Clinical trial results:
An Open-Label, Multicenter, Biomarker Study to Explore the Mechanism of Action of Ocrelizumab and B-Cell Biology in Patients With Relapsing Multiple Sclerosis or Primary Progressive Multiple Sclerosis

Summary

EudraCT number	2015-004616-37
Trial protocol	SE DE
Global end of trial date	11 April 2023

Results information

Result version number	v1 (current)
This version publication date	26 April 2024
First version publication date	26 April 2024

Trial information

Trial identification

Sponsor protocol code	ML29966

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02688985
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genentech, Inc.
Sponsor organisation address	1 DNA Way, Suite 258A, South San Francisco, United States, 4070
Public contact	Medical Communications, Genentech, Inc., 41 800 8218590, genentech@druginfo.com
Scientific contact	Medical Communications, Genentech, Inc., 41 800 8218590, genentech@druginfo.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 March 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is an open-label, multicenter, biomarker study designed to be hypothesis-generating in order to better understand the mechanism of action of ocrelizumab and B-cell biology in RMS or PPMS.

Protection of trial subjects:

This study was conducted in full conformance with the ICH E6 guideline for Good Clinical Practice and the principles of the Declaration of Helsinki, or the laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual. All participants were required to read and sign an informed consent form prior to participation in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 April 2016
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	Canada: 34
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	United States: 81
Worldwide total number of subjects	131
EEA total number of subjects	16

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)	131

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

131 patients enrolled at 17 study locations in the U.S., Canada, Germany, and Sweden

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	RMS Cohort Arm 1: Ocrelizumab + LP

Arm description:

Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP before the start of dosing (Week 1, treatment baseline) with ocrelizumab and a second LP at Week 12. Participants will be asked to have an additional optional LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab
Investigational medicinal product code	
Other name	RO4964913
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab will be administered as IV infusion.

Investigational medicinal product name	Antihistamine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants will receive an antihistamine, such as diphenhydramine, prior to ocrelizumab infusion.

Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants will receive 100 mg of IV methylprenisolone (or an equivalent) prior to ocrelizumab infusion.

Arm title	RMS Cohort Arm 2: Ocrelizumab + LP

Arm description:

Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP before the start of dosing (Week 1, treatment baseline) with ocrelizumab and a second LP at Week 24. Participants will be asked to have an additional optional LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.

Arm type	Experimental

Investigational medicinal product name	Ocrelizumab
Investigational medicinal product code	
Other name	RO4964913
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab will be administered as IV infusion.

Investigational medicinal product name	Antihistamine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants will receive an antihistamine, such as diphenhydramine, prior to ocrelizumab infusion.

Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants will receive 100 mg of IV methylprenisolone (or an equivalent) prior to ocrelizumab infusion.

Arm title	RMS Cohort Arm 3: Ocrelizumab + LP

Arm description:

Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP before the start of dosing (Week 1, treatment baseline) with ocrelizumab and a second LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab
Investigational medicinal product code	
Other name	RO4964913
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab will be administered as IV infusion.

Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants will receive 100 mg of IV methylprenisolone (or an equivalent) prior to ocrelizumab infusion.

Investigational medicinal product name	Antihistamine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants will receive an antihistamine, such as diphenhydramine, prior to ocrelizumab infusion.

Arm title	RMS Cohort Arm 4: Ocrelizumab + LP

Arm description:

Ocrelizumab treatment will be delayed for 12 weeks from pre-treatment baseline. Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP at Week -12 (pre-treatment baseline) and a second LP before the start of dosing (Week 1, treatment baseline). Participants will be asked to have an additional optional LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab
Investigational medicinal product code	
Other name	RO4964913
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab will be administered as IV infusion.

Investigational medicinal product name	Antihistamine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants will receive an antihistamine, such as diphenhydramine, prior to ocrelizumab infusion.

Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants will receive 100 mg of IV methylprenisolone (or an equivalent) prior to ocrelizumab infusion.

Arm title	PPMS Cohort: Ocrelizumab + LP

Arm description:

For the PPMS cohort, ocrelizumab will be administered as two 300-mg IV infusions separated by 14 days at a scheduled interval of every 24 weeks during the treatment period and then as a single 600-mg dose every 24 weeks starting week 72 during the Long-Term Extension period.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab
Investigational medicinal product code	
Other name	RO4964913
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab will be administered as IV infusion.

Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants will receive 100 mg of IV methylprenisolone (or an equivalent) prior to ocrelizumab infusion.

Investigational medicinal product name	Antihistamine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use

Dosage and administration details:

Participants will receive an antihistamine, such as diphenhydramine, prior to ocrelizumab infusion.

Number of subjects in period 1	RMS Cohort Arm 1: Ocrelizumab + LP	RMS Cohort Arm 2: Ocrelizumab + LP	RMS Cohort Arm 3: Ocrelizumab + LP
Started	23	31	28
Completed	0	0	0
Not completed	23	31	28
Adverse event, serious fatal	-	-	-
Physician decision	2	2	-
Consent withdrawn by subject	2	8	7
Adverse event, non-fatal	1	2	2
Study Terminated By Sponsor	-	-	-
Not specified	3	4	1
Continued Onto Commercially Available Ocrelizumab	12	12	14
Non-Compliance With Study Drug	1	3	1
Pregnancy	-	-	2
Lost to follow-up	2	-	1
Lack of efficacy	-	-	-

Number of subjects in period 1	RMS Cohort Arm 4: Ocrelizumab + LP	PPMS Cohort: Ocrelizumab + LP
Started	18	31
Completed	0	1
Not completed	18	30
Adverse event, serious fatal	-	1
Physician decision	-	1
Consent withdrawn by subject	1	4
Adverse event, non-fatal	-	-
Study Terminated By Sponsor	1	-
Not specified	-	-
Continued Onto Commercially Available Ocrelizumab	14	21
Non-Compliance With Study Drug	-	1
Pregnancy	1	-
Lost to follow-up	1	1
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	RMS Cohort Arm 1: Ocrelizumab + LP
Reporting group description:	
Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP before the start of dosing (Week 1, treatment baseline) with ocrelizumab and a second LP at Week 12. Participants will be asked to have an additional optional LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.	
Reporting group title	RMS Cohort Arm 2: Ocrelizumab + LP
Reporting group description:	
Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP before the start of dosing (Week 1, treatment baseline) with ocrelizumab and a second LP at Week 24. Participants will be asked to have an additional optional LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.	
Reporting group title	RMS Cohort Arm 3: Ocrelizumab + LP
Reporting group description:	
Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP before the start of dosing (Week 1, treatment baseline) with ocrelizumab and a second LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.	
Reporting group title	RMS Cohort Arm 4: Ocrelizumab + LP
Reporting group description:	
Ocrelizumab treatment will be delayed for 12 weeks from pre-treatment baseline. Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP at Week -12 (pre-treatment baseline) and a second LP before the start of dosing (Week 1, treatment baseline). Participants will be asked to have an additional optional LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.	
Reporting group title	PPMS Cohort: Ocrelizumab + LP
Reporting group description:	
For the PPMS cohort, ocrelizumab will be administered as two 300-mg IV infusions separated by 14 days at a scheduled interval of every 24 weeks during the treatment period and then as a single 600-mg dose every 24 weeks starting week 72 during the Long-Term Extension period.	

Reporting group values	RMS Cohort Arm 1: Ocrelizumab + LP	RMS Cohort Arm 2: Ocrelizumab + LP	RMS Cohort Arm 3: Ocrelizumab + LP
Number of subjects	23	31	28
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	23	31	28
>=65 years	0	0	0
Age Continuous Units: Years			
arithmetic mean	36.0	38.7	34.6
standard deviation	± 10.4	± 10.4	± 10.8
Sex/Gender, Customized Units: Participants			
Male	8	9	8
Female	15	22	20

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	3	1
White	21	28	25
More than one race	0	0	0
Unknown or Not Reported	0	0	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	2	1
Not Hispanic or Latino	22	28	27
Unknown or Not Reported	0	1	0

Reporting group values	RMS Cohort Arm 4: Ocrelizumab + LP	PPMS Cohort: Ocrelizumab + LP	Total
Number of subjects	18	31	131
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	18	31	131
>=65 years	0	0	0
Age Continuous Units: Years			
arithmetic mean	36.4	44.9	
standard deviation	± 9.8	± 7.4	-
Sex/Gender, Customized Units: Participants			
Male	7	16	48
Female	11	15	83
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	0	9
White	13	29	116
More than one race	1	0	1
Unknown or Not Reported	0	1	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	2	6
Not Hispanic or Latino	17	28	122
Unknown or Not Reported	1	1	3

End points

End points reporting groups

Reporting group title	RMS Cohort Arm 1: Ocrelizumab + LP

Reporting group description:

Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP before the start of dosing (Week 1, treatment baseline) with ocrelizumab and a second LP at Week 12. Participants will be asked to have an additional optional LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.

Reporting group title	RMS Cohort Arm 2: Ocrelizumab + LP

Reporting group description:

Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP before the start of dosing (Week 1, treatment baseline) with ocrelizumab and a second LP at Week 24. Participants will be asked to have an additional optional LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.

Reporting group title	RMS Cohort Arm 3: Ocrelizumab + LP

Reporting group description:

Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP before the start of dosing (Week 1, treatment baseline) with ocrelizumab and a second LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.

Reporting group title	RMS Cohort Arm 4: Ocrelizumab + LP

Reporting group description:

Ocrelizumab treatment will be delayed for 12 weeks from pre-treatment baseline. Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP at Week -12 (pre-treatment baseline) and a second LP before the start of dosing (Week 1, treatment baseline). Participants will be asked to have an additional optional LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.

Reporting group title	PPMS Cohort: Ocrelizumab + LP

Reporting group description:

For the PPMS cohort, ocrelizumab will be administered as two 300-mg IV infusions separated by 14 days at a scheduled interval of every 24 weeks during the treatment period and then as a single 600-mg dose every 24 weeks starting week 72 during the Long-Term Extension period.

Primary: Change in Levels of NfL (neurofilament light) in CSF from Treatment Baseline to Post-Treatment with Ocrelizumab

End point title	Change in Levels of NfL (neurofilament light) in CSF from Treatment Baseline to Post-Treatment with Ocrelizumab[1]

End point description:

End point type	Primary

End point timeframe:

From Baseline to post-treatment (Week 12, 24, 52 according to randomization and Weeks 144 and 240)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No analysis provided

End point values	RMS Cohort Arm 1: Ocrelizumab + LP	RMS Cohort Arm 2: Ocrelizumab + LP	RMS Cohort Arm 3: Ocrelizumab + LP	RMS Cohort Arm 4: Ocrelizumab + LP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	25	22	16
Units: pg/mL				
arithmetic mean (standard deviation)				
Primary Analysis	-1232.97 (± 2060.37)	-1169.13 (± 1739.49)	-1008.13 (± 1132.68)	-931.83 (± 2816.27)
LTE phase Week 144	-2331.89 (± 3334.80)	-644.50 (± 1371.39)	-1287.58 (± 1822.72)	-2544.33 (± 3807.94)
LTE phase Week 240	-2499.98 (± 3606.71)	-791.51 (± 1150.89)	-1060.33 (± 1678.95)	-5488.70 (± 4350.46)

End point values	PPMS Cohort: Ocrelizumab + LP			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: pg/mL				
arithmetic mean (standard deviation)				
Primary Analysis	261.85 (± 1175.72)			
LTE phase Week 144	-925.32 (± 2507.97)			
LTE phase Week 240	-1221.33 (± 2738.19)			

Statistical analyses

No statistical analyses for this end point

Primary: Change in Number of CD19+ B cells in CSF from Treatment Baseline to Post-Treatment with Ocrelizumab

End point title	Change in Number of CD19+ B cells in CSF from Treatment Baseline to Post-Treatment with Ocrelizumab[2]

End point description:

End point type	Primary

End point timeframe:

From Baseline to post-treatment (Week 12, 24, 52 according to randomization and Weeks 144 and 240)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No analysis provided

End point values	RMS Cohort Arm 1: Ocrelizumab + LP	RMS Cohort Arm 2: Ocrelizumab + LP	RMS Cohort Arm 3: Ocrelizumab + LP	RMS Cohort Arm 4: Ocrelizumab + LP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	25	22	16
Units: cells/µL				
arithmetic mean (standard deviation)				
Primary Analysis	-0.22 (± 0.26)	-0.15 (± 0.36)	-0.13 (± 0.32)	-0.18 (± 0.37)
LTE phase Week 144	-0.11 (± 0.08)	-0.14 (± 0.20)	-0.06 (± 0.23)	0.15 (± 0.10)
LTE phase Week 240	-0.08 (± 0.09)	-0.20 (± 0.26)	-0.02 (± 0.01)	-0.04 (± 0.05)

End point values	PPMS Cohort: Ocrelizumab + LP			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: cells/µL				
arithmetic mean (standard deviation)				
Primary Analysis	-0.09 (± 0.11)			
LTE phase Week 144	-0.01 (± 0.09)			
LTE phase Week 240	0.01 (± 0.03)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Number of CD3+ T-Cells in CSF Post-Treatment With Ocrelizumab

End point title	Change From Baseline in Number of CD3+ T-Cells in CSF Post-Treatment With Ocrelizumab[3]

End point description:

End point type	Primary

End point timeframe:

From Baseline to post-treatment (Week 12, 24, 52 according to randomization and Weeks 144 and 240)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No analysis provided

End point values	RMS Cohort Arm 1: Ocrelizumab + LP	RMS Cohort Arm 2: Ocrelizumab + LP	RMS Cohort Arm 3: Ocrelizumab + LP	RMS Cohort Arm 4: Ocrelizumab + LP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	25	22	16
Units: cells/µL				
arithmetic mean (standard deviation)				

Primary Analysis	-6.61 (± 10.48)	-1.92 (± 3.15)	-1.46 (± 2.67)	-1.98 (± 5.10)
LTE phase Week 144	-3.45 (± 2.33)	1.78 (± 9.76)	-0.83 (± 4.64)	2.25 (± 0.17)
LTE phase Week 240	-3.00 (± 3.16)	-3.47 (± 2.31)	-1.41 (± 1.30)	-1.67 (± 2.42)

End point values	PPMS Cohort: Ocrelizumab + LP			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: cells/µL				
arithmetic mean (standard deviation)				
Primary Analysis	-3.25 (± 4.32)			
LTE phase Week 144	-3.62 (± 5.56)			
LTE phase Week 240	-1.37 (± 0.54)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline up to 5 years

Adverse event reporting additional description:

Safety population is defined as all enrolled patients who received at least one infusion of ocrelizumab, even if the infusion was incomplete.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	RMS Cohort Arm 1: Ocrelizumab + LP

Reporting group description:

Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP before the start of dosing (Week 1, treatment baseline) with ocrelizumab and a second LP at Week 12. Participants will be asked to have an additional optional LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.

Reporting group title	RMS Cohort Arm 2: Ocrelizumab + LP

Reporting group description:

Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP before the start of dosing (Week 1, treatment baseline) with ocrelizumab and a second LP at Week 24. Participants will be asked to have an additional optional LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.

Reporting group title	PPMS Cohort: Ocrelizumab + LP

Reporting group description:

For the PPMS cohort, ocrelizumab will be administered as two 300-mg IV infusions separated by 14 days at a scheduled interval of every 24 weeks during the treatment period and then as a single 600-mg dose every 24 weeks starting week 72 during the Long-Term Extension period.

Reporting group title	RMS Cohort Arm 4: Ocrelizumab + LP

Reporting group description:

Ocrelizumab treatment will be delayed for 12 weeks from pre-treatment baseline. Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP at Week -12 (pre-treatment baseline) and a second LP before the start of dosing (Week 1, treatment baseline). Participants will be asked to have an additional optional LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.

Reporting group title	RMS Cohort Arm 3: Ocrelizumab + LP

Reporting group description:

Participants with RMS will receive ocrelizumab as two 300-mg IV infusion on Days 1 and 15 then as single infusion of 600 mg on Weeks 24 and 48. Participants will receive a LP before the start of dosing (Week 1, treatment baseline) with ocrelizumab and a second LP at Week 52. Participants that complete the study and continue to receive ocrelizumab will receive single infusions every 24 weeks starting from Week 72.

Serious adverse events	RMS Cohort Arm 1: Ocrelizumab + LP	RMS Cohort Arm 2: Ocrelizumab + LP	PPMS Cohort: Ocrelizumab + LP
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 23 (21.74%)	5 / 31 (16.13%)	9 / 31 (29.03%)
number of deaths (all causes)	1	0	1

number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Eye injury			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (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
Injury			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (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
Rib fracture			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
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 disorders			
Seizure			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	0 / 31 (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
Myelitis transverse			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple sclerosis relapse			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (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
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn's disease			

subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	0 / 31 (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
Enteritis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	0 / 31 (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
Umbilical hernia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Assisted suicide			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bipolar disorder			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mania			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	0 / 31 (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

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	0 / 31 (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
Seronegative arthritis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (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			
COVID-19 pneumonia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (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
Pneumonia			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Appendicitis			
subjects affected / exposed	2 / 23 (8.70%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	RMS Cohort Arm 4: Ocrelizumab + LP	RMS Cohort Arm 3: Ocrelizumab + LP	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 18 (27.78%)	1 / 28 (3.57%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Eye injury			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelitis transverse			

subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis relapse			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Assisted suicide			

subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar disorder			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seronegative arthritis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Influenza			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	RMS Cohort Arm 1: Ocrelizumab + LP	RMS Cohort Arm 2: Ocrelizumab + LP	PPMS Cohort: Ocrelizumab + LP
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 23 (100.00%)	28 / 31 (90.32%)	31 / 31 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0

Vascular disorders			
Vasculitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Peripheral coldness			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	3 / 31 (9.68%)
occurrences (all)	1	1	3
Influenza like illness			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	2 / 31 (6.45%)
occurrences (all)	0	1	6
Gait disturbance			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
Fatigue			
subjects affected / exposed	1 / 23 (4.35%)	2 / 31 (6.45%)	5 / 31 (16.13%)
occurrences (all)	1	2	10
Facial pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Pain			
subjects affected / exposed	2 / 23 (8.70%)	1 / 31 (3.23%)	1 / 31 (3.23%)
occurrences (all)	2	1	1
Puncture site pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	3 / 31 (9.68%)
occurrences (all)	1	0	4
Pyrexia			

subjects affected / exposed	1 / 23 (4.35%)	3 / 31 (9.68%)	2 / 31 (6.45%)
occurrences (all)	1	4	4
Vessel puncture site pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	1 / 31 (3.23%)
occurrences (all)	1	1	1
Reproductive system and breast disorders			
Breast cyst			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	2 / 23 (8.70%)	1 / 31 (3.23%)	8 / 31 (25.81%)
occurrences (all)	2	1	8
Hiccups			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	2 / 23 (8.70%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	1
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	2 / 23 (8.70%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	2	0	2

Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Depression			
subjects affected / exposed	2 / 23 (8.70%)	2 / 31 (6.45%)	5 / 31 (16.13%)
occurrences (all)	2	2	5
Insomnia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Panic attack			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Restlessness			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Somnambulism			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood iron decreased			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Influenza A virus test positive			
subjects affected / exposed	2 / 23 (8.70%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Occult blood			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Weight increased			

subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Blood uric acid increased			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Chillblains			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
Fall			
subjects affected / exposed	2 / 23 (8.70%)	2 / 31 (6.45%)	5 / 31 (16.13%)
occurrences (all)	2	2	9
Infusion related reaction			
subjects affected / exposed	15 / 23 (65.22%)	9 / 31 (29.03%)	12 / 31 (38.71%)
occurrences (all)	36	13	38
Joint dislocation			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	2 / 23 (8.70%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	2	0	2
Limb injury			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Post lumbar puncture syndrome			
subjects affected / exposed	2 / 23 (8.70%)	4 / 31 (12.90%)	6 / 31 (19.35%)
occurrences (all)	3	5	8
Post procedural contusion			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Procedural dizziness			

subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	1 / 23 (4.35%)	2 / 31 (6.45%)	3 / 31 (9.68%)
occurrences (all)	2	2	3
Road traffic accident			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	4	0	1
Skin abrasion			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Thermal burn			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	4 / 31 (12.90%)
occurrences (all)	1	0	4
Palpitations			
subjects affected / exposed	2 / 23 (8.70%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	3	0	0
Nervous system disorders			
Multiple sclerosis pseudo relapse			
subjects affected / exposed	3 / 23 (13.04%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	5	0	0
Balance disorder			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	4 / 31 (12.90%)
occurrences (all)	0	0	4
Burning sensation			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Cognitive disorder			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Coordination abnormal			

subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	2 / 31 (6.45%)
occurrences (all)	0	1	3
Dysarthria			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 23 (8.70%)	6 / 31 (19.35%)	5 / 31 (16.13%)
occurrences (all)	4	10	5
Hypoaesthesia			
subjects affected / exposed	2 / 23 (8.70%)	1 / 31 (3.23%)	4 / 31 (12.90%)
occurrences (all)	2	1	6
Lhermitte's sign			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	2 / 23 (8.70%)	4 / 31 (12.90%)	0 / 31 (0.00%)
occurrences (all)	2	4	0
Multiple sclerosis			
subjects affected / exposed	3 / 23 (13.04%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	3	0	0
Muscle spasticity			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
Restless arm syndrome			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Sensory disturbance			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Sinus headache			

subjects affected / exposed	0 / 23 (0.00%)	2 / 31 (6.45%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Somnolence			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	1 / 31 (3.23%)
occurrences (all)	0	1	1
Tremor			
subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	2 / 31 (6.45%)
occurrences (all)	1	1	2
Paraesthesia			
subjects affected / exposed	3 / 23 (13.04%)	2 / 31 (6.45%)	4 / 31 (12.90%)
occurrences (all)	4	3	7
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Inner ear inflammation			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	2 / 23 (8.70%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	1
Vertigo			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Eye disorders			

Vision blurred			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Ocular hyperaemia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	1 / 31 (3.23%)
occurrences (all)	0	1	1
Abdominal pain			
subjects affected / exposed	1 / 23 (4.35%)	2 / 31 (6.45%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
Anal incontinence			
subjects affected / exposed	2 / 23 (8.70%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Constipation			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	3 / 23 (13.04%)	1 / 31 (3.23%)	1 / 31 (3.23%)
occurrences (all)	3	1	2
Diverticulum			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Vomiting			

subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	2
Nausea			
subjects affected / exposed	1 / 23 (4.35%)	3 / 31 (9.68%)	2 / 31 (6.45%)
occurrences (all)	1	3	3
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 23 (0.00%)	3 / 31 (9.68%)	2 / 31 (6.45%)
occurrences (all)	0	3	2
Dermatitis allergic			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Hand dermatitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0

Pruritus			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Psoriasis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Rash			
subjects affected / exposed	0 / 23 (0.00%)	2 / 31 (6.45%)	2 / 31 (6.45%)
occurrences (all)	0	2	2
Rosacea			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Rash erythematous			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Urinary hesitation			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
Dysuria			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			

Neck pain			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	3 / 31 (9.68%)
occurrences (all)	1	0	3
Arthralgia			
subjects affected / exposed	2 / 23 (8.70%)	3 / 31 (9.68%)	11 / 31 (35.48%)
occurrences (all)	2	3	14
Back pain			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	9 / 31 (29.03%)
occurrences (all)	1	0	10
Flank pain			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Limb discomfort			
subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	2 / 31 (6.45%)
occurrences (all)	1	1	3
Muscle spasms			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	3 / 31 (9.68%)
occurrences (all)	0	1	4
Muscle tightness			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Muscular weakness			
subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	4 / 31 (12.90%)
occurrences (all)	1	1	5
Musculoskeletal stiffness			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
Myalgia			
subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	3 / 31 (9.68%)
occurrences (all)	1	1	4
Pain in extremity			
subjects affected / exposed	3 / 23 (13.04%)	4 / 31 (12.90%)	3 / 31 (9.68%)
occurrences (all)	3	5	7
Tendonitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0

Tendon disorder			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 23 (4.35%)	2 / 31 (6.45%)	2 / 31 (6.45%)
occurrences (all)	1	2	2
Infected cyst			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 23 (4.35%)	2 / 31 (6.45%)	2 / 31 (6.45%)
occurrences (all)	1	2	3
Gastrointestinal infection			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	3
Gastroenteritis viral			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Ear infection			
subjects affected / exposed	2 / 23 (8.70%)	3 / 31 (9.68%)	0 / 31 (0.00%)
occurrences (all)	2	3	0
Conjunctivitis			
subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	2 / 31 (6.45%)
occurrences (all)	1	2	2
COVID-19			
subjects affected / exposed	4 / 23 (17.39%)	2 / 31 (6.45%)	5 / 31 (16.13%)
occurrences (all)	4	2	5
Bronchitis			
subjects affected / exposed	1 / 23 (4.35%)	5 / 31 (16.13%)	1 / 31 (3.23%)
occurrences (all)	1	5	1
Gastroenteritis			

subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	1 / 31 (3.23%)
occurrences (all)	1	1	1
Upper respiratory tract infection			
subjects affected / exposed	7 / 23 (30.43%)	6 / 31 (19.35%)	13 / 31 (41.94%)
occurrences (all)	10	12	22
Urinary tract infection			
subjects affected / exposed	4 / 23 (17.39%)	5 / 31 (16.13%)	11 / 31 (35.48%)
occurrences (all)	5	6	41
Tooth infection			
subjects affected / exposed	1 / 23 (4.35%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	4 / 23 (17.39%)	10 / 31 (32.26%)	2 / 31 (6.45%)
occurrences (all)	5	13	2
Rhinitis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Pyelonephritis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	1 / 23 (4.35%)	2 / 31 (6.45%)	4 / 31 (12.90%)
occurrences (all)	1	2	4
Pharyngitis streptococcal			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	1 / 31 (3.23%)
occurrences (all)	0	1	1
Oral herpes			
subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	2 / 31 (6.45%)
occurrences (all)	1	1	2
Oral candidiasis			

subjects affected / exposed	0 / 23 (0.00%)	2 / 31 (6.45%)	1 / 31 (3.23%)
occurrences (all)	0	3	1
Nasopharyngitis			
subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	5 / 31 (16.13%)
occurrences (all)	1	1	6
Vaginal infection			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Nail bed infection			
subjects affected / exposed	0 / 23 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 23 (4.35%)	2 / 31 (6.45%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 23 (0.00%)	2 / 31 (6.45%)	1 / 31 (3.23%)
occurrences (all)	0	2	1

Non-serious adverse events	RMS Cohort Arm 4: Ocrelizumab + LP	RMS Cohort Arm 3: Ocrelizumab + LP	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 18 (94.44%)	27 / 28 (96.43%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Vasculitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Peripheral coldness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	

Influenza like illness			
subjects affected / exposed	1 / 18 (5.56%)	2 / 28 (7.14%)	
occurrences (all)	1	4	
Gait disturbance			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	4 / 18 (22.22%)	3 / 28 (10.71%)	
occurrences (all)	8	3	
Facial pain			
subjects affected / exposed	0 / 18 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Chest discomfort			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Puncture site pain			
subjects affected / exposed	2 / 18 (11.11%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Peripheral swelling			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Vessel puncture site pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Reproductive system and breast disorders			

Breast cyst			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 18 (11.11%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	2 / 18 (11.11%)	3 / 28 (10.71%)	
occurrences (all)	2	3	
Hiccups			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Oropharyngeal pain			
subjects affected / exposed	1 / 18 (5.56%)	2 / 28 (7.14%)	
occurrences (all)	2	2	
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Anxiety			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Attention deficit hyperactivity disorder			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Depressed mood			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	0 / 18 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Insomnia			

subjects affected / exposed	1 / 18 (5.56%)	3 / 28 (10.71%)	
occurrences (all)	1	3	
Panic attack			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Restlessness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Somnambulism			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood iron decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Body temperature increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Influenza A virus test positive			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Occult blood			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Weight increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Blood uric acid increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Chillblains			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Contusion			

subjects affected / exposed	3 / 18 (16.67%)	0 / 28 (0.00%)	
occurrences (all)	3	0	
Fall			
subjects affected / exposed	2 / 18 (11.11%)	4 / 28 (14.29%)	
occurrences (all)	2	5	
Infusion related reaction			
subjects affected / exposed	11 / 18 (61.11%)	16 / 28 (57.14%)	
occurrences (all)	16	32	
Joint dislocation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Ligament sprain			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Limb injury			
subjects affected / exposed	2 / 18 (11.11%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Post lumbar puncture syndrome			
subjects affected / exposed	4 / 18 (22.22%)	4 / 28 (14.29%)	
occurrences (all)	4	7	
Post procedural contusion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Procedural dizziness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	2	
Road traffic accident			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Skin abrasion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Thermal burn			

subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Multiple sclerosis pseudo relapse			
subjects affected / exposed	2 / 18 (11.11%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Balance disorder			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Burning sensation			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	3	
Cognitive disorder			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Coordination abnormal			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	0 / 18 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Dysarthria			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	4 / 18 (22.22%)	4 / 28 (14.29%)	
occurrences (all)	5	4	
Hypoaesthesia			

subjects affected / exposed	2 / 18 (11.11%)	4 / 28 (14.29%)	
occurrences (all)	5	4	
Lhermitte's sign			
subjects affected / exposed	0 / 18 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	3	
Migraine			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Multiple sclerosis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Muscle spasticity			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Restless arm syndrome			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Restless legs syndrome			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Sensory disturbance			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Sinus headache			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Somnolence			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	2 / 18 (11.11%)	4 / 28 (14.29%)	
occurrences (all)	3	5	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Lymphadenopathy			
subjects affected / exposed	0 / 18 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Lymphopenia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Inner ear inflammation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Tinnitus			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Vertigo			
subjects affected / exposed	0 / 18 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Eye disorders			
Vision blurred			
subjects affected / exposed	2 / 18 (11.11%)	1 / 28 (3.57%)	
occurrences (all)	2	1	
Ocular hyperaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Eye pain			
subjects affected / exposed	2 / 18 (11.11%)	1 / 28 (3.57%)	
occurrences (all)	2	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			

subjects affected / exposed	2 / 18 (11.11%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Abdominal pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Anal incontinence			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	2 / 18 (11.11%)	2 / 28 (7.14%)	
occurrences (all)	2	2	
Diverticulum			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 28 (0.00%)	
occurrences (all)	3	0	
Vomiting			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	3 / 18 (16.67%)	4 / 28 (14.29%)	
occurrences (all)	3	5	
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 18 (16.67%)	0 / 28 (0.00%)	
occurrences (all)	3	0	
Food poisoning			
subjects affected / exposed	2 / 18 (11.11%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Dysphagia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			

Eczema			
subjects affected / exposed	1 / 18 (5.56%)	2 / 28 (7.14%)	
occurrences (all)	1	2	
Acne			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Alopecia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Dermatitis allergic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Hand dermatitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Psoriasis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	1 / 18 (5.56%)	3 / 28 (10.71%)	
occurrences (all)	1	5	
Rosacea			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Skin fissures			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	

Urticaria			
subjects affected / exposed	0 / 18 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Rash erythematous			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Urinary hesitation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Urinary retention			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Dysuria			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 18 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	4	
Arthralgia			
subjects affected / exposed	2 / 18 (11.11%)	4 / 28 (14.29%)	
occurrences (all)	3	5	
Back pain			
subjects affected / exposed	4 / 18 (22.22%)	2 / 28 (7.14%)	
occurrences (all)	4	2	
Flank pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Limb discomfort			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			

subjects affected / exposed	1 / 18 (5.56%)	3 / 28 (10.71%)	
occurrences (all)	1	5	
Muscle tightness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Muscular weakness			
subjects affected / exposed	2 / 18 (11.11%)	2 / 28 (7.14%)	
occurrences (all)	2	3	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 18 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 28 (0.00%)	
occurrences (all)	3	0	
Pain in extremity			
subjects affected / exposed	3 / 18 (16.67%)	5 / 28 (17.86%)	
occurrences (all)	6	6	
Tendonitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Tendon disorder			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 18 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Infected cyst			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Impetigo			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	

Gastrointestinal infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis viral			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	1 / 18 (5.56%)	2 / 28 (7.14%)	
occurrences (all)	1	2	
Conjunctivitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	4 / 18 (22.22%)	1 / 28 (3.57%)	
occurrences (all)	4	1	
Bronchitis			
subjects affected / exposed	1 / 18 (5.56%)	2 / 28 (7.14%)	
occurrences (all)	1	3	
Gastroenteritis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	2	1	
Upper respiratory tract infection			
subjects affected / exposed	12 / 18 (66.67%)	10 / 28 (35.71%)	
occurrences (all)	28	19	
Urinary tract infection			
subjects affected / exposed	7 / 18 (38.89%)	5 / 28 (17.86%)	
occurrences (all)	14	9	
Tooth infection			
subjects affected / exposed	1 / 18 (5.56%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
Sinusitis			
subjects affected / exposed	1 / 18 (5.56%)	4 / 28 (14.29%)	
occurrences (all)	1	5	
Rhinitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	

Respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Pyelonephritis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Pharyngitis streptococcal			
subjects affected / exposed	0 / 18 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Pharyngitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	2 / 18 (11.11%)	3 / 28 (10.71%)	
occurrences (all)	2	4	
Vaginal infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Nail bed infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Viral infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 28 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 November 2016	The protocol was expanded to include a control arm (Arm 4) to the RMS cohort that would allow for an estimate of the natural variability of the disease when analyzing other cohort arms
29 September 2017	A long-term extension (LTE) phase, beginning at Week 72 and continuing for up to 4 years, was added to collect additional safety and efficacy information
18 December 2020	The protocol was amended to incorporate an optional shorter study drug infusion regimen for patients enrolled in the LTE phase

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported