Clinical trial results:
Effect of MD1003 in spinal progressive multiple sclerosis: a pivotal randomized double blind placebo controlled study

Summary

EudraCT number	2013-002113-35
Trial protocol	FR
Global end of trial date	04 June 2020

Results information

Result version number	v1 (current)
This version publication date	19 November 2020
First version publication date	19 November 2020

Trial information

Trial identification

Sponsor protocol code	MD1003CT2013-02MS-SPI

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medday Pharmaceuticals S.A.
Sponsor organisation address	24-26 rue de la Pépinière, Paris, France,
Public contact	Clinical Trials Information Desk, Medday Pharmaceuticals S.A., +33 0180401465,
Scientific contact	Clinical Trials Information Desk, Medday Pharmaceuticals S.A., +33 0180401465,

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	04 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 February 2015
Global end of trial reached?	Yes
Global end of trial date	04 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the superiority of MD1003 300 mg/day over placebo in clinical improvement of patients with spinal progressive multiple sclerosis.

Protection of trial subjects:

This protocol complied with the principal laid down by the 18th World Medical Assembly (Helsinki, 1964 an following amendments) and all applicable amendments laid down by the World Medical Assemblies, as well as the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. The trial complied with the laws and regulations of the country in which the study was performed, and any applicable guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 September 2013
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	France: 154
Worldwide total number of subjects	154
EEA total number of subjects	154

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)	152
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	166[1]
Number of subjects completed	154

Pre-assignment subject non-completion reasons

Reason: Number of subjects	inclusion/exclusion criteria: 12

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: the difference is the number of screen failures.

Period 1

Period 1 title	Double-blind phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	MD1003

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MD1003
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg 3 times/day (1 capsule in the morning, 1 at noon, 1 in the evening)

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule 3 times/day

Number of subjects in period 1	MD1003	Placebo
Started	103	51
Completed	91	42
Not completed	12	9
Consent withdrawn by subject	5	4
Physician decision	3	2
Adverse event, non-fatal	3	3
Protocol deviation	1	-

Period 2

Period 2 title	Open-label extension phase M12-M78
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MD1003-MD1003

Arm description:

MD1003 300 mg/day for 12 months in the double-blind phase and MD1003 300 mg/day for 66 additional months in the open-label extension phase.

Arm type	Experimental
Investigational medicinal product name	MD1003
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg 3 times/day (1 capsule in the morning, 1 at noon, 1 in the evening)

Arm title	Placebo-MD1003

Arm description:

Placebo for 12 months in the double-blind phase, then switch to MD1003 300 mg/day for 66 additional months in the open-label extension phase.

Arm type	Experimental
Investigational medicinal product name	MD1003
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg 3 times/day (1 capsule in the morning, 1 at noon, 1 in the evening)

Number of subjects in period 2	MD1003-MD1003	Placebo-MD1003
Started	91	42
Completed	36	19
Not completed	55	23
Consent withdrawn by subject	13	8
Adverse event, non-fatal	7	3
Other	9	3
Lack of efficacy	26	9

Baseline characteristics

Reporting groups	
Reporting group title	MD1003
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	MD1003	Placebo	Total
Number of subjects	103	51	154
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	101	0	101
From 65-84 years	2	51	53
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	51.8	50.7	
standard deviation	± 9.1	± 8.4	-
Gender categorical Units: Subjects			
Female	53	30	83
Male	50	21	71
Demographic characteristics at baseline by baseline EDSS Units: Subjects			
EDSS 4.5 to 5.5	28	7	35
EDSS 6 to 7	75	44	119

Subject analysis sets	
Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomized patients who received at least one dose of study medication and with at least one baseline EDSS and one baseline TW25 assessment will be included. All analyses will be performed according to the intent-to-treat principle, i.e. patients will be analyzed according to the treatment arm they were assigned to.

Subject analysis set title	Safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients who received at least one dose of study medication will be included in the Safety population. Patients were analyzed according to the treatment they actually received.

Reporting group values	ITT population	Safety set	
Number of subjects	154	154	
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)	152	152	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	51.4	51.4	
standard deviation	± 8.9	± 8.9	
Gender categorical Units: Subjects			
Female	83	83	
Male	71	71	
Demographic characteristics at baseline by baseline EDSS Units: Subjects			
EDSS 4.5 to 5.5	35	35	
EDSS 6 to 7	119	119	

End points

End points reporting groups

Reporting group title	MD1003
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	MD1003-MD1003
Reporting group description:	
MD1003 300 mg/day for 12 months in the double-blind phase and MD1003 300 mg/day for 66 additional months in the open-label extension phase.	
Reporting group title	Placebo-MD1003
Reporting group description:	
Placebo for 12 months in the double-blind phase, then switch to MD1003 300 mg/day for 66 additional months in the open-label extension phase.	
Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized patients who received at least one dose of study medication and with at least one baseline EDSS and one baseline TW25 assessment will be included. All analyses will be performed according to the intent-to-treat principle, i.e. patients will be analyzed according to the treatment arm they were assigned to.	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received at least one dose of study medication will be included in the Safety population. Patients were analyzed according to the treatment they actually received.	

Primary: Proportion of patients with improvement of either the EDSS or the TW25 at M9 confirmed at M12

End point title	Proportion of patients with improvement of either the EDSS or the TW25 at M9 confirmed at M12

End point description:

• Improvement of Expanded Disability Status Scale (EDSS) at M9 confirmed at M12 is defined as:
  - A decrease of at least ≥ 0.5 point if baseline EDSS within [6; 7]
  - A decrease of at least ≥ 1 point if baseline EDSS within [4.5; 5.5]
• Improvement of Time to Walk 25 Feet (TW25) is defined as a decrease of at least ≥ 20% at M9 confirmed at M12 compared to baseline TW25.

End point type	Primary
End point timeframe:	
M0-M12	

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	51		
Units: Number of patients	13	0		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0051
Method	Fisher exact

Secondary: CGI score at M12

End point title	CGI score at M12

End point description:

The Clinical Global Impression - Improvement scale (CGI-I) is a 7 point scale that requires the clinician to assess how much the patient's illness has improved or worsened relative to a baseline state at the beginning of the intervention. The 7-point scale goes from: 1, very much improved; 2, much improved; 3, minimally improved; 4, no change; 5, minimally worse; 6, much worse; or 7, very much worse.

End point type	Secondary

End point timeframe:

M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	45		
Units: CGI score				
arithmetic mean (standard deviation)	4.05 (± 0.81)	4.62 (± 0.75)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Secondary: Proportions of patients with improvement of both EDSS and TW25 at M9 and confirmed at M12

End point title	Proportions of patients with improvement of both EDSS and TW25 at M9 and confirmed at M12

End point description:

Improvement of both EDSS and TW25 is defined as follows:
- decreased EDSS (at least 0.5 point if baseline EDSS from 6 to 7 and at least 1 point if baseline EDSS from 4.5 to 5.5) and
- decreased TW25 (at least 20%) at M9 confimred at M12.

End point type	Secondary

End point timeframe:

M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	51		
Units: Number of patients				
number (not applicable)	2	0		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Proportion of patients with increased EDSS score at M9 and confirmed at M12

End point title	Proportion of patients with increased EDSS score at M9 and confirmed at M12

End point description:

Increased EDSS score is defined as:
- An increase of at least ≥ 0.5 point if baseline EDSS within the [6; 7] range;
- An increase of at least ≥ 1 point if baseline EDSS within the [4.5; 5.5] range.

End point type	Secondary

End point timeframe:

M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	44		
Units: Number of patients				
number (not applicable)	4	6		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0727
Method	Fisher exact

Secondary: Proportion of patients with stable EDSS score at M9 and confirmed at M12

End point title	Proportion of patients with stable EDSS score at M9 and confirmed at M12

End point description:

The definition of stable EDSS is by default: it corresponds to all patients excluding those with decreased and those with increased EDSS score.

End point type	Secondary

End point timeframe:

M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	51		
Units: Number of patients				
number (not applicable)	81	38		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003 v Placebo

Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6832
Method	Fisher exact

Secondary: Mean change in General Health Sub-score of the SF36 questionnaire between M0 and M12

End point title	Mean change in General Health Sub-score of the SF36 questionnaire between M0 and M12

End point description:

End point type	Secondary

End point timeframe:

M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	51		
Units: SF36 score				
arithmetic mean (standard deviation)	-4.43 (± 16.75)	2.25 (± 16.23)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0349
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in the fatigue impact scale (M-FIS) between M0 and M12

End point title	Mean change in the fatigue impact scale (M-FIS) between M0 and M12

End point description:

End point type	Secondary

End point timeframe:

M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	47		
Units: Fatigue impact scale				
arithmetic mean (standard deviation)	1.38 (± 16.04)	1.30 (± 15.69)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8466
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change of the Nine Hole Peg Test (9HPT) between M0 and M12 (Best hand)

End point title	Mean change of the Nine Hole Peg Test (9HPT) between M0 and M12 (Best hand)

End point description:

End point type	Secondary

End point timeframe:

M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	47		
Units: 9HPT score				
arithmetic mean (standard deviation)	2.06 (± 5.21)	1.40 (± 7.06)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003 v Placebo

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9757
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M12 (visual)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M12 (visual)

End point description:

End point type	Secondary

End point timeframe:

M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	51		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.05 (± 0.81)	-0.10 (± 0.5)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.183
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in EDSS between M0 and M18

End point title	Mean change in EDSS between M0 and M18

End point description:

End point type	Secondary

End point timeframe:

M0-M18

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	41		
Units: EDSS score				
arithmetic mean (standard deviation)	-0.02 (± 0.61)	0.13 (± 0.45)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	Placebo-MD1003 v MD1003-MD1003
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0273
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in EDSS between M0 and M24

End point title	Mean change in EDSS between M0 and M24

End point description:

End point type	Secondary

End point timeframe:

M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	41		
Units: EDSS score				
arithmetic mean (standard deviation)	0.04 (± 0.62)	0.15 (± 0.37)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003

Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1283
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in EDSS between M0 and M30

End point title	Mean change in EDSS between M0 and M30

End point description:

End point type	Secondary

End point timeframe:

M0-M30

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	37		
Units: EDSS score				
arithmetic mean (standard deviation)	0.1 (± 0.68)	0.23 (± 0.3)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.041
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in EDSS between M0 and M36

End point title	Mean change in EDSS between M0 and M36

End point description:

End point type	Secondary

End point timeframe:

M0-M36

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	33		
Units: EDSS score				
arithmetic mean (standard deviation)	0.11 (± 0.69)	0.18 (± 0.33)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4285
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in EDSS between M0 and M42

End point title	Mean change in EDSS between M0 and M42

End point description:

End point type	Secondary

End point timeframe:

M0-M42

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	29		
Units: EDSS score				
arithmetic mean (standard deviation)	0.17 (± 0.73)	0.28 (± 0.56)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3653
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in EDSS between M0 and M48

End point title	Mean change in EDSS between M0 and M48
End point description:	

End point type	Secondary
End point timeframe:	
M0-M48	

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	26		
Units: EDSS score				
arithmetic mean (standard deviation)	0.16 (± 0.77)	0.4 (± 0.49)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	Placebo-MD1003 v MD1003-MD1003
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1742
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in EDSS between M0 and M54

End point title	Mean change in EDSS between M0 and M54
End point description:	

End point type	Secondary
End point timeframe:	
M0-M54	

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	23		
Units: EDSS score				
arithmetic mean (standard deviation)	0.17 (± 0.75)	0.43 (± 0.51)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.135
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in EDSS between M0 and M60

End point title	Mean change in EDSS between M0 and M60

End point description:

End point type	Secondary

End point timeframe:

M0-M60

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	22		
Units: EDSS score				
arithmetic mean (standard deviation)	0.21 (± 0.75)	0.39 (± 0.43)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.25
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in the MS walking scale (MSWS) between M0 and M24

End point title	Mean change in the MS walking scale (MSWS) between M0 and M24

End point description:

End point type	Secondary

End point timeframe:

M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	38		
Units: MSWS				
arithmetic mean (standard deviation)	2.06 (± 17.22)	5.05 (± 27.07)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6415
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in the MS walking scale (MSWS) between M0 and M12

End point title	Mean change in the MS walking scale (MSWS) between M0 and M12

End point description:

End point type	Secondary

End point timeframe:

M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	46		
Units: MSWS				
arithmetic mean (standard deviation)	0.79 (± 17.12)	5.26 (± 22.51)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8118
Method	Wilcoxon (Mann-Whitney)

Secondary: CGI score at M24

End point title	CGI score at M24

End point description:

The Clinical Global Impression - Improvement scale (CGI-I) is a 7 point scale that requires the clinician to assess how much the patient's illness has improved or worsened relative to a baseline state at the beginning of the intervention. The 7-point scale goes from: 1, very much improved; 2, much improved; 3, minimally improved; 4, no change; 5, minimally worse; 6, much worse; or 7, very much worse.

End point type	Secondary

End point timeframe:

M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	42		
Units: CGI score				
arithmetic mean (standard deviation)	4.17 (± 0.97)	4.24 (± 0.73)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	Placebo-MD1003 v MD1003-MD1003

Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8173
Method	Wilcoxon (Mann-Whitney)

Secondary: CGI score at M36

End point title	CGI score at M36

End point description:

End point type	Secondary

End point timeframe:

M36

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	42		
Units: CGI score				
arithmetic mean (standard deviation)	4.28 (± 0.97)	4.29 (± 0.81)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9648
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean percent change in TW25 between M0 and M12

End point title	Mean percent change in TW25 between M0 and M12

End point description:

End point type	Secondary

End point timeframe:

M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	42		
Units: TW25				
arithmetic mean (standard deviation)	67.71 (± 203.27)	98.18 (± 253.73)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	Placebo v MD1003
Number of subjects included in analysis	136
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.6393
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean percent change in TW25 between M0 and M24

End point title	Mean percent change in TW25 between M0 and M24

End point description:

End point type	Secondary

End point timeframe:

M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	39		
Units: TW25				
arithmetic mean (standard deviation)	95.77 (± 221.26)	121.51 (± 256.29)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003

Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.823
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean percent change in TW25 between M0 and M36

End point title	Mean percent change in TW25 between M0 and M36

End point description:

End point type	Secondary

End point timeframe:

M0-M36

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	30		
Units: TW25				
arithmetic mean (standard deviation)	125.28 (± 387.7)	165.11 (± 297.1)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4669
Method	Wilcoxon (Mann-Whitney)

Secondary: Proportions of patients with improvement of both EDSS and TW25 at M18 and confirmed at M24

End point title	Proportions of patients with improvement of both EDSS and TW25 at M18 and confirmed at M24

End point description:

Improvement of both EDSS and TW25 is defined as follows:
- decreased EDSS (at least 0.5 point if baseline EDSS from 6 to 7 and at least 1 point if baseline EDSS from 4.5 to 5.5) and
- decreased TW25 (at least 20%) at the corresponding visit confirmed at the next visit compared to the baseline value.

End point type	Secondary

End point timeframe:
M18-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Number of patients				
number (not applicable)	2	0		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Proportions of patients with improvement of both EDSS and TW25 at M24 and confirmed at M30

End point title	Proportions of patients with improvement of both EDSS and TW25 at M24 and confirmed at M30

End point description:

Improvement of both EDSS and TW25 is defined as follows:
- decreased EDSS (at least 0.5 point if baseline EDSS from 6 to 7 and at least 1 point if baseline EDSS from 4.5 to 5.5) and
- decreased TW25 (at least 20%) at the corresponding visit confirmed at the next visit compared to the baseline value.

End point type	Secondary

End point timeframe:
M24-M30

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Number of patients				
number (not applicable)	1	0		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Proportions of patients with improvement of both EDSS and TW25 at M36 and confirmed at M42

End point title	Proportions of patients with improvement of both EDSS and TW25 at M36 and confirmed at M42

End point description:

Improvement of both EDSS and TW25 is defined as follows:
- decreased EDSS (at least 0.5 point if baseline EDSS from 6 to 7 and at least 1 point if baseline EDSS from 4.5 to 5.5) and
- decreased TW25 (at least 20%) at the corresponding visit confirmed at the next visit compared to the baseline value.

End point type	Secondary

End point timeframe:

M36-M42

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Number of patients				
number (not applicable)	0	0		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003

Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0 [1]
Method	Fisher exact

Notes:

[1] - No p-value had been calculated

Secondary: Proportions of patients with improvement of both EDSS and TW25 at M30 and confirmed at M36

End point title	Proportions of patients with improvement of both EDSS and TW25 at M30 and confirmed at M36

End point description:

Improvement of both EDSS and TW25 is defined as follows:
- decreased EDSS (at least 0.5 point if baseline EDSS from 6 to 7 and at least 1 point if baseline EDSS from 4.5 to 5.5) and
- decreased TW25 (at least 20%) at the corresponding visit confirmed at the next visit compared to the baseline value.

End point type	Secondary

End point timeframe:

M30-M36

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Number of patients				
number (not applicable)	0	0		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0 [2]
Method	Fisher exact

Notes:

[2] - No p-value had been calculated

Secondary: Proportions of patients with improvement of both EDSS and TW25 at M42 and confirmed at M48

End point title	Proportions of patients with improvement of both EDSS and TW25 at M42 and confirmed at M48

End point description:

Improvement of both EDSS and TW25 is defined as follows:

- decreased EDSS (at least 0.5 point if baseline EDSS from 6 to 7 and at least 1 point if baseline EDSS from 4.5 to 5.5) and
- decreased TW25 (at least 20%) at the corresponding visit confirmed at the next visit compared to the baseline value.

End point type	Secondary

End point timeframe:

M42-M48

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Number of patients				
number (not applicable)	0	0		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	Placebo-MD1003 v MD1003-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0 [3]
Method	Fisher exact

Notes:

[3] - No p-value had been calculated

Secondary: Proportions of patients with improvement of both EDSS and TW25 at M48 and confirmed at M54

End point title	Proportions of patients with improvement of both EDSS and TW25 at M48 and confirmed at M54

End point description:

Improvement of both EDSS and TW25 is defined as follows:
- decreased EDSS (at least 0.5 point if baseline EDSS from 6 to 7 and at least 1 point if baseline EDSS from 4.5 to 5.5) and
- decreased TW25 (at least 20%) at the corresponding visit confirmed at the next visit compared to the baseline value.

End point type	Secondary

End point timeframe:

M48-M54

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Number of patients				
number (not applicable)	0	0		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0 [4]
Method	Fisher exact

Notes:

[4] - No p-value had been calculated

Secondary: Proportion of patients with increased EDSS score at M18 confirmed at M24

End point title	Proportion of patients with increased EDSS score at M18 confirmed at M24

End point description:

Increased EDSS score is defined as:
- An increase of at least ≥ 0.5 point if baseline EDSS within the [6; 7] range;
- An increase of at least ≥ 1 point if baseline EDSS within the [4.5; 5.5] range.

End point type	Secondary

End point timeframe:

M18-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	41		
Units: Number of patients				
number (not applicable)	8	13		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003

Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0045
Method	Fisher exact

Secondary: Proportion of patients with increased EDSS score at M12 and confirmed at M18

End point title	Proportion of patients with increased EDSS score at M12 and confirmed at M18

End point description:

Increased EDSS score is defined as:
- An increase of at least ≥ 0.5 point if baseline EDSS within the [6; 7] range;
- An increase of at least ≥ 1 point if baseline EDSS within the [4.5; 5.5] range.

End point type	Secondary

End point timeframe:

M12-M18

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	40		
Units: Number of patients				
number (not applicable)	7	7		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1332
Method	Fisher exact

Secondary: Proportion of patients with increased EDSS score at M24 and confirmed at M30

End point title	Proportion of patients with increased EDSS score at M24 and confirmed at M30

End point description:

Increased EDSS score is defined as:
- An increase of at least ≥ 0.5 point if baseline EDSS within the [6; 7] range;
- An increase of at least ≥ 1 point if baseline EDSS within the [4.5; 5.5] range.

End point type	Secondary

End point timeframe: M24-M30

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	36		
Units: Number of patients				
number (not applicable)	10	10		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1199
Method	Fisher exact

Secondary: Proportion of patients with increased EDSS score at M30 and confirmed at M36

End point title	Proportion of patients with increased EDSS score at M30 and confirmed at M36

End point description:

Increased EDSS score is defined as:
- An increase of at least ≥ 0.5 point if baseline EDSS within the [6; 7] range;
- An increase of at least ≥ 1 point if baseline EDSS within the [4.5; 5.5] range.

End point type	Secondary

End point timeframe:

M30-M36

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	33		
Units: Number of patients				
number (not applicable)	12	9		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4357
Method	Fisher exact

Secondary: Proportion of patients with increased EDSS score at M36 and confirmed at M42

End point title	Proportion of patients with increased EDSS score at M36 and confirmed at M42

End point description:

Increased EDSS score is defined as:
- An increase of at least ≥ 0.5 point if baseline EDSS within the [6; 7] range;
- An increase of at least ≥ 1 point if baseline EDSS within the [4.5; 5.5] range.

End point type	Secondary

End point timeframe:

M36-M42

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	29		
Units: Number of patients				
number (not applicable)	14	8		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Proportion of patients with increased EDSS score at M42 and confirmed at M48

End point title	Proportion of patients with increased EDSS score at M42 and confirmed at M48

End point description:

Increased EDSS score is defined as:

- An increase of at least ≥ 0.5 point if baseline EDSS within the [6; 7] range;
- An increase of at least ≥ 1 point if baseline EDSS within the [4.5; 5.5] range.

End point type	Secondary

End point timeframe:

M42-M48

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	26		
Units: Number of patients				
number (not applicable)	12	8		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5851
Method	Fisher exact

Secondary: Proportion of patients with increased EDSS score at M48 and confirmed at M54

End point title	Proportion of patients with increased EDSS score at M48 and confirmed at M54

End point description:

Increased EDSS score is defined as:
- An increase of at least ≥ 0.5 point if baseline EDSS within the [6; 7] range;
- An increase of at least ≥ 1 point if baseline EDSS within the [4.5; 5.5] range.

End point type	Secondary

End point timeframe:

M48-M54

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	23		
Units: Number of patients				
number (not applicable)	12	8		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7792
Method	Fisher exact

Secondary: Proportion of patients with increased EDSS score at M54 and confirmed at M60

End point title	Proportion of patients with increased EDSS score at M54 and confirmed at M60

End point description:

Increased EDSS score is defined as:
- An increase of at least ≥ 0.5 point if baseline EDSS within the [6; 7] range;
- An increase of at least ≥ 1 point if baseline EDSS within the [4.5; 5.5] range.

End point type	Secondary

End point timeframe:

M54-M60

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	22		
Units: Number of patients				
number (not applicable)	14	8		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Proportion of patients with stable EDSS score at M12 and confirmed at M18

End point title	Proportion of patients with stable EDSS score at M12 and confirmed at M18

End point description:

The definition of stable EDSS is by default: it corresponds to all patients excluding those with decreased and those with increased EDSS score.

End point type	Secondary

End point timeframe:

M12-M18

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Number of patients				
number (not applicable)	72	32		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8216
Method	Fisher exact

Secondary: Proportion of patients with stable EDSS score at M24 and confirmed at M30

End point title	Proportion of patients with stable EDSS score at M24 and confirmed at M30

End point description:

The definition of stable EDSS is by default: it corresponds to all patients excluding those with decreased and those with increased EDSS score.

End point type	Secondary

End point timeframe:

M24-M30

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Number of patients				
number (not applicable)	53	26		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7089
Method	Fisher exact

Secondary: Proportion of patients with stable EDSS score at M36 and confirmed at M42

End point title	Proportion of patients with stable EDSS score at M36 and confirmed at M42

End point description:

The definition of stable EDSS is by default: it corresponds to all patients excluding those with decreased and those with increased EDSS score.

End point type	Secondary

End point timeframe:

M36-M42

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Number of patients				
number (not applicable)	33	21		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1833
Method	Fisher exact

Secondary: Proportion of patients with stable EDSS score at M48 and confirmed at M54

End point title	Proportion of patients with stable EDSS score at M48 and confirmed at M54

End point description:

The definition of stable EDSS is by default: it corresponds to all patients excluding those with decreased and those with increased EDSS score.

End point type	Secondary

End point timeframe:

M48-M54

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Number of patients				
number (not applicable)	24	15		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3083
Method	Fisher exact

Secondary: Mean change of the General Health Sub-score of the SF36 questionnaire between M0 and M24

End point title	Mean change of the General Health Sub-score of the SF36 questionnaire between M0 and M24

End point description:

End point type	Secondary

End point timeframe:
M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: SF36 score				
arithmetic mean (standard deviation)	-3.95 (± 15.68)	1.37 (± 19.26)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.1722
Method	Wilcoxon (Mann-Whitney)

Notes:
[5] - The LOCF method was used.

Secondary: Mean change in the fatigue impact scale (M-FIS) between M0 and M24

End point title	Mean change in the fatigue impact scale (M-FIS) between M0 and M24

End point description:

End point type	Secondary

End point timeframe:
M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	38		
Units: FIS				
arithmetic mean (standard deviation)	-0.40 (± 13.49)	0.79 (± 13.88)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9716
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change of the Nine Hole Peg Test (9HPT) between M0 and M24 (best hand)

End point title	Mean change of the Nine Hole Peg Test (9HPT) between M0 and M24 (best hand)

End point description:

End point type	Secondary

End point timeframe:

M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	38		
Units: 9HPT score				
arithmetic mean (standard deviation)	3.43 (± 8.44)	2.76 (± 9.20)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7713
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change of the Nine Hole Peg Test (9HPT) between M0 and M24 (worst hand)

End point title	Mean change of the Nine Hole Peg Test (9HPT) between M0 and M24 (worst hand)

End point description:

End point type	Secondary

End point timeframe:
M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	40		
Units: 9HPT score				
arithmetic mean (standard deviation)	8.87 (± 33.86)	7.70 (± 32.17)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7694
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M12 (brain stem)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M12 (brain stem)

End point description:

End point type	Secondary

End point timeframe:
M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	51		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.10 (± 0.69)	-0.08 (± 0.82)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1912
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M12 (pyramidal)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M12 (pyramidal)

End point description:

End point type	Secondary

End point timeframe:

M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	51		
Units: Kurztke fonctionnal score				
arithmetic mean (standard deviation)	-0.03 (± 0.55)	0.04 (± 0.53)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5404
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M12 (cerebellar)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M12 (cerebellar)

End point description:

End point type	Secondary

End point timeframe:
M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	49		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.19 (± 0.86)	0.14 (± 1.12)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5376
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M12 (sensory)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M12 (sensory)

End point description:

End point type	Secondary

End point timeframe:
M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	51		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	-0.25 (± 0.93)	0.06 (± 0.88)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0896
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M12 (bowel and bladder)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M12 (bowel and bladder)

End point description:

End point type	Secondary

End point timeframe:

M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	51		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.14 (± 0.83)	0.20 (± 0.98)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	Placebo v MD1003
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6801
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M12 (cerebral)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M12 (cerebral)

End point description:

End point type	Secondary

End point timeframe:
M0-M12

End point values	MD1003	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	51		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	-0.08 (± 0.76)	0.08 (± 0.91)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003 v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2619
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M24 (visual)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M24 (visual)

End point description:

End point type	Secondary

End point timeframe:
M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.04 (± 1)	0.17 (± 1.19)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7312
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M24 (brain stem)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M24 (brain stem)

End point description:

End point type	Secondary

End point timeframe:

M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.09 (± 0.89)	0.14 (± 0.84)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5761
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M24 (pyramidal)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M24 (pyramidal)

End point description:

End point type	Secondary

End point timeframe:
M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.12 (± 0.61)	0.12 (± 0.59)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.878
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M24 (cerebellar)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M24 (cerebellar)

End point description:

End point type	Secondary

End point timeframe:
M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	41		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.09 (± 0.91)	0.05 (± 1.53)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8181
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M24 (sensory)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M24 (sensory)

End point description:

End point type	Secondary

End point timeframe:

M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	-0.08 (± 0.96)	-0.17 (± 0.99)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6394
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M24 (bowel and bladder)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M24 (bowel and bladder)

End point description:

End point type	Secondary

End point timeframe:
M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.12 (± 0.89)	0.02 (± 0.92)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8062
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M24 (cerebral)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M24 (cerebral)

End point description:

End point type	Secondary

End point timeframe:
M0-M24

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	-0.01 (± 0.89)	0 (± 0.96)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7453
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M36 (visual)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M36 (visual)

End point description:

End point type	Secondary

End point timeframe:

M0-M36

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.03 (± 1.08)	0.12 (± 1.15)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	Placebo-MD1003 v MD1003-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.921
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M36 (brain stem)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M36 (brain stem)

End point description:

End point type	Secondary

End point timeframe: M0-M36

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.08 (± 0.91)	0 (± 0.83)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8211
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M36 (pyramidal)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M36 (pyramidal)

End point description:

End point type	Secondary

End point timeframe:
M0-M36

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.16 (± 0.75)	0.19 (± 0.74)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7737
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M36 (cerebellar)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M36 (cerebellar)

End point description:

End point type	Secondary

End point timeframe:

M0-M36

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	41		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.13 (± 1.04)	0.22 (± 1.37)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8437
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M36 (sensory)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M36 (sensory)

End point description:

End point type	Secondary

End point timeframe:
M0-M36

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	-0.16 (± 0.93)	-0.02 (± 1)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	Placebo-MD1003 v MD1003-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4809
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M36 (bowel and bladder)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M36 (bowel and bladder)

End point description:

End point type	Secondary

End point timeframe:
M0-M36

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.13 (± 0.96)	0.19 (± 0.97)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5514
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M36 (cerebral)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M36 (cerebral)

End point description:

End point type	Secondary

End point timeframe:

M0-M36

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	-0.03 (± 0.87)	0.07 (± 0.92)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5806
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M48 (visual)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M48 (visual)

End point description:

End point type	Secondary

End point timeframe:
M0-M48

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.03 (± 1.06)	-0.1 (± 0.73)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4782
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M48 (brain stem)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M48 (brain stem)

End point description:

End point type	Secondary

End point timeframe:
M0-M48

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.14 (± 0.88)	0.05 (± 0.85)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8818
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M48 (pyramidal)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M48 (pyramidal)

End point description:

End point type	Secondary

End point timeframe:

M0-M48

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.21 (± 0.77)	0.26 (± 0.83)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7643
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M48 (cerebellar)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M48 (cerebellar)

End point description:

End point type	Secondary

End point timeframe:
M0-M48

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	41		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.18 (± 1.05)	0.12 (± 1.5)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8652
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M48 (sensory)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M48 (sensory)

End point description:

End point type	Secondary

End point timeframe:
M0-M48

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	-0.11 (± 1)	0.12 (± 0.97)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2847
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M48 (bowel and bladder)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M48 (bowel and bladder)

End point description:

End point type	Secondary

End point timeframe:

M0-M48

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.1 (± 0.98)	0.26 (± 0.94)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2531
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M48 (cerebral)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M48 (cerebral)

End point description:

End point type	Secondary

End point timeframe:
M0-M48

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.02 (± 1.05)	0.1 (± 0.93)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4569
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M60 (visual)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M60 (visual)

End point description:

End point type	Secondary

End point timeframe:
M0-M60

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.05 (± 1.07)	-0.07 (± 0.81)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4438
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M60 (brain stem)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M60 (brain stem)

End point description:

End point type	Secondary

End point timeframe:

M0-M60

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.12 (± 0.88)	0.05 (± 0.88)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8021
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M60 (pyramidal)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M60 (pyramidal)

End point description:

End point type	Secondary

End point timeframe: M0-M60

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.22 (± 0.73)	0.26 (± 0.8)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.664
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M60 (cerebellar)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M60 (cerebellar)

End point description:

End point type	Secondary

End point timeframe:
M0-M60

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	41		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.16 (± 1.09)	0.12 (± 1.5)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	Placebo-MD1003 v MD1003-MD1003
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7363
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M60 (sensory)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M60 (sensory)

End point description:

End point type	Secondary

End point timeframe:

M0-M60

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	-0.09 (± 1.03)	0.12 (± 0.99)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2937
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M60 (bowel and bladder)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M60 (bowel and bladder)

End point description:

End point type	Secondary

End point timeframe:
M0-M60

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	0.25 (± 1.08)	0.24 (± 0.93)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	MD1003-MD1003 v Placebo-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8206
Method	Wilcoxon (Mann-Whitney)

Secondary: Mean change in sub-score of the Kurtzke functional score between M0 and M60 (cerebral)

End point title	Mean change in sub-score of the Kurtzke functional score between M0 and M60 (cerebral)

End point description:

End point type	Secondary

End point timeframe:
M0-M60

End point values	MD1003-MD1003	Placebo-MD1003		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	42		
Units: Kurtzke fonctionnal score				
arithmetic mean (standard deviation)	-0.01 (± 0.9)	-0.02 (± 0.95)		

Statistical analyses

Statistical analysis title	Mann-Whitney's U test
Comparison groups	Placebo-MD1003 v MD1003-MD1003
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9151
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From ICF signature to M84	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16
Reporting groups	
Reporting group title	MD1003
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	MD1003-MD1003 extension phase
Reporting group description: -	
Reporting group title	Placebo-MD1003 extension phase
Reporting group description: -	

Serious adverse events	MD1003	Placebo	MD1003-MD1003 extension phase
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 103 (20.39%)	12 / 51 (23.53%)	32 / 91 (35.16%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Phlebitis			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Cholecystectomy			
subjects affected / exposed	0 / 103 (0.00%)	1 / 51 (1.96%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma radiation therapy to brain			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hospitalisation			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac ablation			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip arthroplasty			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intrathecal pump insertion			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rehabilitation therapy			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary cystectomy			

subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urostomy			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthmatic crisis			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			

subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Mental disorder			
subjects affected / exposed	0 / 103 (0.00%)	1 / 51 (1.96%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Inflammatory marker increased			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laboratory test interference			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural			

complications			
Fibula fracture			
subjects affected / exposed	0 / 103 (0.00%)	1 / 51 (1.96%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 103 (0.00%)	1 / 51 (1.96%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 103 (0.00%)	1 / 51 (1.96%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fractured sacrum			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			

subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation necrosis			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 103 (0.00%)	1 / 51 (1.96%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple sclerosis			

subjects affected / exposed	1 / 103 (0.97%)	1 / 51 (1.96%)	4 / 91 (4.40%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple sclerosis relapse			
subjects affected / exposed	6 / 103 (5.83%)	4 / 51 (7.84%)	11 / 91 (12.09%)
occurrences causally related to treatment / all	0 / 8	0 / 4	5 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle spasticity			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Epilepsy			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal neuralgia			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uhthoff's phenomenon			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune thrombocytopenia			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 103 (0.00%)	1 / 51 (1.96%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Mucocutaneous rash			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 103 (0.00%)	1 / 51 (1.96%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract disorder			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Myopathy			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Enterocolitis infectious			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	1 / 103 (0.97%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis infective staphylococcal			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo-MD1003 extension phase		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 42 (38.10%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			

subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal cancer				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep vein thrombosis				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Phlebitis				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Cholecystectomy				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gamma radiation therapy to brain				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hospitalisation				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac ablation				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip arthroplasty				

subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intrathecal pump insertion				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rehabilitation therapy				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary cystectomy				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urostomy				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Condition aggravated				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	2 / 42 (4.76%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Breast mass				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Prostatitis				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Asthmatic crisis				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung disorder				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Completed suicide				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mental disorder				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Inflammatory marker increased				

subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laboratory test interference				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Weight decreased				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Fibula fracture				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clavicle fracture				

subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fractured sacrum				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic fracture				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Radiation necrosis				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Supraventricular tachycardia				

subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Haemorrhage intracranial				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple sclerosis				
subjects affected / exposed	3 / 42 (7.14%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Multiple sclerosis relapse				
subjects affected / exposed	5 / 42 (11.90%)			
occurrences causally related to treatment / all	1 / 7			
deaths causally related to treatment / all	0 / 0			
Muscle spasticity				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorder				

subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Trigeminal neuralgia				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uhthoff's phenomenon				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune thrombocytopenia				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenitis				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				

subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Mucocutaneous rash			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract disorder			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Myopathy			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Enterocolitis infectious			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Bursitis infective staphylococcal			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			

subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	MD1003	Placebo	MD1003-MD1003 extension phase
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 103 (20.39%)	13 / 51 (25.49%)	78 / 91 (85.71%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	5 / 91 (5.49%)
occurrences (all)	0	0	5
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	2 / 91 (2.20%)
occurrences (all)	0	0	2
Cardiac disorders			
Oedema peripheral			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	8 / 91 (8.79%)
occurrences (all)	0	0	9
Nervous system disorders			
Multiple sclerosis relapse			
subjects affected / exposed	6 / 103 (5.83%)	4 / 51 (7.84%)	14 / 91 (15.38%)
occurrences (all)	8	4	21
Headache			
subjects affected / exposed	4 / 103 (3.88%)	3 / 51 (5.88%)	0 / 91 (0.00%)
occurrences (all)	5	7	0
General disorders and administration site conditions			
Back pain			
subjects affected / exposed	4 / 103 (3.88%)	3 / 51 (5.88%)	6 / 91 (6.59%)
occurrences (all)	4	3	6
Fatigue			
subjects affected / exposed	1 / 103 (0.97%)	4 / 51 (7.84%)	0 / 91 (0.00%)
occurrences (all)	1	5	0
Asthenia			

subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	5 / 91 (5.49%)
occurrences (all)	0	0	6
Immune system disorders			
Multiple sclerosis			
subjects affected / exposed	12 / 103 (11.65%)	7 / 51 (13.73%)	9 / 91 (9.89%)
occurrences (all)	13	9	10
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	1 / 91 (1.10%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Muscle spasticity			
subjects affected / exposed	4 / 103 (3.88%)	6 / 51 (11.76%)	3 / 91 (3.30%)
occurrences (all)	4	7	3
Arthralgia			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	7 / 91 (7.69%)
occurrences (all)	0	0	7
Ligament sprain			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	5 / 91 (5.49%)
occurrences (all)	0	0	5
Osteoporosis			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	4 / 91 (4.40%)
occurrences (all)	0	0	4
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	11 / 103 (10.68%)	6 / 51 (11.76%)	18 / 91 (19.78%)
occurrences (all)	13	9	33
Bronchitis			
subjects affected / exposed	5 / 103 (4.85%)	6 / 51 (11.76%)	6 / 91 (6.59%)
occurrences (all)	5	6	7
Nasopharyngitis			
subjects affected / exposed	5 / 103 (4.85%)	3 / 51 (5.88%)	5 / 91 (5.49%)
occurrences (all)	5	4	8
Influenza			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	5 / 91 (5.49%)
occurrences (all)	0	0	5

Influenza like illness			
subjects affected / exposed	0 / 103 (0.00%)	0 / 51 (0.00%)	3 / 91 (3.30%)
occurrences (all)	0	0	4

Non-serious adverse events	Placebo-MD1003 extension phase		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 42 (90.48%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Cardiac disorders			
Oedema peripheral			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Multiple sclerosis relapse			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	9		
Headache			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Back pain			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Immune system disorders			

Multiple sclerosis			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	7		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Muscle spasticity			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Arthralgia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Ligament sprain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Osteoporosis			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	11 / 42 (26.19%)		
occurrences (all)	24		
Bronchitis			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Nasopharyngitis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 September 2013	I) Modification of the study design II) Addition of the ancillary study III) Modification of one of the non-inclusion criteria IV) Addition of a non inclusion criteria
22 January 2014	I) Modification of the primary endpoint II) Modification of the secondary endpoints III) Modification of the age inclusion crietria IV) Modification of a non inclusion criteria V) Deletion of the exclusion criteria VI) Creation of a Data and Safety Monitoring Board (DSMB) VII) Modification of the number of patients included in the study
02 May 2014	I) Clarification of the primary endpoint II) Addition of a secondary endpoint III) Addition of a homostasis assessment during and at the end of the study
06 June 2014	Clarification on the primary endpoint without any change on patients' safety
22 July 2014	Addition of a secondary endpoint
22 January 2015	I) Update of the investigator's brochure with new non clinical data having an impact on patients' safety and the trial protocol II) Update of the number of included patients III) Modification of the protocol according to new clinical and non clinical events IV) Modification of the protocol with addition of a brain MRI at M24 V) Clarification on the MRI follow up protocol and addition of new MRI analyses VI) Clarification on protocol for the interim analysis of the results related to the double blind 12-month period. VII) Modification of the patient information sheet following new clinical and non clinical events and clarification on the MRI follow up protocol with addition of new analyses of MRI data
07 September 2015	Extension of the follow-up period for the patients' cohort up to 3 year follow-up
15 June 2016	To increase the follow-up period of the patients' cohort, it is proposed to continue the study up to 4 year follow-up (until M48) + update of sponsor's contact details + update of investigators' list.
08 June 2017	In order to increase the duration of cohorts follow-up, it is proposed to continue the study until Marketing Authorisation is obtained, with visits every 6 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported