



Clinical trial results:

Clarifying the mechanism of action of cladribine in relapsing multiple sclerosis

Summary

EudraCT number	2018-004557-24
Trial protocol	DE
Global end of trial date	23 September 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	UKM17_0056
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Universität Münster
Sponsor organisation address	Schlossplatz 2, Münster, Germany, 48149
Public contact	Coordinating investigator, Universitätsklinikum Münster, Klinik für Neurologie, luisa.klotz@ukmuenster.de
Scientific contact	Coordinating investigator, Universitätsklinikum Münster, Klinik für Neurologie, luisa.klotz@ukmuenster.de

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	15 August 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 September 2024
Global end of trial reached?	Yes
Global end of trial date	23 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Analysis of the T cell receptor repertoire of CD4 and CD8 T cells, and the B cell receptor repertoire of CD19 B cells before and during the first year after onset of cladribine treatment in patients with relapsing-remitting multiple sclerosis (RRMS).

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and the ICH Guidelines in Good Clinical Practice. The study was not started before the competent ethics committee had given a favorable opinion. Written informed consent was obtained from all patients and the study was only conducted as approved by the Ethics committee and the competent authority. Amendments were only implemented after approval.

Background therapy:

If the lymphocyte count dropped below 200 cells/mm³, anti-herpes prophylaxis was considered in accordance with local standard practice for the duration of grade 4 lymphopenia. In the event of infections (e.g. herpes zoster), anti-infective treatment was initiated as clinically indicated.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	28 October 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

24 patients with RRMS were recruited for this study from October 2019 until January 2022.

Pre-assignment

Screening details:

Each patient's eligibility was verified during a screening visit. Informed consent was obtained prior to any clinical procedures performed solely for study-related purposes.

Period 1

Period 1 title	Month 0
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Month 0
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Arm description:

Cladribine-treated patients at month 0.

Arm type	Experimental
Investigational medicinal product name	MAVENCLAD
Investigational medicinal product code	
Other name	Cladribine
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The recommended cumulative dose of MAVENCLAD was 3.5 mg/kg body weight over 2 years, administered as one treatment course of 1.75 mg/kg per year. Each treatment course consisted of two 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 consisted of 4 or 5 days on which a patient received 10 mg or 20 mg (one or two tablets) as a single daily dose, depending on body weight.

Number of subjects in period 1	Month 0
Started	24
Completed	24

Period 2

Period 2 title	Month 3
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Month 3
Arm description: Cladribine-treated patients at month 3.	
Arm type	Experimental
Investigational medicinal product name	MAVENCLAD
Investigational medicinal product code	
Other name	Cladribine
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The recommended cumulative dose of MAVENCLAD was 3.5 mg/kg body weight over 2 years, administered as one treatment course of 1.75 mg/kg per year. Each treatment course consisted of two 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 consisted of 4 or 5 days on which a patient received 10 mg or 20 mg (one or two tablets) as a single daily dose, depending on body weight.

Number of subjects in period 2	Month 3
Started	24
Completed	23
Not completed	1
Consent withdrawn by subject	1

Period 3

Period 3 title	Month 12
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Month 12
Arm description: Cladribine-treated patients at month 12.	
Arm type	Experimental
Investigational medicinal product name	MAVENCLAD
Investigational medicinal product code	
Other name	Cladribine
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The recommended cumulative dose of MAVENCLAD was 3.5 mg/kg body weight over 2 years, administered as one treatment course of 1.75 mg/kg per year. Each treatment course consisted of two 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 consisted of 4 or 5 days on which a patient received 10 mg or 20 mg (one or two tablets) as a single daily dose, depending on body weight.

Number of subjects in period 3	Month 12
Started	23
Completed	23

Period 4

Period 4 title	Month 24
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Month 24
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Arm description:

Cladribine-treated patients at month 24.

Arm type	Experimental
Investigational medicinal product name	MAVENCLAD
Investigational medicinal product code	
Other name	Cladribine
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The recommended cumulative dose of MAVENCLAD was 3.5 mg/kg body weight over 2 years, administered as one treatment course of 1.75 mg/kg per year. Each treatment course consisted of two 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 consisted of 4 or 5 days on which a patient received 10 mg or 20 mg (one or two tablets) as a single daily dose, depending on body weight.

Number of subjects in period 4	Month 24
Started	23
Completed	23

Baseline characteristics

Reporting groups

Reporting group title	Month 0
Reporting group description:	
Demographics and disease characteristics for cladribine-treated patients with RRMS at month 0.	

Reporting group values	Month 0	Total	
Number of subjects	24	24	
Age categorical			
Units: Subjects			
Adults (18-64 years)	24	24	
Age continuous			
Units: years			
median	36.5		
full range (min-max)	21 to 56	-	
Gender categorical			
Units: Subjects			
Female	15	15	
Male	9	9	
John Cunningham (JC) virus screening			
Units: Subjects			
Negative	7	7	
Positive	17	17	
Number of patients who already received a MS therapy			
Units: Subjects			
Patient received a MS therapy	18	18	
Unknown	6	6	
Last MS therapy received			
Units: Subjects			
Interferon Beta	1	1	
Dimethyl Fumarate	4	4	
Glatirameracetat	1	1	
Fingolimod	3	3	
Natalizumab	6	6	
Ocrelizumab	2	2	
Other	1	1	
Unknown	6	6	
Time from MS diagnosis to baseline visit			
Units: Years			
arithmetic mean	5.19		
full range (min-max)	0.05 to 26.17	-	
Time from first MS symptoms to baseline visit			
Units: Years			
arithmetic mean	5.36		
full range (min-max)	0.05 to 26.17	-	
Number of relapses since MS diagnosis			

Units: Number of relapses			
median	2		
full range (min-max)	1 to 10	-	
Time from most recent relapse to baseline visit			
Units: Months			
median	4.12		
full range (min-max)	0.59 to 112.56	-	

End points

End points reporting groups

Reporting group title	Month 0
Reporting group description: Cladribine-treated patients at month 0.	
Reporting group title	Month 3
Reporting group description: Cladribine-treated patients at month 3.	
Reporting group title	Month 12
Reporting group description: Cladribine-treated patients at month 12.	
Reporting group title	Month 24
Reporting group description: Cladribine-treated patients at month 24.	
Subject analysis set title	Month 0 - unstable disease
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cladribine-treated patients with unstable disease at month 0.	
Subject analysis set title	Month 0 - stable disease
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cladribine-treated patients with stable disease at month 0.	
Subject analysis set title	Month 12 - unstable disease
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cladribine-treated patients with unstable disease at month 12.	
Subject analysis set title	Month 12 - stable disease
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cladribine-treated patients with stable disease at month 12.	
Subject analysis set title	Month 24 - unstable disease
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cladribine-treated patients with unstable disease at month 24.	
Subject analysis set title	Month 24 - stable disease
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cladribine-treated patients with stable disease at month 24.	
Subject analysis set title	Month 3 - Kaplan-Meier method
Subject analysis set type	Full analysis
Subject analysis set description: Month 3 - Kaplan-Meier method	
Subject analysis set title	Month 6 - Kaplan-Meier method
Subject analysis set type	Full analysis
Subject analysis set description: Month 6 - Kaplan-Meier method	
Subject analysis set title	Month 12 - Kaplan-Meier method
Subject analysis set type	Full analysis

Subject analysis set description:

Month 12 - Kaplan-Meier method

Subject analysis set title	Month 18 - Kaplan-Meier method
Subject analysis set type	Full analysis

Subject analysis set description:

Month 18 - Kaplan-Meier method

Subject analysis set title	Month 24 - Kaplan-Meier method
Subject analysis set type	Full analysis

Subject analysis set description:

Month 24 - Kaplan-Meier method

Subject analysis set title	Overall study
Subject analysis set type	Full analysis

Subject analysis set description:

All patients in the study

Primary: T cell receptor repertoire – Number of clones

End point title	T cell receptor repertoire – Number of clones
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End point description:

Due to insufficient availability of blood sample material, only 20 patients were analysed.

End point type	Primary
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End point timeframe:

Month 0, 12 and 24

End point values	Month 0	Month 12	Month 24	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	18	19	
Units: Number of clones				
arithmetic mean (standard deviation)	1479299.45 (\pm 514265.58)	1287672.72 (\pm 516730.09)	1117550.79 (\pm 548980.80)	

Statistical analyses

Statistical analysis title	Absolute change from month 0 to month 12
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Statistical analysis description:

This study was intended as an explorative study, i.e. all results were interpreted as hypotheses-generating. The absolute change from month 0 to month 12 and from month 0 to month 24 were analyzed descriptively. Additionally, exploratory inferential analyses were performed. To assess the difference between two different time points, Student's t-test for paired samples and Wilcoxon signed-rank test were used.

Comparison groups	Month 12 v Month 0
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1335
Method	Student's t-test for paired samples

Statistical analysis title	Absolute change from month 0 to month 12
Comparison groups	Month 12 v Month 0
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1297
Method	Wilcoxon signed-rank test

Statistical analysis title	Absolute change from month 0 to month 24
Comparison groups	Month 24 v Month 0
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008
Method	Student's t-test for paired samples

Statistical analysis title	Absolute change from month 0 to month 24
Comparison groups	Month 24 v Month 0
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0017
Method	Wilcoxon signed-rank test

Secondary: T cell receptor repertoire – Number of unique clones	
End point title	T cell receptor repertoire – Number of unique clones
End point description: Due to insufficient availability of blood sample material, only 20 patients were analysed.	
End point type	Secondary
End point timeframe: Month 0, 12 and 24	

End point values	Month 0	Month 12	Month 24	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	18	19	
Units: Number of unique clones				
arithmetic mean (standard deviation)	862025.60 (\pm 409681.87)	693093.61 (\pm 362987.09)	633434.42 (\pm 407096.02)	

Statistical analyses

Statistical analysis title	Absolute change from month 0 to month 12
Comparison groups	Month 0 v Month 12
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0063
Method	Student's t-test for paired samples

Statistical analysis title	Absolute change from month 0 to month 12
Comparison groups	Month 0 v Month 12
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0056
Method	Wilcoxon signed-rank test

Statistical analysis title	Absolute change from month 0 to month 24
Comparison groups	Month 0 v Month 24
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0012
Method	Student's t-test for paired samples

Statistical analysis title	Absolute change from month 0 to month 24
Comparison groups	Month 0 v Month 24

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0024
Method	Wilcoxon signed-rank test

Secondary: T cell receptor repertoire – Clonality

End point title	T cell receptor repertoire – Clonality
End point description:	Due to insufficient availability of blood sample material, only 20 patients were analysed.
End point type	Secondary
End point timeframe:	Month 0, 12 and 24

End point values	Month 0	Month 12	Month 24	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	18	19	
Units: Clonality				
arithmetic mean (standard deviation)	0.096 (± 0.052)	0.105 (± 0.061)	0.119 (± 0.084)	

Statistical analyses

Statistical analysis title	Absolute change from month 0 to month 12
Comparison groups	Month 0 v Month 12
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3262
Method	Student's t-test for paired samples

Statistical analysis title	Absolute change from month 0 to month 12
Comparison groups	Month 0 v Month 12
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0385
Method	Wilcoxon signed-rank test

Statistical analysis title	Absolute change from month 0 to month 24
Comparison groups	Month 0 v Month 24
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0961
Method	Student's t-test for paired samples

Statistical analysis title	Absolute change from month 0 to month 24
Comparison groups	Month 0 v Month 24
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0401
Method	Wilcoxon signed-rank test

Secondary: B cell receptor repertoire – Number of clones	
End point title	B cell receptor repertoire – Number of clones
End point description: Due to insufficient availability of blood sample material, only 22 patients were analysed.	
End point type	Secondary
End point timeframe: Month 0 and 24	

End point values	Month 0	Month 24		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Number of clones				
arithmetic mean (standard deviation)	44494.91 (± 20894.87)	56806.27 (± 19366.05)		

Statistical analyses	
Statistical analysis title	Absolute change from month 0 to month 24
Comparison groups	Month 0 v Month 24

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0402
Method	Student's t-test for paired samples

Statistical analysis title	Absolute change from month 0 to month 24
Comparison groups	Month 0 v Month 24
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0271
Method	Wilcoxon signed-rank test

Secondary: B cell receptor repertoire – Number of unique clones

End point title	B cell receptor repertoire – Number of unique clones
End point description: Due to insufficient availability of blood sample material, only 22 patients were analysed.	
End point type	Secondary
End point timeframe: Month 0 and 24	

End point values	Month 0	Month 24		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Number of unique clones				
arithmetic mean (standard deviation)	42846.41 (± 20321.30)	55449.27 (± 18954.07)		

Statistical analyses

Statistical analysis title	Absolute change from month 0 to month 24
Comparison groups	Month 0 v Month 24
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0316
Method	Student's t-test for paired samples

Statistical analysis title	Absolute change from month 0 to month 24
Comparison groups	Month 0 v Month 24
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0246
Method	Wilcoxon signed-rank test

Secondary: B cell receptor repertoire – Clonality

End point title	B cell receptor repertoire – Clonality
End point description:	Due to insufficient availability of blood sample material, only 22 patients were analysed.
End point type	Secondary
End point timeframe:	Month 0 and 24

End point values	Month 0	Month 24		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Clonality				
arithmetic mean (standard deviation)	0.022 (± 0.005)	0.018 (± 0.002)		

Statistical analyses

Statistical analysis title	Absolute change from month 0 to month 24
Comparison groups	Month 0 v Month 24
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	Student's t-test for paired samples Stat

Statistical analysis title	Absolute change from month 0 to month 24
Comparison groups	Month 0 v Month 24

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon signed-rank test

Post-hoc: T cell receptor repertoire – Number of clones (disease status)

End point title	T cell receptor repertoire – Number of clones (disease status)
End point description: Patients were grouped according to their disease status ("unstable disease" (n = 12) vs "stable disease" (n = 8)) and compared with each other. Due to insufficient availability of blood sample material, only 20 patients were analysed.	
End point type	Post-hoc
End point timeframe: Month 0, 12 and 24	

End point values	Month 0 - unstable disease	Month 0 - stable disease	Month 12 - unstable disease	Month 12 - stable disease
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	8	11	7
Units: Number of clones				
arithmetic mean (standard deviation)	1456939.92 (± 603571.35)	1512838.75 (± 378461.58)	1183882.18 (± 582672.29)	1450772.14 (± 374030.43)

End point values	Month 24 - unstable disease	Month 24 - stable disease		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	7		
Units: Number of clones				
arithmetic mean (standard deviation)	1043145.08 (± 609179.72)	1245103.43 (± 440154.70)		

Statistical analyses

Statistical analysis title	Comparison of disease status at month 0
Statistical analysis description: Comparison of disease status ("no unstable disease" vs "stable disease") at month 0, month 12 and month 24 using Student's t-test for unpaired sample or the Mann Whitney U test.	
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease

Number of subjects included in analysis	20
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.9101
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 0
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease
Number of subjects included in analysis	20
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.802
Method	t-test (Satterthwaite)

Statistical analysis title	Comparison of disease status at month 12
Comparison groups	Month 12 - unstable disease v Month 12 - stable disease
Number of subjects included in analysis	18
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.3749
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 12
Comparison groups	Month 12 - unstable disease v Month 12 - stable disease
Number of subjects included in analysis	18
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.2539
Method	t-test (Satterthwaite)

Statistical analysis title	Comparison of disease status at month 24
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	19
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.1003
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 24
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	19
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.4164
Method	t-test (Satterthwaite)

Statistical analysis title	Change from month 0 to month 12
Statistical analysis description: The mean (\pm SD) number of clones changed from baseline to month 12 by -239449.55 ± 444762.39 for patients without stable disease and by -26870.43 ± 378013.67 for patients with stable disease.	
Comparison groups	Month 12 - stable disease v Month 12 - unstable disease v Month 0 - stable disease v Month 0 - unstable disease
Number of subjects included in analysis	38
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.3283
Method	Mann-Whitney U-test

Statistical analysis title	Change from month 0 to month 12
Statistical analysis description: The mean (\pm SD) number of clones changed from baseline to month 12 by -239449.55 ± 444762.39 for patients without stable disease and by -26870.43 ± 378013.67 for patients with stable disease.	
Comparison groups	Month 12 - stable disease v Month 12 - unstable disease v Month 0 - stable disease v Month 0 - unstable disease
Number of subjects included in analysis	38
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.2957
Method	t-test (Satterthwaite)

Statistical analysis title	Change from month 0 to month 24
Statistical analysis description: The mean (\pm SD) number of clones changed from baseline to month 24 by -413794.83 ± 413915.08 for patients without stable disease and by -313157.43 ± 419823.15 for patients with stable disease.	
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease v Month 0 - stable disease v Month 0 - unstable disease
Number of subjects included in analysis	39
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.5918
Method	Mann-Whitney U-test

Statistical analysis title	Change from month 0 to month 24
Statistical analysis description: The mean (\pm SD) number of clones changed from baseline to month 24 by -413794.83 ± 413915.08 for patients without stable disease and by -313157.43 ± 419823.15 for patients with stable disease.	
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease v Month 0 - stable disease v Month 0 - unstable disease
Number of subjects included in analysis	39
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.6212
Method	t-test (Satterthwaite)

Post-hoc: T cell receptor repertoire – Number of unique clones (disease status)

End point title	T cell receptor repertoire – Number of unique clones (disease status)
End point description: Patients were grouped according to their disease status ("unstable disease" (n = 12) vs "stable disease" (n = 8)) and compared with each other. Due to insufficient availability of blood sample material, only 20 patients were analysed.	
End point type	Post-hoc
End point timeframe: Month 0, 12 and 24	

End point values	Month 0 - unstable disease	Month 0 - stable disease	Month 12 - unstable disease	Month 12 - stable disease
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	8	11	7
Units: Number of unique clones				
arithmetic mean (standard deviation)	824845.92 (\pm 475027.78)	917795.13 (\pm 308292.59)	607361.09 (\pm 383500.92)	827816.14 (\pm 305854.61)

End point values	Month 24 - unstable disease	Month 24 - stable disease		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	7		
Units: Number of unique clones				
arithmetic mean (standard deviation)	568364.50 (\pm 450424.63)	744982.86 (\pm 319758.46)		

Statistical analyses

Statistical analysis title	Comparison of disease status at month 0
Comparison groups	Month 0 - stable disease v Month 0 - unstable disease
Number of subjects included in analysis	20
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.7345
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 0
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease
Number of subjects included in analysis	20
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.6022
Method	t-test (Satterthwaite)

Statistical analysis title	Comparison of disease status at month 12
Comparison groups	Month 12 - unstable disease v Month 12 - stable disease
Number of subjects included in analysis	18
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.2854
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 12
Comparison groups	Month 12 - unstable disease v Month 12 - stable disease
Number of subjects included in analysis	18
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.1976
Method	t-test (Satterthwaite)

Statistical analysis title	Comparison of disease status at month 24
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Comparison groups	Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	19
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.1198
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 24
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	19
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.3345
Method	t-test (Satterthwaite)

Statistical analysis title	Change from month 0 to month 12
Statistical analysis description: The mean (\pm SD) number of unique clones changed from baseline to month 12 by -183363.36 \pm 237060.54 for patients without stable disease and by -103843.57 \pm 154785.88 for patients with stable disease.	
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 12 - unstable disease v Month 12 - stable disease
Number of subjects included in analysis	38
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.7914
Method	Mann-Whitney U-test

Statistical analysis title	Change from month 0 to month 12
Statistical analysis description: The mean (\pm SD) number of unique clones changed from baseline to month 12 by -183363.36 \pm 237060.54 for patients without stable disease and by -103843.57 \pm 154785.88 for patients with stable disease.	
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 12 - unstable disease v Month 12 - stable disease
Number of subjects included in analysis	38
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.402
Method	t-test (Satterthwaite)

Statistical analysis title	Change from month 0 to month 24
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Statistical analysis description:

The mean (\pm SD) number of unique clones changed from baseline to month 24 by -256481.42 ± 271551.50 for patients without stable disease and by -200192.43 ± 277061.57 for patients with stable disease.

Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	39
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.8369
Method	Mann-Whitney U-test

Statistical analysis title

Change from month 0 to month 24

Statistical analysis description:

The mean (\pm SD) number of unique clones changed from baseline to month 24 by -256481.42 ± 271551.50 for patients without stable disease and by -200192.43 ± 277061.57 for patients with stable disease.

Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	39
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.6743
Method	t-test (Satterthwaite)

Post-hoc: T cell receptor repertoire – Clonality (disease status)

End point title	T cell receptor repertoire – Clonality (disease status)
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End point description:

Patients were grouped according to their disease status ("unstable disease" (n = 12) vs "stable disease" (n = 8)) and compared with each other. Due to insufficient availability of blood sample material, only 20 patients were analysed.

End point type	Post-hoc
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End point timeframe:

Month 0, 12 and 24

End point values	Month 0 - unstable disease	Month 0 - stable disease	Month 12 - unstable disease	Month 12 - stable disease
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	8	11	7
Units: Clonality				
arithmetic mean (standard deviation)	0.101 (\pm 0.060)	0.089 (\pm 0.042)	0.100 (\pm 0.068)	0.112 (\pm 0.052)

End point values	Month 24 - unstable disease	Month 24 - stable disease		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	7		
Units: Clonality				
arithmetic mean (standard deviation)	0.113 (\pm 0.090)	0.130 (\pm 0.076)		

Statistical analyses

Statistical analysis title	Comparison of disease status at month 0
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease
Number of subjects included in analysis	20
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.9101
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 0
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease
Number of subjects included in analysis	20
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.6045
Method	t-test (Satterthwaite)

Statistical analysis title	Comparison of disease status at month 12
Comparison groups	Month 12 - unstable disease v Month 12 - stable disease
Number of subjects included in analysis	18
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.5962
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 12
Comparison groups	Month 12 - unstable disease v Month 12 - stable disease

Number of subjects included in analysis	18
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.6839
Method	t-test (Satterthwaite)

Statistical analysis title	Comparison of disease status at month 24
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	19
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.3845
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 24
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	19
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.6684
Method	t-test (Satterthwaite)

Statistical analysis title	Change from month 0 to month 12
Comparison groups	Month 0 - stable disease v Month 0 - unstable disease v Month 12 - unstable disease v Month 12 - stable disease
Number of subjects included in analysis	38
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0154
Method	Mann-Whitney U-test

Statistical analysis title	Change from month 0 to month 12
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 12 - unstable disease v Month 12 - stable disease
Number of subjects included in analysis	38
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0346
Method	t-test (Satterthwaite)

Statistical analysis title	Change from month 0 to month 24
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	39
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.2614
Method	Mann-Whitney U-test

Statistical analysis title	Change from month 0 to month 24
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	39
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.3195
Method	t-test (Satterthwaite)

Post-hoc: B cell receptor repertoire – Number of clones (disease status)

End point title	B cell receptor repertoire – Number of clones (disease status)
End point description: Patients were grouped according to their disease status ("unstable disease" (n = 14) vs "stable disease" (n = 8)) and compared with each other. Due to insufficient availability of blood sample material, only 22 patients were analysed.	
End point type	Post-hoc
End point timeframe: Month 0 and 24	

End point values	Month 0 - unstable disease	Month 0 - stable disease	Month 24 - unstable disease	Month 24 - stable disease
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	8	14	8
Units: Number of clones				
arithmetic mean (standard deviation)	43029.36 (± 23966.08)	47059.63 (± 15207.93)	57424.57 (± 20380.44)	55724.25 (± 18752.12)

Statistical analyses

Statistical analysis title	Comparison of disease status at month 0
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease
Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.5699
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 0
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease
Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.6352
Method	t-test (Satterthwaite)

Statistical analysis title	Comparison of disease status at month 24
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.8676
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 24
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.8454
Method	t-test (Satterthwaite)

Statistical analysis title	Change from month 0 to month 24
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 24 - unstable disease v Month 24 - stable disease

Number of subjects included in analysis	44
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.5252
Method	Mann-Whitney U-test

Statistical analysis title	Change from month 0 to month 24
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	44
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.6017
Method	t-test (Satterthwaite)

Post-hoc: B cell receptor repertoire – Number of unique clones (disease status)

End point title	B cell receptor repertoire – Number of unique clones (disease status)
End point description:	Patients were grouped according to their disease status ("unstable disease" (n = 14) vs "stable disease" (n = 8)) and compared with each other. Due to insufficient availability of blood sample material, only 22 patients were analysed.
End point type	Post-hoc
End point timeframe:	Month 0 and 24

End point values	Month 0 - unstable disease	Month 0 - stable disease	Month 24 - unstable disease	Month 24 - stable disease
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	8	14	8
Units: Number of unique clones				
arithmetic mean (standard deviation)	41430.00 (± 23450.22)	45325.13 (± 14372.34)	56134.71 (± 19948.17)	54249.75 (± 18335.04)

Statistical analyses

Statistical analysis title	Comparison of disease status at month 0
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease

Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.5699
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 0
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease
Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.6346
Method	t-test (Satterthwaite)

Statistical analysis title	Comparison of disease status at month 24
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.8676
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 24
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.8252
Method	t-test (Satterthwaite)

Statistical analysis title	Change from month 0 to month 24
Statistical analysis description: The mean (\pm SD) number of unique clones changed from baseline to month 24 by 14704.71 ± 29107.94 for patients without stable disease and by 8924.63 ± 19485.86 for patients with stable disease.	
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 24 - unstable disease v Month 24 - stable disease

Number of subjects included in analysis	44
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.5252
Method	Mann-Whitney U-test

Statistical analysis title	Change from month 0 to month 24
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Statistical analysis description:

The mean (\pm SD) number of unique clones changed from baseline to month 24 by 14704.71 ± 29107.94 for patients without stable disease and by 8924.63 ± 19485.86 for patients with stable disease.

Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	44
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.5844
Method	t-test (Satterthwaite)

Post-hoc: B cell receptor repertoire – Clonality (disease status)

End point title	B cell receptor repertoire – Clonality (disease status)
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End point description:

Patients were grouped according to their disease status ("unstable disease" (n = 14) vs "stable disease" (n = 8)) and compared with each other. Due to insufficient availability of blood sample material, only 22 patients were analysed.

End point type	Post-hoc
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End point timeframe:

Month 0 and 24

End point values	Month 0 - unstable disease	Month 0 - stable disease	Month 24 - unstable disease	Month 24 - stable disease
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	8	14	8
Units: Clonality				
arithmetic mean (standard deviation)	0.023 (\pm 0.006)	0.020 (\pm 0.002)	0.018 (\pm 0.002)	0.018 (\pm 0.002)

Statistical analyses

Statistical analysis title	Comparison of disease status at month 0
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease

Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.289
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 0
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease
Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.1233
Method	t-test (Satterthwaite)

Statistical analysis title	Comparison of disease status at month 24
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.2731
Method	Mann-Whitney-U test

Statistical analysis title	Comparison of disease status at month 24
Comparison groups	Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.3185
Method	t-test (Satterthwaite)

Statistical analysis title	Change from month 0 to month 24
Statistical analysis description: The mean (\pm SD) number of clonality changed from baseline to month 24 by -0.006 ± 0.005 for patients without stable disease and by -0.002 ± 0.002 for patients with stable disease.	
Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 24 - unstable disease v Month 24 - stable disease

Number of subjects included in analysis	44
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0668
Method	Mann-Whitney U-test

Statistical analysis title	Change from month 0 to month 24
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Statistical analysis description:

The mean (\pm SD) number of clonality changed from baseline to month 24 by -0.006 ± 0.005 for patients without stable disease and by -0.002 ± 0.002 for patients with stable disease.

Comparison groups	Month 0 - unstable disease v Month 0 - stable disease v Month 24 - unstable disease v Month 24 - stable disease
Number of subjects included in analysis	44
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0301
Method	t-test (Satterthwaite)

Post-hoc: Relapse evaluation

End point title	Relapse evaluation
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End point description:

The percentage of patients without a relapse was analyzed with the Kaplan-Meier method.

End point type	Post-hoc
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End point timeframe:

Month 3, 6, 12, 18 and 24.

End point values	Month 3 - Kaplan-Meier method	Month 6 - Kaplan-Meier method	Month 12 - Kaplan-Meier method	Month 18 - Kaplan-Meier method
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: Percentage without relapse				
number (confidence interval 95%)	83.3 (61.5 to 93.4)	74.6 (51.9 to 87.7)	61.4 (38.9 to 77.8)	57.0 (34.8 to 74.1)

End point values	Month 24 - Kaplan-Meier method			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Percentage without relapse				
number (confidence interval 95%)	57.0 (34.8 to 74.1)			

Statistical analyses

No statistical analyses for this end point

Post-hoc: Annualized relapse rate

End point title	Annualized relapse rate
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End point description:

Annualized relapse rate calculated with Poisson regression.

End point type	Post-hoc
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End point timeframe:

In the course of the study.

End point values	Overall study			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Annualized relapse rate				
number (confidence interval 95%)	0.34 (0.21 to 0.56)			

Statistical analyses

No statistical analyses for this end point

Post-hoc: EDSS (expanded disability status scale) score

End point title	EDSS (expanded disability status scale) score
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End point description:

End point type	Post-hoc
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End point timeframe:

Month 0, 3, 12 and 24.

End point values	Month 0	Month 3	Month 12	Month 24
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	24	23	23
Units: EDSS score				
median (full range (min-max))	1.5 (0 to 4.5)	1.25 (0 to 5.5)	1 (0 to 5.5)	1 (0 to 4)

Statistical analyses

No statistical analyses for this end point

Post-hoc: MSFC (multiple sclerosis functional composite) score

End point title	MSFC (multiple sclerosis functional composite) score
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End point description:

End point type	Post-hoc
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End point timeframe:

Month 0, 3, 12 and 24.

End point values	Month 0	Month 3	Month 12	Month 24
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	21	22	18
Units: MSFC score				
median (full range (min-max))	0.35 (-0.51 to 1.25)	0.74 (-0.10 to 1.30)	0.77 (-0.06 to 1.29)	0.55 (0.10 to 1.13)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from the time the informed consent was signed up to the study termination visit.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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Reporting groups

Reporting group title	All patients
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Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 24 (37.50%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Weight decreased			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple sclerosis relapse			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Spinal pain			

subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 24 (100.00%)		
Vascular disorders			
Peripheral coldness			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Surgical and medical procedures			
Skin neoplasm excision			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 24 (20.83%)		
occurrences (all)	6		
Illness			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	2		
Immune system disorders			
Mycotic allergy			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Seasonal allergy			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Reproductive system and breast disorders			

Endometriosis subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Paranasal cyst subjects affected / exposed occurrences (all) Rhinitis allergic subjects affected / exposed occurrences (all)	4 / 24 (16.67%) 4 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1		
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Listless subjects affected / exposed occurrences (all) Panic attack subjects affected / exposed occurrences (all) Sleep disorder subjects affected / exposed occurrences (all) Somatic symptom disorder subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 5 / 24 (20.83%) 6 1 / 24 (4.17%) 1		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Epicondylitis subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 2 1 / 24 (4.17%) 1		

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	2		
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Dysarthria			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	10		
Hypoaesthesia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Multiple sclerosis relapse			
subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	6		
Paraesthesia			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Post-traumatic neuralgia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Sensory disturbance			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Blood and lymphatic system disorders			

Lymphopenia subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Ear and labyrinth disorders Paraesthesia ear subjects affected / exposed occurrences (all) Tinnitus subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 2 1 / 24 (4.17%) 1		
Eye disorders Cyclitis subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dysphagia subjects affected / exposed occurrences (all) Enteritis subjects affected / exposed occurrences (all) Gastric disorder subjects affected / exposed occurrences (all) Gastrointestinal disorder subjects affected / exposed occurrences (all) Toothache	1 / 24 (4.17%) 1 3 / 24 (12.50%) 4 2 / 24 (8.33%) 2 1 / 24 (4.17%) 1 1 / 24 (4.17%) 1 2 / 24 (8.33%) 2 1 / 24 (4.17%) 1		

subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Hyperhidrosis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Nail bed inflammation			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Sensitive skin			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Renal and urinary disorders			
Albuminuria			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Bladder dysfunction			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Renal pain			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Urinary retention			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	4		
Back pain			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	2		
Muscle spasms			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	5		
Tenosynovitis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Bronchitis bacterial			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	10 / 24 (41.67%)		
occurrences (all)	11		
Coronavirus infection			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	4		
Cystitis			

subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	3		
Fungal infection			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Fungal skin infection			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Gastroenteritis viral			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Herpes simplex			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Herpes zoster			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	4		
Hordeolum			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	12 / 24 (50.00%)		
occurrences (all)	17		
Oral herpes			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	2		
Tonsillitis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	2		
Upper respiratory tract infection			

subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	3		
Vitamin D deficiency			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 July 2019	<ul style="list-style-type: none">Inclusion and exclusion criteria were amended. All MS prior therapies were permitted. Nevertheless, time interval between a prior therapy and administration of Mavenclad had to be observed.The procedure of patient screening regarding the prescription of Mavenclad was amended.
03 March 2020	<ul style="list-style-type: none">Inclusion and exclusion criteria were amended. The time intervals to be observed for certain prior therapies were updated.The adjusted shelf life of Mavenclad was updated.
09 July 2021	<ul style="list-style-type: none">It was planned to enrol 30 patients in the study. The study was terminated early after the enrolment of 24 patients. The patients included were examined in accordance with the study protocol until their individual end of the study.
20 April 2022	<ul style="list-style-type: none">Administrative changes in the study were implemented. New safety data on Mavenclad regarding side effects, precautions and warnings were added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/38084102>