Clinical trial results:
Phase II, Multicenter, Randomized, Parallel-Group, Partially Blinded, Placebo and Avonex Controlled Dose Finding Study to Evaluate the Efficacy As Measured by Brain MRI Lesions, and Safety of 2 Dose Regimens of Ocrelizumab in Patients With RRMS

Summary

EudraCT number	2007-006338-32
Trial protocol	FR GB DE ES CZ SK DK BE NL FI BG IT
Global end of trial date	08 November 2023

Results information

Result version number	v2 (current)
This version publication date	10 November 2024
First version publication date	22 March 2015
Version creation reason	
Summary attachment (see zip file)	WA21493 (CSR synopsis) (CSR WA21493_Redacted.pdf)

Trial information

Trial identification

Sponsor protocol code	ACT4422g

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00676715
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4058
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	Medical Communications, F. Hoffmann-La Roche AG, +41 616878333, 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	08 November 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was a Avonex (interferon beta-1a) controlled dose finding study to evaluate the efficacy as measured by brain MRI lesions, and safety of 2 dose regimens of ocrelizumab in participants with relapsing remitting multiple sclerosis (RRMS).

Protection of trial subjects:

All study participants were required to read and sign an informed consent form (ICF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 July 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	84 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Bulgaria: 11
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Czechia: 14
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Russian Federation: 17
Country: Number of subjects enrolled	Romania: 4
Country: Number of subjects enrolled	Serbia: 34
Country: Number of subjects enrolled	Slovakia: 14
Country: Number of subjects enrolled	Ukraine: 26
Country: Number of subjects enrolled	United States: 47

Worldwide total number of subjects	218
EEA total number of subjects	72

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)	218
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 220 participants were randomized, of which 218 received study treatment. Participants took part in the study at 79 investigative sites across 18 countries from July 17, 2008, to November 08, 2023.

Pre-assignment

Screening details:

The study consisted of a 96-week Treatment Period (TP) followed by a Treatment-free period (TFP). Participants who completed both TP & TFP (at least Week 120) were invited to participate in the optional Open-label Extension (OLE) period.

Period 1

Period 1 title	Treatment Period (TP)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Avonex/Ocrelizumab 600 mg (Active Comparator) group was open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo / Ocrelizumab 600 mg

Arm description:

In the Treatment Period, participants received placebo as intravenous (IV) infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 milligrams (mg), IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600 mg, once every 24 weeks (Q24W).

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab 600 mg
Investigational medicinal product code	RO4964913
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab was administered 300 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by, 600 mg, IV, on Day 1 of Cycle 2 and 600 mg, IV, on Day 1 of Cycles 3 and 4.

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

Dosage and administration details:

Placebo was administered on Day 1, and Day 15 in Cycle 1 (1 Cycle = 168 days)

Arm title	Ocrelizumab 600 mg / Ocrelizumab 600 mg

Arm description:

In the Treatment Period, participants received ocrelizumab 300 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 600 mg, IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4.

Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600 mg, Q24W.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab 600 mg
Investigational medicinal product code	RO4964913
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab was administered 300 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by, 600 mg, IV, on Day 1 of Cycle 2 and 600 mg, IV, on Day 1 of Cycles 3 and 4.

Arm title	Ocrelizumab 1000 mg / Ocrelizumab 600 mg

Arm description:

In the Treatment Period, participants received ocrelizumab 1000 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 1000 mg IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 1000 mg, IV, on Day 1 of Cycle 3 and ocrelizumab, 600 mg, IV, on Day 1 of Cycle 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600 mg, Q24W.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab 600 mg
Investigational medicinal product code	RO4964913
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab was administered 300 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by, 600 mg, IV, on Day 1 of Cycle 2 and 600 mg, IV, on Day 1 of Cycles 3 and 4.

Investigational medicinal product name	Ocrelizumab 1000 mg
Investigational medicinal product code	RO4964913
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab was administered 1000 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by, 1000 mg, IV, on Day 1 of Cycle 2 and placebo IV on Day 15 of Cycle 2 followed by ocrelizumab, 1000 mg, IV, on Day 1 of Cycles 3 and 4.

Arm title	Avonex / Ocrelizumab 600 mg

Arm description:

In the Treatment Period, participants received Avonex 30 micrograms (mcg) as intramuscular (IM) injection once every week of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600 mg, Q24W.

Arm type	Active comparator
Investigational medicinal product name	Ocrelizumab 600 mg
Investigational medicinal product code	RO4964913
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:	
Ocrelizumab administered 300 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by, 600 mg, IV, on Day 1 of Cycle 2 and 600 mg, IV, on Day 1 of Cycles 3 and 4.	
Investigational medicinal product name	Avonex
Investigational medicinal product code	
Other name	Interferon beta-1a
Pharmaceutical forms	Powder and solvent for concentrate for solution for infusion
Routes of administration	Intramuscular use
Dosage and administration details:	
Avonex was administered 30 mcg as IM injection every week of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 2 and 600 mg, IV, on Day 1 of Cycles 3 and 4.	

Number of subjects in period 1	Placebo / Ocrelizumab 600 mg	Ocrelizumab 600 mg / Ocrelizumab 600 mg	Ocrelizumab 1000 mg / Ocrelizumab 600 mg
Started	54	55	55
Completed	48	46	43
Not completed	6	9	12
Adverse event, serious fatal	-	-	1
Insufficient therapeutic response	1	1	2
Failure to return	1	-	-
Administrative	-	-	-
Adverse event, non-fatal	-	3	2
Violation of selection criteria at entry	-	-	1
Refused treatment/did not cooperate	1	2	3
Withdrew consent	3	3	3

Number of subjects in period 1	Avonex / Ocrelizumab 600 mg
Started	54
Completed	46
Not completed	8
Adverse event, serious fatal	-
Insufficient therapeutic response	1
Failure to return	-
Administrative	1
Adverse event, non-fatal	2
Violation of selection criteria at entry	-
Refused treatment/did not cooperate	1
Withdrew consent	3

Period 2

Period 2 title	Treatment-free Period (TFP)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/ Ocrelizumab 600 mg

Arm description:

In the Treatment Period, participants received placebo as intravenous (IV) infusion on Days 1 and 15 of Cycle 1 (1Cycle=168 days), followed by ocrelizumab, 300 milligrams (mg), IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, once every 24 weeks (Q24W).

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Ocrelizumab 600 mg/Ocrelizumab 600 mg

Arm description:

In the Treatment Period, participants received ocrelizumab 300 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 600 mg, IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Ocrelizumab 1000 mg/ Ocrelizumab 600 mg

Arm description:

In the Treatment Period, participants received ocrelizumab 1000 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 1000 mg IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 1000 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Avonex/ Ocrelizumab 600 mg

Arm description:

In the Treatment Period, participants received Avonex 30 micrograms (mcg) as intramuscular (IM) injection every week of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Placebo/ Ocrelizumab 600 mg	Ocrelizumab 600 mg/Ocrelizumab 600 mg	Ocrelizumab 1000 mg/ Ocrelizumab 600 mg
Started	48	46	43
Completed	35	32	30
Not completed	14	16	20
Adverse event, serious fatal	1	1	1
Consent withdrawn by subject	3	3	4
Adverse event, non-fatal	-	-	1
Lost to follow-up	2	2	6
Reason not provided	8	10	8
Joined	1	2	7
Participants Joined from TP.	1	2	7

Number of subjects in period 2	Avonex/ Ocrelizumab 600 mg
Started	46
Completed	35
Not completed	14
Adverse event, serious fatal	-
Consent withdrawn by subject	5
Adverse event, non-fatal	-
Lost to follow-up	2
Reason not provided	7
Joined	3
Participants Joined from TP.	3

Period 3	
Period 3 title	Open Label Extension (OLE)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes

Arm title	Placebo/ Ocrelizumab 600 mg

Arm description:

In the Treatment Period, participants received placebo as intravenous (IV) infusion on Days 1 and 15 of Cycle 1 (1Cycle=168 days), followed by ocrelizumab, 300 milligrams (mg), IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, once every 24 weeks (Q24W).

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab 600 mg
Investigational medicinal product code	RO4964913
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab 300mg was administered IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of 600mg, Q24W.

Arm title	Ocrelizumab 600 mg/Ocrelizumab 600 mg

Arm description:

In the Treatment Period, participants received ocrelizumab 300 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 600 mg, IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab 600 mg
Investigational medicinal product code	RO4964913
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab 300mg was administered IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of 600mg, Q24W.

Arm title	Ocrelizumab 1000 mg/ Ocrelizumab 600 mg

Arm description:

In the Treatment Period, participants received ocrelizumab 1000 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 1000 mg IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 1000 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab 600 mg
Investigational medicinal product code	RO4964913
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab 300mg was administered IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of 600mg, Q24W.

Arm title	Avonex/ Ocrelizumab 600 mg

Arm description:

In the Treatment Period, participants received Avonex 30 micrograms (mcg) as intramuscular (IM) injection every week of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Arm type	Active comparator
Investigational medicinal product name	Ocrelizumab 600 mg
Investigational medicinal product code	RO4964913
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ocrelizumab 300mg was administered IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of 600mg, Q24W.

Number of subjects in period 3[1]	Placebo/ Ocrelizumab 600 mg	Ocrelizumab 600 mg/Ocrelizumab 600 mg	Ocrelizumab 1000 mg/ Ocrelizumab 600 mg
Started	29	32	19
Completed	22	21	11
Not completed	7	11	8
Adverse event, serious fatal	2	-	2
Consent withdrawn by subject	2	4	3
Adverse event, non-fatal	-	3	1
Lost to follow-up	-	-	1
Reason not provided	3	4	1

Number of subjects in period 3[1]	Avonex/ Ocrelizumab 600 mg
Started	24
Completed	14
Not completed	10
Adverse event, serious fatal	2
Consent withdrawn by subject	3
Adverse event, non-fatal	-
Lost to follow-up	1
Reason not provided	4

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Participants who have completed both the Treatment Period and the Treatment-Free Period will be invited to participate in the OLE. Participants will be re-consented for participation and enter the OLE screening period where they will undergo an evaluation for continued eligibility. Participants who are not eligible, or choose not to enter the OLE will complete the trial after their B-cells have repleted.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo / Ocrelizumab 600 mg
Reporting group description:	
In the Treatment Period, participants received placebo as intravenous (IV) infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 milligrams (mg), IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600 mg, once every 24 weeks (Q24W).	
Reporting group title	Ocrelizumab 600 mg / Ocrelizumab 600 mg
Reporting group description:	
In the Treatment Period, participants received ocrelizumab 300 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 600 mg, IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600 mg, Q24W.	
Reporting group title	Ocrelizumab 1000 mg / Ocrelizumab 600 mg
Reporting group description:	
In the Treatment Period, participants received ocrelizumab 1000 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 1000 mg IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 1000 mg, IV, on Day 1 of Cycle 3 and ocrelizumab, 600 mg, IV, on Day 1 of Cycle 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600 mg, Q24W.	
Reporting group title	Avonex / Ocrelizumab 600 mg
Reporting group description:	
In the Treatment Period, participants received Avonex 30 micrograms (mcg) as intramuscular (IM) injection once every week of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600 mg, Q24W.	

Reporting group values	Placebo / Ocrelizumab 600 mg	Ocrelizumab 600 mg / Ocrelizumab 600 mg	Ocrelizumab 1000 mg / Ocrelizumab 600 mg
Number of subjects	54	55	55
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	38.0	35.6	38.5
standard deviation	± 8.8	± 8.5	± 8.7
Gender, Male/Female Units: participants			
Female	36	35	38
Male	18	20	17

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	3	2
White	52	51	53
More than one race	0	0	0
Unknown or Not Reported	1	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	6	6	7
Not Hispanic or Latino	48	49	48
Unknown or Not Reported	0	0	0

Reporting group values	Avonex / Ocrelizumab 600 mg	Total	
Number of subjects	54	218	
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	38.1		
standard deviation	± 9.3	-	
Gender, Male/Female Units: participants			
Female	32	141	
Male	22	77	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	0	1	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	6	
White	53	209	
More than one race	0	0	
Unknown or Not Reported	0	1	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	7	26	
Not Hispanic or Latino	47	192	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Placebo / Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received placebo as intravenous (IV) infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 milligrams (mg), IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600 mg, once every 24 weeks (Q24W).

Reporting group title	Ocrelizumab 600 mg / Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received ocrelizumab 300 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 600 mg, IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600 mg, Q24W.

Reporting group title	Ocrelizumab 1000 mg / Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received ocrelizumab 1000 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 1000 mg IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 1000 mg, IV, on Day 1 of Cycle 3 and ocrelizumab, 600 mg, IV, on Day 1 of Cycle 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600 mg, Q24W.

Reporting group title	Avonex / Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received Avonex 30 micrograms (mcg) as intramuscular (IM) injection once every week of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600 mg, Q24W.

Reporting group title	Placebo/ Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received placebo as intravenous (IV) infusion on Days 1 and 15 of Cycle 1 (1Cycle=168 days), followed by ocrelizumab, 300 milligrams (mg), IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, once every 24 weeks (Q24W).

Reporting group title	Ocrelizumab 600 mg/Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received ocrelizumab 300 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 600 mg, IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Reporting group title	Ocrelizumab 1000 mg/ Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received ocrelizumab 1000 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 1000 mg IV, on Day 1 and placebo IV on Day 15

of Cycle 2. Participants then received ocrelizumab, 1000 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Reporting group title	Avonex/ Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received Avonex 30 micrograms (mcg) as intramuscular (IM) injection every week of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Reporting group title	Placebo/ Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received placebo as intravenous (IV) infusion on Days 1 and 15 of Cycle 1 (1Cycle=168 days), followed by ocrelizumab, 300 milligrams (mg), IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, once every 24 weeks (Q24W).

Reporting group title	Ocrelizumab 600 mg/Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received ocrelizumab 300 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 600 mg, IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Reporting group title	Ocrelizumab 1000 mg/ Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received ocrelizumab 1000 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 1000 mg IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 1000 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Reporting group title	Avonex/ Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received Avonex 30 micrograms (mcg) as intramuscular (IM) injection every week of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Primary: Total Number of Gadolinium-Enhancing T1 Lesions Observed on Magnetic R4esonance Imaging (MRI) Scans of the Brain

End point title	Total Number of Gadolinium-Enhancing T1 Lesions Observed on Magnetic R4esonance Imaging (MRI) Scans of the Brain

End point description:

Mean of total number of gadolinium-enhancing T1 lesions observed on MRI scans of the brain at Weeks 12, 16, 20, 24 was determined using average imputation method. The intent-to-treat population includes all randomized participants who had received any study drug. Here, number analysed signifies the participants who were evaluable for the outcome.

End point type	Primary

End point timeframe:

Week 12 to Week 24

End point values	Placebo / Ocrelizumab 600 mg	Ocrelizumab 600 mg / Ocrelizumab 600 mg	Ocrelizumab 1000 mg / Ocrelizumab 600 mg	Avonex / Ocrelizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	51	52	52
Units: lesions				
arithmetic mean (standard deviation)	5.6 (± 12.53)	0.6 (± 1.52)	0.2 (± 0.65)	6.9 (± 16.01)

Statistical analyses

Statistical analysis title	Placebo vs Ocrelizumab 600 mg

Statistical analysis description:

Van Elteren test is stratified by region and presence of baseline gadolinium-enhancing lesions (absent or present).

Comparison groups	Placebo / Ocrelizumab 600 mg v Ocrelizumab 600 mg / Ocrelizumab 600 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Van Elteren Test (stratified)

Statistical analysis title	Placebo vs Avonex

Statistical analysis description:

Van Elteren test is stratified by region and presence of baseline gadolinium-enhancing lesions (absent or present).

Comparison groups	Placebo / Ocrelizumab 600 mg v Avonex / Ocrelizumab 600 mg
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7496
Method	Van Elteren Test (stratified)

Statistical analysis title	Placebo vs Ocrelizumab 1000 mg

Statistical analysis description:

Van Elteren test is stratified by region and presence of baseline gadolinium-enhancing lesions (absent or present).

Comparison groups	Placebo / Ocrelizumab 600 mg v Ocrelizumab 1000 mg / Ocrelizumab 600 mg

Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Van Elteren Test (stratified)

Secondary: Annualized Protocol Defined Relapse Rate at Week 24

End point title	Annualized Protocol Defined Relapse Rate at Week 24

End point description:

Adjusted annualized relapse rate for geographical region is reported here. The relapse rate was calculated as the total number of relapses for each participant divided by the total number of patient-years. The intent-to-treat population includes all randomized participants who had received any study drug.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo / Ocrelizumab 600 mg	Ocrelizumab 600 mg / Ocrelizumab 600 mg	Ocrelizumab 1000 mg / Ocrelizumab 600 mg	Avonex / Ocrelizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	54
Units: relapses per year				
number (confidence interval 95%)	0.557 (0.370 to 0.839)	0.127 (0.054 to 0.299)	0.213 (0.110 to 0.414)	0.364 (0.220 to 0.602)

Statistical analyses

Statistical analysis title	Placebo vs Ocrelizumab 600 mg

Statistical analysis description:

Poisson model was fitted for adjusting for geographic region only.

Comparison groups	Placebo / Ocrelizumab 600 mg v Ocrelizumab 600 mg / Ocrelizumab 600 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0019
Method	Poisson model

Statistical analysis title	Placebo vs Avonex

Statistical analysis description:

Poisson model was fitted for adjusting for geographic region only.

Comparison groups	Placebo / Ocrelizumab 600 mg v Avonex / Ocrelizumab 600 mg

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1814
Method	Poisson model

Statistical analysis title	Placebo vs Ocrelizumab 1000 mg
Statistical analysis description: Poisson model was fitted for adjusting for geographic region only.	
Comparison groups	Placebo / Ocrelizumab 600 mg v Ocrelizumab 1000 mg / Ocrelizumab 600 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0136
Method	Poisson model

Secondary: Percentage of Participants Who Remained Relapse Free at Week 24

End point title	Percentage of Participants Who Remained Relapse Free at Week 24
End point description: Percentage of participants who remained relapse free at Week 24 were reported. The intent-to-treat population includes all randomized participants who had received any study drug. Percentages have been rounded off to the first decimal.	
End point type	Secondary
End point timeframe: Week 24	

End point values	Placebo / Ocrelizumab 600 mg	Ocrelizumab 600 mg / Ocrelizumab 600 mg	Ocrelizumab 1000 mg / Ocrelizumab 600 mg	Avonex / Ocrelizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	54
Units: percentage of participants				
number (confidence interval 95%)	75.9 (64.5 to 87.3)	85.5 (76.1 to 94.8)	87.3 (78.5 to 96.1)	77.8 (66.7 to 88.9)

Statistical analyses

Statistical analysis title	Placebo vs Ocrelizumab 600 mg
Comparison groups	Placebo / Ocrelizumab 600 mg v Ocrelizumab 600 mg / Ocrelizumab 600 mg

Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1978
Method	Cochran-Mantel-Haenszel chi-square test
Parameter estimate	Relative risk (RR)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	1.34

Statistical analysis title	Placebo vs Avonex
Comparison groups	Placebo / Ocrelizumab 600 mg v Avonex / Ocrelizumab 600 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8206
Method	CMH chi-square tes
Parameter estimate	Relative risk (RR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	1.84

Statistical analysis title	Placebo vs Ocrelizumab 1000 mg
Comparison groups	Placebo / Ocrelizumab 600 mg v Ocrelizumab 1000 mg / Ocrelizumab 600 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.131
Method	CMH chi-square test
Parameter estimate	Relative risk (RR)
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	1.22

Secondary: Change From Baseline in Total Volume of T2 Lesions on MRI Scans of the Brain at Week 24

End point title	Change From Baseline in Total Volume of T2 Lesions on MRI Scans of the Brain at Week 24

End point description:

Change from baseline in total volume of T2 lesions on MRI scans of the brain at Week 24 was reported. The intent-to-treat population includes all randomized participants who had received any study drug. Overall number of participants analyzed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo / Ocrelizumab 600 mg	Ocrelizumab 600 mg / Ocrelizumab 600 mg	Ocrelizumab 1000 mg / Ocrelizumab 600 mg	Avonex / Ocrelizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	55	55	54
Units: cubic millimeter (mm^3)				
arithmetic mean (standard deviation)				
Baseline (n= 47, 51, 53, 49)	8950.84 (± 9776.261)	13972.61 (± 19930.158)	13178.30 (± 14271.383)	13209.11 (± 17206.511)
Change at Week 24 (n= 43, 45, 46, 46)	-112.31 (± 1464.206)	-878.84 (± 2756.839)	-600.89 (± 2105.964)	1040.06 (± 4510.140)

Statistical analyses

Statistical analysis title	Placebo vs Ocrelizumab 600 mg
Comparison groups	Placebo / Ocrelizumab 600 mg v Ocrelizumab 600 mg / Ocrelizumab 600 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1391
Method	Van Elteren Test (stratified)

Statistical analysis title	Placebo vs Avonex
Comparison groups	Placebo / Ocrelizumab 600 mg v Avonex / Ocrelizumab 600 mg
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.474
Method	Van Elteren Test (stratified)

Statistical analysis title	Placebo vs Ocrelizumab 1000 mg
Comparison groups	Placebo / Ocrelizumab 600 mg v Ocrelizumab 1000 mg / Ocrelizumab 600 mg
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1596
Method	Van Elteren Test (stratified)

Secondary: Total Number of Gadolinium-Enhancing T1 Lesions

End point title	Total Number of Gadolinium-Enhancing T1 Lesions

End point description:

Total number of gadolinium-enhancing T1 lesions from Week 4 to Week 24 were reported. The intent-to-treat population includes all randomized participants who had received any study drug. Overall number of participants analyzed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Weeks 4 to Week 24

End point values	Placebo / Ocrelizumab 600 mg	Ocrelizumab 600 mg / Ocrelizumab 600 mg	Ocrelizumab 1000 mg / Ocrelizumab 600 mg	Avonex / Ocrelizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	51	52	52
Units: lesions				
arithmetic mean (standard deviation)	8.7 (± 17.54)	2.5 (± 5.10)	1.8 (± 5.26)	10.3 (± 22.15)

Statistical analyses

Statistical analysis title	Placebo vs Ocrelizumab 600 mg
Comparison groups	Placebo / Ocrelizumab 600 mg v Ocrelizumab 600 mg / Ocrelizumab 600 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0004
Method	Van Elteren Test (stratified)

Statistical analysis title	Placebo vs Ocrelizumab 600 mg
Comparison groups	Placebo / Ocrelizumab 600 mg v Avonex / Ocrelizumab 600 mg

Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2725
Method	Van Elteren Test (stratified)

Statistical analysis title	Placebo vs Ocrelizumab 1000 mg
Comparison groups	Placebo / Ocrelizumab 600 mg v Ocrelizumab 1000 mg / Ocrelizumab 600 mg
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Van Elteren Test (stratified)

Secondary: Total Number of New Gadolinium-Enhancing T1 Lesions Observed by MRI Scans of the Brain

End point title	Total Number of New Gadolinium-Enhancing T1 Lesions Observed by MRI Scans of the Brain

End point description:

Total number of new gadolinium-enhancing T1 lesions observed by MRI scans of the brain were reported. The intent-to-treat population includes all randomized participants who had received any study drug. Overall number of participants analyzed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Weeks 4 to Week 24

End point values	Placebo / Ocrelizumab 600 mg	Ocrelizumab 600 mg / Ocrelizumab 600 mg	Ocrelizumab 1000 mg / Ocrelizumab 600 mg	Avonex / Ocrelizumab 600 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	51	52	52
Units: lesions				
arithmetic mean (standard deviation)	5.1 (± 11.99)	0.8 (± 1.95)	0.8 (± 2.16)	6.2 (± 13.79)

Statistical analyses

Statistical analysis title	Placebo vs Ocrelizumab 600 mg
Comparison groups	Placebo / Ocrelizumab 600 mg v Ocrelizumab 600 mg / Ocrelizumab 600 mg

Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Van Elteren Test (stratified)

Statistical analysis title	Placebo vs Avonex
Comparison groups	Placebo / Ocrelizumab 600 mg v Avonex / Ocrelizumab 600 mg
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4985
Method	Van Elteren Test (stratified)

Statistical analysis title	Placebo vs Ocrelizumab 1000 mg
Comparison groups	Placebo / Ocrelizumab 600 mg v Ocrelizumab 1000 mg / Ocrelizumab 600 mg
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Van Elteren Test (stratified)

Adverse events information

Timeframe for reporting adverse events:

Up to 787 Weeks

Adverse event reporting additional description:

The safety population included all participants who received any study drug and underwent at least one assessment of safety. As per planned analysis adverse events from both the TP and TFP were combined and reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Placebo/Ocrelizumab 600mg

Reporting group description:

In the Treatment Period, participants received placebo as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Reporting group title	Ocrelizumab 600mg/Ocrelizumab 600mg

Reporting group description:

In the Treatment Period, participants received ocrelizumab 300 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 600 mg, IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W

Reporting group title	Ocrelizumab 600 mg Open Label Extension (OLE)

Reporting group description:

Participants who opted to enroll in the OLE received two IV infusions of ocrelizumab, 300mg on Days 1 and 15 of Cycle 5, followed by a single infusion of ocrelizumab, 600mg, once Q24W

Reporting group title	Avonex/Ocrelizumab 600 mg

Reporting group description:

In the Treatment Period, participants received Avonex 30 mcg as IM injection once every week of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 300 mg, IV, on Days 1 and 15 of Cycle 2. Participants then received ocrelizumab, 600 mg, IV, on Day 1 of Cycles 3 and 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Reporting group title	Ocrelizumab 1000mg/Ocrelizumab 600mg

Reporting group description:

In the Treatment Period, participants received ocrelizumab 1000 mg as IV infusion on Days 1 and 15 of Cycle 1 (1 Cycle = 168 days), followed by ocrelizumab, 1000 mg IV, on Day 1 and placebo IV on Day 15 of Cycle 2. Participants then received ocrelizumab, 1000 mg, IV, on Day 1 of Cycle 3 and ocrelizumab, 600 mg, IV, on Day 1 of Cycle 4. Participants who completed the TP then entered the TFP which was of variable duration. Participants who completed the TP and the TFP (at least through Week 120) and opted to enroll in the OLE period received ocrelizumab, 300mg, IV, on Days 1 and 15 of Cycle 5 followed by a single infusion of ocrelizumab, 600mg, Q24W.

Serious adverse events	Placebo/Ocrelizumab 600mg	Ocrelizumab 600mg/Ocrelizumab 600mg	Ocrelizumab 600 mg Open Label Extension (OLE)
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 54 (20.37%)	17 / 55 (30.91%)	28 / 103 (27.18%)
number of deaths (all causes)	3	1	6
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BREAST CANCER			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
LUNG NEOPLASM MALIGNANT			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
PREGNANCY			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	0 / 103 (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
General disorders and administration site conditions			
DRUG WITHDRAWAL SYNDROME			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
SYSTEMIC INFLAMMATORY			

RESPONSE SYNDROME			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
DEATH			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
PYREXIA			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
HYPERSENSITIVITY			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	0 / 103 (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
Reproductive system and breast disorders			
OVARIAN MASS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
UTERINE PROLAPSE			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 1	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	1 / 54 (1.85%)	0 / 55 (0.00%)	2 / 103 (1.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Psychiatric disorders			
DEPRESSION			

subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
ACUTE PSYCHOSIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
SUSPECTED SUICIDE ATTEMPT			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
ANXIETY			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
SUICIDAL IDEATION			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
Investigations			
AMYLASE INCREASED			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD POTASSIUM INCREASED			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMEAR CERVIX ABNORMAL			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	0 / 103 (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
Injury, poisoning and procedural complications			

INFUSION RELATED REACTION			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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	1 / 54 (1.85%)	0 / 55 (0.00%)	0 / 103 (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
SUBDURAL HAEMATOMA			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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			
CARDIAC ARREST			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	1 / 103 (0.97%)
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			
MULTIPLE SCLEROSIS RELAPSE			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
SEIZURE			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
EPILEPSY			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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 DISORDER			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MULTIPLE SCLEROSIS PSEUDO RELAPSE			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	2 / 103 (1.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCLE SPASTICITY			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	0 / 103 (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
Blood and lymphatic system disorders			
NEUTROPENIA			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAEMIA			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMMUNE THROMBOCYTOPENIA			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	0 / 103 (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
Eye disorders			
RETINAL ARTERY OCCLUSION			

subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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 UPPER			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	0 / 103 (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 STRANGULATED			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
SUBILEUS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	0 / 103 (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
SALIVARY DUCT INFLAMMATION			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	0 / 103 (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
COLITIS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	0 / 103 (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
LARGE INTESTINE POLYP			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
OESOPHAGITIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	1 / 103 (0.97%)
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 CHRONIC			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
ERYTHEMA NODOSUM			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
URETEROLITHIASIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
Endocrine disorders			
ADRENAL CYST			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
RHEUMATOID ARTHRITIS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACK PAIN			
subjects affected / exposed	1 / 54 (1.85%)	1 / 55 (1.82%)	2 / 103 (1.94%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
BRONCHITIS			

subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL ABSCESS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	0 / 103 (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
INFLUENZA			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
UROSEPSIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
TRACHEOBRONCHITIS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	2 / 103 (1.94%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
PNEUMONIA			
subjects affected / exposed	2 / 54 (3.70%)	1 / 55 (1.82%)	4 / 103 (3.88%)
occurrences causally related to treatment / all	1 / 2	1 / 1	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	0 / 103 (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
COVID-19			

subjects affected / exposed	1 / 54 (1.85%)	1 / 55 (1.82%)	4 / 103 (3.88%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
GINGIVITIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
COVID-19 PNEUMONIA			
subjects affected / exposed	3 / 54 (5.56%)	3 / 55 (5.45%)	6 / 103 (5.83%)
occurrences causally related to treatment / all	0 / 3	1 / 3	1 / 6
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
CELLULITIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORAL HERPES			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	0 / 103 (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
CYSTITIS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	0 / 103 (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
PYELONEPHRITIS ACUTE			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
HEPATITIS A			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			

subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	3 / 103 (2.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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
INFECTION			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COMPLICATED APPENDICITIS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENCEPHALITIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	0 / 103 (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

Serious adverse events	Avonex/Ocrelizumab 600 mg	Ocrelizumab 1000mg/Ocrelizumab 600mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 54 (29.63%)	16 / 55 (29.09%)	
number of deaths (all causes)	2	3	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BREAST CANCER			

subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG NEOPLASM MALIGNANT			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
PREGNANCY			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
DRUG WITHDRAWAL SYNDROME			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
DEATH			

subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
HYPERSENSITIVITY			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
OVARIAN MASS			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UTERINE PROLAPSE			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (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	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE PSYCHOSIS			

subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUSPECTED SUICIDE ATTEMPT			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANXIETY			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUICIDAL IDEATION			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
AMYLASE INCREASED			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD POTASSIUM INCREASED			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SMEAR CERVIX ABNORMAL			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
INFUSION RELATED REACTION			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (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	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBDURAL HAEMATOMA			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FALL			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
CARDIAC ARREST			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
MULTIPLE SCLEROSIS RELAPSE			
subjects affected / exposed	2 / 54 (3.70%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEIZURE			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPILEPSY			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NERVOUS SYSTEM DISORDER			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

MULTIPLE SCLEROSIS PSEUDO RELAPSE			
subjects affected / exposed	1 / 54 (1.85%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCLE SPASTICITY			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
NEUTROPENIA			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAEMIA			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
IMMUNE THROMBOCYTOPENIA			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
RETINAL ARTERY OCCLUSION			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			

subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INGUINAL HERNIA STRANGULATED			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBILEUS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SALIVARY DUCT INFLAMMATION			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARGE INTESTINE POLYP			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGITIS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLECYSTITIS CHRONIC			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

ERYTHEMA NODOSUM			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
URETEROLITHIASIS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
ADRENAL CYST			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (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			
RHEUMATOID ARTHRITIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACK PAIN			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAL ABSCESS			

subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (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	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
TRACHEOBRONCHITIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
PNEUMONIA			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 54 (3.70%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
GINGIVITIS			

subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 PNEUMONIA			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (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 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORAL HERPES			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYSTITIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYELONEPHRITIS ACUTE			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATITIS A			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 54 (0.00%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIVERTICULITIS			

subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COMPLICATED APPENDICITIS			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENCEPHALITIS			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (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	Placebo/Ocrelizumab 600mg	Ocrelizumab 600mg/Ocrelizumab 600mg	Ocrelizumab 600 mg Open Label Extension (OLE)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 54 (96.30%)	47 / 55 (85.45%)	85 / 103 (82.52%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	4 / 54 (7.41%)	6 / 55 (10.91%)	4 / 103 (3.88%)
occurrences (all)	4	7	4
General disorders and administration site conditions			
ASTHENIA			

subjects affected / exposed	3 / 54 (5.56%)	2 / 55 (3.64%)	3 / 103 (2.91%)
occurrences (all)	5	2	3
CHILLS			
subjects affected / exposed	0 / 54 (0.00%)	2 / 55 (3.64%)	1 / 103 (0.97%)
occurrences (all)	0	2	1
PYREXIA			
subjects affected / exposed	3 / 54 (5.56%)	8 / 55 (14.55%)	11 / 103 (10.68%)
occurrences (all)	3	8	12
FATIGUE			
subjects affected / exposed	5 / 54 (9.26%)	7 / 55 (12.73%)	8 / 103 (7.77%)
occurrences (all)	8	7	12
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 54 (1.85%)	2 / 55 (3.64%)	3 / 103 (2.91%)
occurrences (all)	1	2	3
OEDEMA PERIPHERAL			
subjects affected / exposed	3 / 54 (5.56%)	1 / 55 (1.82%)	2 / 103 (1.94%)
occurrences (all)	3	1	2
Immune system disorders			
HYPOGAMMAGLOBULINAEMIA			
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)	4 / 103 (3.88%)
occurrences (all)	1	3	4
SEASONAL ALLERGY			
subjects affected / exposed	1 / 54 (1.85%)	1 / 55 (1.82%)	3 / 103 (2.91%)
occurrences (all)	1	1	3
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	2 / 103 (1.94%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
RHINORRHOEA			
subjects affected / exposed	0 / 54 (0.00%)	3 / 55 (5.45%)	3 / 103 (2.91%)
occurrences (all)	0	3	3
COUGH			
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)	5 / 103 (4.85%)
occurrences (all)	1	5	7
DYSPNOEA			

subjects affected / exposed	2 / 54 (3.70%)	1 / 55 (1.82%)	2 / 103 (1.94%)
occurrences (all)	3	1	3
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	2 / 54 (3.70%)	7 / 55 (12.73%)	5 / 103 (4.85%)
occurrences (all)	2	8	5
INSOMNIA			
subjects affected / exposed	2 / 54 (3.70%)	3 / 55 (5.45%)	4 / 103 (3.88%)
occurrences (all)	3	4	4
ANXIETY			
subjects affected / exposed	3 / 54 (5.56%)	5 / 55 (9.09%)	4 / 103 (3.88%)
occurrences (all)	3	7	4
Injury, poisoning and procedural complications			
SKIN LACERATION			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences (all)	0	1	1
INFUSION RELATED REACTION			
subjects affected / exposed	29 / 54 (53.70%)	25 / 55 (45.45%)	23 / 103 (22.33%)
occurrences (all)	63	60	39
FALL			
subjects affected / exposed	1 / 54 (1.85%)	1 / 55 (1.82%)	2 / 103 (1.94%)
occurrences (all)	1	1	2
THERMAL BURN			
subjects affected / exposed	3 / 54 (5.56%)	1 / 55 (1.82%)	0 / 103 (0.00%)
occurrences (all)	4	1	0
CONTUSION			
subjects affected / exposed	2 / 54 (3.70%)	3 / 55 (5.45%)	3 / 103 (2.91%)
occurrences (all)	3	3	3
LIGAMENT SPRAIN			
subjects affected / exposed	2 / 54 (3.70%)	1 / 55 (1.82%)	1 / 103 (0.97%)
occurrences (all)	2	1	1
Cardiac disorders			
PALPITATIONS			
subjects affected / exposed	1 / 54 (1.85%)	1 / 55 (1.82%)	3 / 103 (2.91%)
occurrences (all)	1	1	3
Nervous system disorders			

MULTIPLE SCLEROSIS RELAPSE			
subjects affected / exposed	26 / 54 (48.15%)	19 / 55 (34.55%)	28 / 103 (27.18%)
occurrences (all)	70	39	68
HEADACHE			
subjects affected / exposed	15 / 54 (27.78%)	9 / 55 (16.36%)	7 / 103 (6.80%)
occurrences (all)	33	16	11
DIZZINESS			
subjects affected / exposed	5 / 54 (9.26%)	4 / 55 (7.27%)	2 / 103 (1.94%)
occurrences (all)	6	4	2
PARAESTHESIA			
subjects affected / exposed	1 / 54 (1.85%)	4 / 55 (7.27%)	0 / 103 (0.00%)
occurrences (all)	1	4	0
SYNCOPE			
subjects affected / exposed	3 / 54 (5.56%)	0 / 55 (0.00%)	0 / 103 (0.00%)
occurrences (all)	4	0	0
HYPOAESTHESIA			
subjects affected / exposed	1 / 54 (1.85%)	2 / 55 (3.64%)	3 / 103 (2.91%)
occurrences (all)	1	3	3
MIGRAINE			
subjects affected / exposed	5 / 54 (9.26%)	4 / 55 (7.27%)	4 / 103 (3.88%)
occurrences (all)	6	6	5
SCIATICA			
subjects affected / exposed	3 / 54 (5.56%)	1 / 55 (1.82%)	3 / 103 (2.91%)
occurrences (all)	3	1	3
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 54 (3.70%)	3 / 55 (5.45%)	2 / 103 (1.94%)
occurrences (all)	2	3	2
Eye disorders			
VISION BLURRED			
subjects affected / exposed	0 / 54 (0.00%)	2 / 55 (3.64%)	3 / 103 (2.91%)
occurrences (all)	0	3	3
Gastrointestinal disorders			
HAEMORRHOIDS			
subjects affected / exposed	3 / 54 (5.56%)	1 / 55 (1.82%)	2 / 103 (1.94%)
occurrences (all)	3	1	2
NAUSEA			

subjects affected / exposed	1 / 54 (1.85%)	2 / 55 (3.64%)	5 / 103 (4.85%)
occurrences (all)	1	3	5
DIARRHOEA			
subjects affected / exposed	3 / 54 (5.56%)	4 / 55 (7.27%)	5 / 103 (4.85%)
occurrences (all)	3	6	7
CONSTIPATION			
subjects affected / exposed	3 / 54 (5.56%)	3 / 55 (5.45%)	4 / 103 (3.88%)
occurrences (all)	3	3	4
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	3 / 54 (5.56%)	2 / 55 (3.64%)	3 / 103 (2.91%)
occurrences (all)	3	3	3
SKIN LESION			
subjects affected / exposed	3 / 54 (5.56%)	1 / 55 (1.82%)	2 / 103 (1.94%)
occurrences (all)	3	1	2
ALOPECIA			
subjects affected / exposed	1 / 54 (1.85%)	4 / 55 (7.27%)	1 / 103 (0.97%)
occurrences (all)	1	4	1
Renal and urinary disorders			
RENAL CYST			
subjects affected / exposed	3 / 54 (5.56%)	1 / 55 (1.82%)	2 / 103 (1.94%)
occurrences (all)	3	1	2
NEPHROLITHIASIS			
subjects affected / exposed	0 / 54 (0.00%)	3 / 55 (5.45%)	4 / 103 (3.88%)
occurrences (all)	0	5	5
Musculoskeletal and connective tissue disorders			
PAIN IN EXTREMITY			
subjects affected / exposed	7 / 54 (12.96%)	2 / 55 (3.64%)	8 / 103 (7.77%)
occurrences (all)	11	2	10
MYALGIA			
subjects affected / exposed	0 / 54 (0.00%)	3 / 55 (5.45%)	3 / 103 (2.91%)
occurrences (all)	0	3	3
ARTHRALGIA			
subjects affected / exposed	8 / 54 (14.81%)	9 / 55 (16.36%)	13 / 103 (12.62%)
occurrences (all)	15	10	18
BACK PAIN			

subjects affected / exposed	9 / 54 (16.67%)	5 / 55 (9.09%)	6 / 103 (5.83%)
occurrences (all)	11	7	7
MUSCULAR WEAKNESS			
subjects affected / exposed	2 / 54 (3.70%)	4 / 55 (7.27%)	4 / 103 (3.88%)
occurrences (all)	2	5	4
Infections and infestations			
SINUSITIS			
subjects affected / exposed	5 / 54 (9.26%)	4 / 55 (7.27%)	5 / 103 (4.85%)
occurrences (all)	7	4	6
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 54 (0.00%)	5 / 55 (9.09%)	1 / 103 (0.97%)
occurrences (all)	0	7	1
BRONCHITIS			
subjects affected / exposed	7 / 54 (12.96%)	4 / 55 (7.27%)	10 / 103 (9.71%)
occurrences (all)	12	4	17
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)	2 / 103 (1.94%)
occurrences (all)	1	3	2
HERPES ZOSTER			
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)	2 / 103 (1.94%)
occurrences (all)	1	3	2
INFLUENZA			
subjects affected / exposed	7 / 54 (12.96%)	4 / 55 (7.27%)	10 / 103 (9.71%)
occurrences (all)	8	4	14
NASOPHARYNGITIS			
subjects affected / exposed	10 / 54 (18.52%)	15 / 55 (27.27%)	20 / 103 (19.42%)
occurrences (all)	15	32	41
VAGINAL INFECTION			
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)	3 / 103 (2.91%)
occurrences (all)	1	3	3
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	10 / 54 (18.52%)	14 / 55 (25.45%)	15 / 103 (14.56%)
occurrences (all)	17	25	32
PNEUMONIA			

subjects affected / exposed	3 / 54 (5.56%)	1 / 55 (1.82%)	7 / 103 (6.80%)
occurrences (all)	5	1	10
GASTROENTERITIS			
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)	5 / 103 (4.85%)
occurrences (all)	1	3	5
ORAL HERPES			
subjects affected / exposed	4 / 54 (7.41%)	3 / 55 (5.45%)	6 / 103 (5.83%)
occurrences (all)	17	7	18
CYSTITIS			
subjects affected / exposed	4 / 54 (7.41%)	2 / 55 (3.64%)	4 / 103 (3.88%)
occurrences (all)	5	4	4
COVID-19			
subjects affected / exposed	12 / 54 (22.22%)	7 / 55 (12.73%)	26 / 103 (25.24%)
occurrences (all)	13	8	30
PHARYNGITIS			
subjects affected / exposed	6 / 54 (11.11%)	3 / 55 (5.45%)	5 / 103 (4.85%)
occurrences (all)	7	6	6
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	8 / 54 (14.81%)	5 / 55 (9.09%)	8 / 103 (7.77%)
occurrences (all)	18	8	9
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	2 / 54 (3.70%)	3 / 55 (5.45%)	3 / 103 (2.91%)
occurrences (all)	2	6	4
URINARY TRACT INFECTION			
subjects affected / exposed	14 / 54 (25.93%)	10 / 55 (18.18%)	23 / 103 (22.33%)
occurrences (all)	29	24	58
VIRAL INFECTION			
subjects affected / exposed	3 / 54 (5.56%)	0 / 55 (0.00%)	1 / 103 (0.97%)
occurrences (all)	3	0	1
PYELONEPHRITIS			
subjects affected / exposed	3 / 54 (5.56%)	0 / 55 (0.00%)	3 / 103 (2.91%)
occurrences (all)	4	0	3
Metabolism and nutrition disorders			
VITAMIN D DEFICIENCY			

subjects affected / exposed	2 / 54 (3.70%)	3 / 55 (5.45%)	5 / 103 (4.85%)
occurrences (all)	2	3	5

Non-serious adverse events	Avonex/Ocrelizumab 600 mg	Ocrelizumab 1000mg/Ocrelizumab 600mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 54 (83.33%)	45 / 55 (81.82%)	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 54 (1.85%)	2 / 55 (3.64%)	
occurrences (all)	1	3	
CHILLS			
subjects affected / exposed	3 / 54 (5.56%)	1 / 55 (1.82%)	
occurrences (all)	3	1	
PYREXIA			
subjects affected / exposed	2 / 54 (3.70%)	3 / 55 (5.45%)	
occurrences (all)	2	4	
FATIGUE			
subjects affected / exposed	4 / 54 (7.41%)	11 / 55 (20.00%)	
occurrences (all)	4	14	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	11 / 54 (20.37%)	2 / 55 (3.64%)	
occurrences (all)	15	2	
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
HYPOGAMMAGLOBULINAEMIA			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences (all)	0	0	
SEASONAL ALLERGY			
subjects affected / exposed	0 / 54 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	3	

Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	3 / 54 (5.56%)	1 / 55 (1.82%)	
occurrences (all)	3	1	
Respiratory, thoracic and mediastinal disorders			
RHINORRHOEA			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences (all)	2	0	
COUGH			
subjects affected / exposed	4 / 54 (7.41%)	3 / 55 (5.45%)	
occurrences (all)	4	3	
DYSPNOEA			
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)	
occurrences (all)	1	3	
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	4 / 54 (7.41%)	5 / 55 (9.09%)	
occurrences (all)	5	5	
INSOMNIA			
subjects affected / exposed	1 / 54 (1.85%)	9 / 55 (16.36%)	
occurrences (all)	1	12	
ANXIETY			
subjects affected / exposed	6 / 54 (11.11%)	3 / 55 (5.45%)	
occurrences (all)	6	3	
Injury, poisoning and procedural complications			
SKIN LACERATION			
subjects affected / exposed	0 / 54 (0.00%)	4 / 55 (7.27%)	
occurrences (all)	0	4	
INFUSION RELATED REACTION			
subjects affected / exposed	20 / 54 (37.04%)	29 / 55 (52.73%)	
occurrences (all)	33	60	
FALL			
subjects affected / exposed	0 / 54 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	3	
THERMAL BURN			

subjects affected / exposed	0 / 54 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	3	
CONTUSION			
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)	
occurrences (all)	1	3	
LIGAMENT SPRAIN			
subjects affected / exposed	1 / 54 (1.85%)	5 / 55 (9.09%)	
occurrences (all)	1	6	
Cardiac disorders			
PALPITATIONS			
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)	
occurrences (all)	1	3	
Nervous system disorders			
MULTIPLE SCLEROSIS RELAPSE			
subjects affected / exposed	29 / 54 (53.70%)	21 / 55 (38.18%)	
occurrences (all)	58	72	
HEADACHE			
subjects affected / exposed	12 / 54 (22.22%)	10 / 55 (18.18%)	
occurrences (all)	19	14	
DIZZINESS			
subjects affected / exposed	1 / 54 (1.85%)	4 / 55 (7.27%)	
occurrences (all)	1	6	
PARAESTHESIA			
subjects affected / exposed	1 / 54 (1.85%)	5 / 55 (9.09%)	
occurrences (all)	1	5	
SYNCOPE			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences (all)	0	0	
HYPOAESTHESIA			
subjects affected / exposed	3 / 54 (5.56%)	5 / 55 (9.09%)	
occurrences (all)	4	5	
MIGRAINE			
subjects affected / exposed	1 / 54 (1.85%)	2 / 55 (3.64%)	
occurrences (all)	1	2	
SCIATICA			

subjects affected / exposed	1 / 54 (1.85%)	1 / 55 (1.82%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
VISION BLURRED			
subjects affected / exposed	0 / 54 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
HAEMORRHOIDS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	2	
NAUSEA			
subjects affected / exposed	4 / 54 (7.41%)	7 / 55 (12.73%)	
occurrences (all)	5	10	
DIARRHOEA			
subjects affected / exposed	2 / 54 (3.70%)	5 / 55 (9.09%)	
occurrences (all)	2	6	
CONSTIPATION			
subjects affected / exposed	2 / 54 (3.70%)	4 / 55 (7.27%)	
occurrences (all)	2	4	
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	4 / 54 (7.41%)	4 / 55 (7.27%)	
occurrences (all)	4	4	
SKIN LESION			
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)	
occurrences (all)	0	0	
ALOPECIA			
subjects affected / exposed	1 / 54 (1.85%)	2 / 55 (3.64%)	
occurrences (all)	2	2	
Renal and urinary disorders			
RENAL CYST			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	

NEPHROLITHIASIS			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
PAIN IN EXTREMITY			
subjects affected / exposed	2 / 54 (3.70%)	8 / 55 (14.55%)	
occurrences (all)	2	10	
MYALGIA			
subjects affected / exposed	3 / 54 (5.56%)	2 / 55 (3.64%)	
occurrences (all)	3	2	
ARTHRALGIA			
subjects affected / exposed	5 / 54 (9.26%)	5 / 55 (9.09%)	
occurrences (all)	8	8	
BACK PAIN			
subjects affected / exposed	7 / 54 (12.96%)	4 / 55 (7.27%)	
occurrences (all)	9	5	
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)	
occurrences (all)	1	4	
Infections and infestations			
SINUSITIS			
subjects affected / exposed	2 / 54 (3.70%)	3 / 55 (5.45%)	
occurrences (all)	2	4	
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
BRONCHITIS			
subjects affected / exposed	2 / 54 (3.70%)	6 / 55 (10.91%)	
occurrences (all)	2	11	
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	0 / 54 (0.00%)	2 / 55 (3.64%)	
occurrences (all)	0	2	
HERPES ZOSTER			
subjects affected / exposed	1 / 54 (1.85%)	1 / 55 (1.82%)	
occurrences (all)	1	1	
INFLUENZA			

subjects affected / exposed	4 / 54 (7.41%)	7 / 55 (12.73%)		
occurrences (all)	5	11		
NASOPHARYNGITIS				
subjects affected / exposed	9 / 54 (16.67%)	12 / 55 (21.82%)		
occurrences (all)	25	25		
VAGINAL INFECTION				
subjects affected / exposed	0 / 54 (0.00%)	0 / 55 (0.00%)		
occurrences (all)	0	0		
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	7 / 54 (12.96%)	11 / 55 (20.00%)		
occurrences (all)	10	26		
PNEUMONIA				
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)		
occurrences (all)	1	4		
GASTROENTERITIS				
subjects affected / exposed	1 / 54 (1.85%)	2 / 55 (3.64%)		
occurrences (all)	1	2		
ORAL HERPES				
subjects affected / exposed	4 / 54 (7.41%)	2 / 55 (3.64%)		
occurrences (all)	5	3		
CYSTITIS				
subjects affected / exposed	0 / 54 (0.00%)	5 / 55 (9.09%)		
occurrences (all)	0	6		
COVID-19				
subjects affected / exposed	2 / 54 (3.70%)	5 / 55 (9.09%)		
occurrences (all)	4	5		
PHARYNGITIS				
subjects affected / exposed	3 / 54 (5.56%)	1 / 55 (1.82%)		
occurrences (all)	4	1		
RESPIRATORY TRACT INFECTION				
subjects affected / exposed	3 / 54 (5.56%)	2 / 55 (3.64%)		
occurrences (all)	5	5		
RESPIRATORY TRACT INFECTION VIRAL				

subjects affected / exposed	1 / 54 (1.85%)	1 / 55 (1.82%)	
occurrences (all)	1	1	
URINARY TRACT INFECTION			
subjects affected / exposed	10 / 54 (18.52%)	15 / 55 (27.27%)	
occurrences (all)	17	39	
VIRAL INFECTION			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
PYELONEPHRITIS			
subjects affected / exposed	1 / 54 (1.85%)	1 / 55 (1.82%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
VITAMIN D DEFICIENCY			
subjects affected / exposed	0 / 54 (0.00%)	2 / 55 (3.64%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 June 2008	The following changes were made as per amendment B: •Collection of persisting gadolinium-enhancing T1 lesions was added. •The transition to Cycle 2 for participants enrolled into Group D was clarified. •An exclusion criterion relating to potential hypersensitivity as a result of human serum albumin contained in the Avonex vials was added. •A risk-benefit reassessment/stopping rule was added. •Consistency was provided in the Expanded Disability Status Scale (EDSS) increase for assessment of disability progression within the protocol. •The difference between treatment withdrawal and study withdrawal was clarified. •The window for study Magnetic Resonance Imaging (MRI) scans was clarified; it was also clarified that the sites would not receive reports from the central MRI reading center. •The requirement of blood samples in order to have baseline values for participants in Group D prior to first Ocrelizumab (OCR) dose was added. •The assessment of protocol-defined relapses was clarified. •A standardized questionnaire for the telephone interview was provided. •The frequency of John Cunningham Virus (JCV) plasma sampling was increased. •Procedures for sample analysis for suspected progressive multifocal leukoencephalopathy (PML) were provided. •An exploratory investigation of patient-reported outcome (PRO) scales for potential implementation in Phase III was added. •Retreatment criteria were provided. •The requirement for clinical evaluations prior to re-dosing with OCR was clarified. •Reporting of clinical relapses and secondary progressive Multiple Sclerosis (MS) as Adverse Events (AEs) was included. •Consistent terminology for the grading of infusion reaction intensity was provided.
15 October 2011	The following changes were made as per amendment C: the addition of an Open Label Extension (OLE) period of the study following the Treatment free period (TFP).
03 April 2012	The following changes were made as per Amendment D: the window for the Week 144 visit to allow participants the opportunity to enter the OLE following the TFP was increased from 24 weeks to 96 weeks.
22 December 2015	The following changes as per amendment E •The duration of OLE period was extended for the participants having completed their 4 years of open-label ocrelizumab treatment. •The permittance of alternative MS treatments and prolongation of the monitoring period for participants switching to other MS therapies post-ocrelizumab was clarified. •Voluntary collection of pregnancy outcomes and infant health information on the first year of life was added. •The telephone interview script was updated to clarify the purpose of the telephone interview. •The activities of the independent Data Monitoring Committee (iDMC) for the OLE period were clarified. •Minor changes and clarifications were made to the schedule of assessments for the OLE period of the study to improve consistency
04 August 2016	The following changes were made as per amendment F: •The version of ocrelizumab that would be administered across the program was changed such that each vial contains 300 mg ocrelizumab. Updated guidance on the storage of infusion bags and a requirement on the use of an infusion set with an infusion set with an in-line filter was added. •The safety section was updated to align the safety language with the Investigator's Brochure, reflecting the outcome from the Phase III clinical studies.

01 February 2017	The following change was made as per amendment G: OLE period of the study was extended to provide participants with the opportunity to continue receiving benefit from ocrelizumab treatment based on positive Phase III relapse multiple sclerosis (RMS) data.
27 September 2017	The following changes were made as per amendment H: •The protocol safety wording was updated for the following risks associated with ocrelizumab treatment: infusion-related reaction (IRR) risk, infection risk, delayed return of peripheral B cells, decrease in immunoglobulins, malignancy including breast cancer risk, progressive multifocal leukoencephalopathy (PML), including the guidance for PML diagnosis, neutropenia, serious infections related to decrease in immunoglobulins, hypersensitivity reactions, and impaired response to immunization. The following risks associated with ocrelizumab treatment have been removed after the latest benefit–risk assessments: cardiovascular disorders and immunogenicity. •Adverse Events of Special Interest (AESIs) were required to be reported by the Investigator to the Sponsor immediately (i.e., no more than 24 hours after learning of the event). •With antihistamines considered as part of the pretreatment regimen, the risks associated with antihistamine use were added (Warnings and Precautions). •Contraception requirements for male participants and female partner pregnancy reporting were removed. •Contraception requirements, duration of contraception, and procedures for pregnant women during OLE period were updated.
15 August 2018	The following changes were made as per amendment I: •The OLE treatment period was extended to 31 December 2020 to provide additional long-term efficacy and safety data. •Language was updated pertaining to impairment of vaccination response. •Retreatment with ocrelizumab for participants with active tuberculosis and for pregnant or breastfeeding female participants was clarified. •Information regarding exposure in utero to ocrelizumab and administration of live or live-attenuated vaccines to neonates and infants were added. •Language related specially to Case Report Forms (CRFs) was deleted to allow for conversion to electronic capture.
09 February 2020	The following changes were made as per amendment J: •For the first participant entering OLE period, the maximum duration was modified to 11 years. •The safety risks for ocrelizumab were updated. •The pharmacokinetic/anti-drug antibody (ADA) collection/analysis was removed because immunogenicity incidence with ocrelizumab is very low (<1%) with no safety risks identified, so continuous monitoring in this population is unnecessary. •The plasma and urine sample collection for John Cunningham virus (JCV) was removed because there is no evidence that JCV antibody index (or similar) informs the risk of PML for participants on ocrelizumab. •Guidance for diagnosis of PML was updated. •Guidance for reporting abortions was updated. •Reference to Medical Monitor was changed where applicable and the emergency contact information was updated.
31 July 2020	The following change was made as per amendment K: The option of a shorter study drug infusion regimen was added to reduce burden on participants and infusion centers during the OLE period.
17 November 2021	The following changes were made as per amendment L: •The benefit-risk assessment for concomitant use of SARS-CoV-2 vaccines was updated. •Language was added to clarify that participants who complete or who discontinue the OLE period treatment early, for any reason, would be followed up for a maximum of 48 weeks after the last infusion of ocrelizumab. Continued B-cell monitoring for participants whose B cells are not repleted (i.e., returned to baseline levels or the lower limit of normal, whichever is lower) was removed because no increased safety risk was identified in the ocrelizumab clinical development program following cessation of treatment. •Language was added to clarify that participants who switch to commercial ocrelizumab after entering B-cell monitoring or enter into treatment with another Disease modifying therapy (DMT) would be discontinued from B-cell monitoring and from the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported