stable or improving neurological status of at least 30 days.

End point type	Secondary

End point timeframe:

From Month 24 after the initial dose of Mavenclad® tablets in parent study until the end of extension study (approximately 2 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219[8]			
Units: Months				
median (confidence interval 95%)	9.99999 (9.99999 to 9.99999)			

Notes:

[8] - 9.99999 denotes values not calculable as fewer than 50% of participants experienced an event.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Confirmed Disability Progression (CDP) as measured by Expanded Disability Status Scale (EDSS) During Extension Study Period

End point title	Time to First Confirmed Disability Progression (CDP) as measured by Expanded Disability Status Scale (EDSS) During Extension Study Period

End point description:

he EDSS is an ordinal clinical rating scale in half-point increments. It assesses the following eight functional systems, areas of the central nervous system that control bodily functions: Pyramidal (ability to walk), Cerebellar (coordination), Brain stem (speech and swallowing), Sensory (touch and pain), Bowel and bladder functions, Visual, Mental, Other (includes any other neurological findings due to Multiple Sclerosis [MS]). EDSS overall score ranging from 0 (normal) to 10 (death due to MS) The 6MCDP during Extension Study Period is defined as sustained increase in EDSS score that started during the Period. Six-month CDP was considered.

End point type	Secondary

End point timeframe:

From Month 24 after the initial dose of Mavenclad® tablets in parent study until the end of extension study (approximately 2 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219[9]			
Units: months				
median (confidence interval 95%)	9.99999 (9.99999 to 9.99999)			

Notes:

[9] - 9.99999 denotes values not calculable as fewer than 50% of participants experienced an event.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Treatment Start with Other Disease Modifying Drugs (DMDs) During Extension Study Period

End point title	Time to Treatment Start with Other Disease Modifying Drugs (DMDs) During Extension Study Period

End point description:

End point type	Secondary

End point timeframe:

From Month 24 after the initial dose of Mavenclad® tablets in parent study until the end of extension study (approximately 2 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219[10]			
Units: months				
median (confidence interval 95%)	9.99999 (9.99999 to 9.99999)			

Notes:

[10] - 9.99999 denotes values not calculable as fewer than 50% of participants experienced an event.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Recurrent Qualifying Relapse During Extension Study Period

End point title	Time to Recurrent Qualifying Relapse During Extension Study Period

End point description:

A qualifying relapse is defined as new, worsening or recurrent neurological symptoms attributed to Multiple Sclerosis (MS) that last for at least 24 hours without fever or infection, or adverse reaction to prescribed medication, preceded by a stable or improving neurological status of at least 30 days.

End point type	Secondary

End point timeframe:

From Month 24 after the initial dose of Mavenclad® tablets in parent study until the end of extension study (approximately 2 years)

End point values	Cladribine			
Subject group type	Reporting group			
Number of subjects analysed	219[11]			
Units: months				
median (confidence interval 95%)	9.99999 (9.99999 to 9.99999)			

Notes:

[11] - 9.99999 denotes values not calculable as fewer than 50% of participants experienced an event.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Month 24 after the initial dose of Mavenclad tablets in parent study until the end of extension study (approximately 4 years)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Cladribine

Reporting group description:

Participants received oral Cladribine (tradename MavencladÂ®) over 2 years, administered as 1 treatment course of 1.75 mg/kg body weight per year. The treatment course consists of 2 treatment weeks, one at the beginning of the first month and one at the beginning of the second month of the respective treatment year. Each treatment week consists of 4 or 5 days on which a patient receives 10 mg or 20 mg (one or two tablets) as a single daily dose, depending on body weight.

Serious adverse events	Cladribine		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 219 (5.94%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 219 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nodular melanoma			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 219 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Plasma cell myeloma			
alternative dictionary used: MedDRA 26.0			

subjects affected / exposed	1 / 219 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostatic adenoma				
alternative dictionary used: MedDRA 26.0				
subjects affected / exposed	1 / 219 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thyroid neoplasm				
alternative dictionary used: MedDRA 26.0				
subjects affected / exposed	1 / 219 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac failure acute				
alternative dictionary used: MedDRA 26.0				
subjects affected / exposed	1 / 219 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Multiple sclerosis relapse				
alternative dictionary used: MedDRA 26.0				
subjects affected / exposed	1 / 219 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pregnancy, puerperium and perinatal conditions				
Abortion missed				
alternative dictionary used: MedDRA 26.0				
subjects affected / exposed	1 / 219 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Malignant gastrointestinal obstruction				

alternative dictionary used: MedDRA 26.0				
subjects affected / exposed	1 / 219 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
alternative dictionary used: MedDRA 26.0				
subjects affected / exposed	1 / 219 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
alternative dictionary used: MedDRA 26.0				
subjects affected / exposed	1 / 219 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary embolism				
alternative dictionary used: MedDRA 26.0				
subjects affected / exposed	1 / 219 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Intervertebral disc protrusion				
alternative dictionary used: MedDRA 26.0				
subjects affected / exposed	1 / 219 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lumbar spinal stenosis				
alternative dictionary used: MedDRA 26.0				
subjects affected / exposed	1 / 219 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				

Bronchitis			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 219 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 219 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 219 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peritonsillitis			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 219 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peritonitis			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 219 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Cladribine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 219 (36.07%)		
Nervous system disorders			
Headache			
alternative dictionary used: MedDRA 26.0			

subjects affected / exposed	16 / 219 (7.31%)		
occurrences (all)	16		
Infections and infestations			
COVID-19			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	50 / 219 (22.83%)		
occurrences (all)	50		
Influenza			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	11 / 219 (5.02%)		
occurrences (all)	11		
Upper respiratory tract infection			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	12 / 219 (5.48%)		
occurrences (all)	12		
Nasopharyngitis			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	15 / 219 (6.85%)		
occurrences (all)	15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

NEDA-3 may be limited by sparse measurement of EDSS this may have resulted in an overestimation of NEDA-3 rate each year. The 6mCDP needs confirmatory visit however most subjects had only 1 visit during each period which may led to underestimation.

Notes: