Clinical trial results:
AN OPEN-LABEL, SINGLE-ARM STUDY TO EVALUATE THE EFFECTIVENESS AND SAFETY OF OCRELIZUMAB IN PATIENTS WITH EARLY STAGE RELAPSING REMITTING MULTIPLE SCLEROSIS

Summary

EudraCT number	2016-002937-31
Trial protocol	NO SE AT DK DE PT BE HU PL SK ES BG SI NL GB FR HR IT
Global end of trial date	27 April 2023

Results information

Result version number	v1
This version publication date	12 May 2024
First version publication date	12 May 2024

Trial information

Trial identification

Sponsor protocol code	MA30143

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, 4058
Public contact	Roche Trial Information Hotline, Hoffmann-La Roche, +41 61 6878333,
Scientific contact	Medical Communications, Hoffmann-La Roche, +1 8008218590, 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	27 April 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 April 2023
Global end of trial reached?	Yes
Global end of trial date	27 April 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

TO EVALUATE THE EFFECTIVENESS AND SAFETY OF OCRELIZUMAB IN PATIENTS WITH EARLY STAGE RELAPSING REMITTING MULTIPLE SCLEROSIS

Protection of trial subjects:

The study was conducted in accordance with the principles of the "Declaration of Helsinki" and Good Clinical Practice (GCP) guidelines according to the regulations and procedures described in the protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 14
Country: Number of subjects enrolled	Australia: 55
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	Belgium: 39
Country: Number of subjects enrolled	Bulgaria: 28
Country: Number of subjects enrolled	Brazil: 21
Country: Number of subjects enrolled	Canada: 67
Country: Number of subjects enrolled	Switzerland: 21
Country: Number of subjects enrolled	Germany: 78
Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	Spain: 36
Country: Number of subjects enrolled	France: 69
Country: Number of subjects enrolled	United Kingdom: 52
Country: Number of subjects enrolled	Croatia: 36
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Italy: 60
Country: Number of subjects enrolled	Kuwait: 5
Country: Number of subjects enrolled	Lebanon: 6
Country: Number of subjects enrolled	Mexico: 72
Country: Number of subjects enrolled	Netherlands: 24
Country: Number of subjects enrolled	Norway: 6

Country: Number of subjects enrolled	Poland: 153
Country: Number of subjects enrolled	Portugal: 27
Country: Number of subjects enrolled	Romania: 19
Country: Number of subjects enrolled	Slovakia: 28
Country: Number of subjects enrolled	Slovenia: 12
Country: Number of subjects enrolled	Sweden: 10
Country: Number of subjects enrolled	Türkiye: 47
Country: Number of subjects enrolled	United States: 203
Worldwide total number of subjects	1225
EEA total number of subjects	662

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)	1225
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Full cohort includes both 1st Enrollment Cohort in the ''original'' study and 2nd Enrollment Cohort to participate in the shorter infusion substudy.

Period 1

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

Arms

Arm title	Ocrelizumab

Arm description:

First Enrollment Cohort. Ocrelizumab was administered intravenously (IV) as two 300-milligram (mg) infusions on Days 1 and 15, followed by one 600-mg infusion dose every 24 weeks (+/- 14 days) for a maximum of 8 doses throughout the 192 weeks treatment period

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

Dosage and administration details:

Ocrelizumab was administered intravenously (IV) as two 300-milligram (mg) infusions on Days 1 and 15, followed by one 600-mg infusion dose every 24 weeks (+/- 14 days)

Number of subjects in period 1	Ocrelizumab
Started	1225
Treatment Period	1225
Safety Follow-up Period	59 [1]
Completed	1010
Not completed	215
Adverse event, serious fatal	12
Site Closure	3
Physician decision	13
planned pregnancy	17
Consent withdrawn by subject	77
Changed to Commercial Ocrelizumab	4
Adverse event, non-fatal	25
Pregnancy	7

Terminated By Sponsor	14
Lost to follow-up	17
disease progression	1
Protocol deviation	15
Lack of efficacy	10

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

Baseline characteristics

Reporting groups	
Reporting group title	Ocrelizumab
Reporting group description:	
First Enrollment Cohort. Ocrelizumab was administered intravenously (IV) as two 300-milligram (mg) infusions on Days 1 and 15, followed by one 600-mg infusion dose every 24 weeks (+/- 14 days) for a maximum of 8 doses throughout the 192 weeks treatment period	

Reporting group values	Ocrelizumab	Total	
Number of subjects	1225	1225	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	1225	1225	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	32.7		
standard deviation	± 9.1	-	
Sex: Female, Male Units:			
Female	784	784	
Male	441	441	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	11	11	
Asian	19	19	
Native Hawaiian or Other Pacific Islander	2	2	
Black or African American	34	34	
White	1007	1007	
More than one race	37	37	
Unknown or Not Reported	115	115	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	145	145	
Not Hispanic or Latino	960	960	
Unknown or Not Reported	120	120	

End points

End points reporting groups

Reporting group title	Ocrelizumab
Reporting group description:	
First Enrollment Cohort. Ocrelizumab was administered intravenously (IV) as two 300-milligram (mg) infusions on Days 1 and 15, followed by one 600-mg infusion dose every 24 weeks (+/- 14 days) for a maximum of 8 doses throughout the 192 weeks treatment period	

Primary: Time to Onset of Confirmed Disability Progression (CDP) Sustained for at Least 24 and 48 Weeks, As Measured Using Expanded Disability Status Scale (EDSS)

End point title	Time to Onset of Confirmed Disability Progression (CDP) Sustained for at Least 24 and 48 Weeks, As Measured Using Expanded Disability Status Scale (EDSS)[1]
End point description:	
The EDSS is a disability scale that ranges in 0.5-point steps from 0 (normal) to 10 (death).	
End point type	Primary
End point timeframe:	
Baseline up to 4 years	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Event-free Rate Estimate %				
median (confidence interval 95%)				
Sustained 24 Wks Event-free estimate 24 Wks	99.55 (98.62 to 99.86)			
Sustained 24 Wks Event-free estimate 48 Wks	97.3 (95.75 to 98.29)			
Sustained 24 Wks Event-free estimate 72 Wks	93.97 (91.87 to 95.54)			
Sustained 24 Wks Event-free estimate 96 Wks	91.65 (89.26 to 93.52)			
Sustained 24 Wks Event-free estimate 120 Wks	90.07 (87.51 to 92.13)			
Sustained 24 Wks Event-free estimate 144 Wks	88.61 (85.91 to 90.83)			
Sustained 24 Wks Event-free estimate 168 Wks	85.98 (83.04 to 88.44)			
Sustained 24 Wks Event-free estimate 192 Wks	84.18 (81.08 to 86.81)			
Sustained 48 Wks Event-free estimate Wk 24	99.55 (98.62 to 99.86)			
Sustained 48 Wks Event-free estimate Wk 48	98.05 (96.67 to 98.87)			
Sustained 48 Wks Event-free estimate Wk 72	95.18 (93.25 to 96.56)			
Sustained 48 Wks Event-free estimate Wk 96	93.47 (91.30 to 95.12)			

Sustained 48 Wks Event-free estimate Wk 120	91.73 (89.34 to 93.61)			
Sustained 48 Wks Event-free estimate Wk 144	90.12 (87.55 to 92.18)			
Sustained 48 Wks Event-free estimate Wk 168	87.98 (85.20 to 90.27)			
Sustained 48 Wks Event-free estimate Wk 192	86.48 (83.54 to 88.93)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With CDP Sustained for At Least 24 and 48 Weeks at Year 1, As Measured Using EDSS

End point title	Percentage of Participants With CDP Sustained for At Least 24 and 48 Weeks at Year 1, As Measured Using EDSS[2]

End point description:

This Outcome Measure is reported in the Outcome Measure 1: Time to Onset of Confirmed Disability Progression (CDP) Sustained for at Least 24 and 48 Weeks, As Measured Using Expanded Disability Status Scale (EDSS)

End point type	Primary

End point timeframe:

Year 1

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Percentage of Participants				
median (confidence interval 95%)	(to)			

Notes:

[3] - No data

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With CDI at Year 4, As Measured Using EDSS

End point title	Percentage of Participants With CDI at Year 4, As Measured Using EDSS[4]

End point description:

End point type	Primary

End point timeframe:

Year 4

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Percentage of Participants				
median (confidence interval 95%)				
Week 144	100.00 (100.00 to 100.00)			
Week 168	99.54 (96.77 to 99.93)			
Week 192	93.77 (89.51 to 96.34)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With CDP Sustained for At Least 24 and 48 Weeks at Year 4, As Measured Using EDSS

End point title	Percentage of Participants With CDP Sustained for At Least 24 and 48 Weeks at Year 4, As Measured Using EDSS[5]

End point description:

This Outcome Measure is reported in the Outcome Measure 1: Time to Onset of Confirmed Disability Progression (CDP) Sustained for at Least 24 and 48 Weeks, As Measured Using Expanded Disability Status Scale (EDSS)

End point type	Primary

End point timeframe:

Year 4

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: Percentage of Participants				
median (confidence interval 95%)	(to)			

Notes:

[6] - No data

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Have Improved, Stable, or Worsened Disability Compared to Baseline at Year 1, As Measured Using EDSS

End point title	Percentage of Participants Who Have Improved, Stable, or Worsened Disability Compared to Baseline at Year 1, As Measured Using EDSS[7]

End point description:

End point type	Primary

End point timeframe:

Year 1 (Week 48)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Percentage of Participants				
number (not applicable)				
Week 48 Worsened (>0.5)	9.3			
Week 48 Stable (Change <= 0.5 and >= -0.5)	73.3			
Week 48 Improved (<-0.5)	17.5			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With CDP Sustained for At Least 24 and 48 Weeks at Year 2, As Measured Using EDSS

End point title	Percentage of Participants With CDP Sustained for At Least 24 and 48 Weeks at Year 2, As Measured Using EDSS[8]

End point description:

This Outcome Measure is reported in the Outcome Measure 1: Time to Onset of Confirmed Disability Progression (CDP) Sustained for at Least 24 and 48 Weeks, As Measured Using Expanded Disability Status Scale (EDSS)

End point type	Primary

End point timeframe:

Year 2

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	0[9]			
Units: Percentage of Particiopants				
median (confidence interval 95%)	(to)			

Notes:

[9] - No data

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Have Improved, Stable, or Worsened Disability Compared to Baseline at Year 2, As Measured Using EDSS

End point title	Percentage of Participants Who Have Improved, Stable, or Worsened Disability Compared to Baseline at Year 2, As Measured Using EDSS[10]

End point description:

End point type	Primary

End point timeframe:

Year 2 (Week 96)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Percentage of Participants				
number (not applicable)				
Week 96 Worsened (>0.5)	11.9			
Week 96 Stable (Change <= 0.5 and >= -0.5)	76.6			
Week 96 Improved (<-0.5)	11.6			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in EDSS Score at Week 24

End point title	Mean Change From Baseline in EDSS Score at Week 24[11]

End point description:

End point type	Primary

End point timeframe:

From Baseline to Week 24

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	671			
Units: Change in Total EDSS				
arithmetic mean (standard deviation)	-0.14 (± 0.68)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in EDSS Score at Week 48

End point title	Mean Change From Baseline in EDSS Score at Week 48[12]

End point description:

End point type	Primary

End point timeframe:

From Baseline to Week 48

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	659			
Units: Change in Total EDSS				
arithmetic mean (standard deviation)	-0.14 (± 0.77)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in EDSS Score at Week 192

End point title	Mean Change From Baseline in EDSS Score at Week 192[13]

End point description:

End point type	Primary

End point timeframe:

Baseline, Week 192

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	562			
Units: Change in Total EDSS				
arithmetic mean (standard deviation)	-0.06 (± 1.06)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to First Protocol-Defined Event of Disease Activity

End point title	Time to First Protocol-Defined Event of Disease Activity[14]

End point description:

Protocol-defined event of disease activity is defined as having at least one of the following: (1). protocol defined relapse (occurrence of new or worsening neurological symptoms attributable to Multiple Sclerosis [MS], as determined using EDSS/Functional Systems Score [FSS] assessment). (2). CDP, as determined using EDSS. (3). a T1 Gd-enhanced lesion after Week 8 (4). a new and/or enlarging T2 hyperintense lesion on magnetic resonance imaging (MRI) after Week 8 compared to the Week 8 MRI scan.

End point type	Primary

End point timeframe:

Baseline up to 4 years

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Event-free Rate Estimate %				
median (confidence interval 95%)				
Week 24	95.98 (94.20 to 97.23)			
Week 48	88.94 (86.30 to 91.09)			
Week 72	83.94 (80.92 to 86.52)			
Week 96	80.38 (77.14 to 83.21)			
Week 120	77.38 (73.99 to 80.39)			
Week 144	75.76 (72.28 to 78.86)			
Week 168	72.79 (69.18 to 76.05)			

Week 192	70.67 (66.97 to 74.04)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in EDSS Score at Week 168

End point title	Mean Change From Baseline in EDSS Score at Week 168[15]

End point description:

End point type	Primary

End point timeframe:

Baseline, Week 168

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	560			
Units: Change in Total EDSS				
arithmetic mean (standard error)	-0.05 (± 1.05)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in EDSS Score at Week 144

End point title	Mean Change From Baseline in EDSS Score at Week 144[16]

End point description:

End point type	Primary

End point timeframe:

Baseline, Week 144

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	561			
Units: Change in Total EDSS				
arithmetic mean (standard error)	-0.10 (± 1.00)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in EDSS Score at Week 96

End point title	Mean Change From Baseline in EDSS Score at Week 96[17]

End point description:

End point type	Primary

End point timeframe:

Baseline, Week 96

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	637			
Units: Change in Total EDSS				
arithmetic mean (standard error)	-0.12 (± 0.95)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in EDSS Score at Week 120

End point title	Mean Change From Baseline in EDSS Score at Week 120[18]

End point description:

End point type	Primary

End point timeframe:

Baseline, Week 120

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	579			
Units: Change in Total EDSS				
arithmetic mean (standard deviation)	-0.10 (± 0.94)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change From Baseline in EDSS Score at Week 72

End point title	Mean Change From Baseline in EDSS Score at Week 72[19]

End point description:

End point type	Primary

End point timeframe:

From Baseline to Week 72

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	651			
Units: Change in Total EDSS				
arithmetic mean (standard deviation)	-0.09 (± 0.89)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to First Relapse

End point title	Time to First Relapse[20]

End point description:

Relapse is defined as occurrence of new or worsening neurological symptoms attributable to MS, as determined using EDSS/FSS assessment.

End point type	Primary

End point timeframe:

Baseline up to 4 years

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Event free Rate Estimate %				
median (confidence interval 95%)				
Week 24	98.52 (97.26 to 99.20)			
Week 48	97.91 (96.50 to 98.76)			
Week 72	96.25 (94.49 to 97.45)			
Week 96	95.32 (93.41 to 96.69)			
Week 120	93.90 (91.78 to 95.49)			
Week 144	93.09 (90.85 to 94.79)			
Week 168	92.43 (90.10 to 94.23)			
Week 192	91.56 (89.12 to 93.48)			

Statistical analyses

No statistical analyses for this end point

Primary: Annualized Relapse Rate

End point title	Annualized Relapse Rate[21]

End point description:

Relapse is defined as occurrence of new or worsening neurological symptoms attributable to MS, as determined using EDSS/FSS assessment. The adjusted annualized relapse rate is reported which is: Adjusted by age at disease diagnosis, Baseline EDSS, Presence of T1 Gd-enhanced lesion at screening and Presence of relapses in the last year prior to enrollment. Log-transformed exposure time is included as an offset variable.
The report contains data up to week 192 of the treatment period of each individual participant.

End point type	Primary

End point timeframe:

Baseline up to 4 years

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Annualized Relapse Rate %				
least squares mean (confidence interval 95%)	0.02 (0.015 to 0.027)			

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of Participants with Infusion Related Reactions (IRRs) Occurring During or Within 24 Hours Following the First Infusion After Randomization to the Shorter Infusion Substudy

End point title	Proportion of Participants with Infusion Related Reactions (IRRs) Occurring During or Within 24 Hours Following the First Infusion After Randomization to the Shorter Infusion Substudy[22]

End point description:

End point type	Primary

End point timeframe:

From Week 24 through Week 192

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	1225			
Units: Participants	677			

Statistical analyses

No statistical analyses for this end point

Primary: Time to onset of 24 weeks Confirmed Disability Improvement (CDI) during the Year 1 treatment period

End point title	Time to onset of 24 weeks Confirmed Disability Improvement (CDI) during the Year 1 treatment period[23]

End point description:

CDI is defined as an improvement of 1 point on the EDSS score confirmed at a regular scheduled visit at least 24 weeks after the initial documentation of neurological worsening (measured only patients with a baseline EDSS of ≥2.0).

End point type	Primary

End point timeframe:

Year 1

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	309			
Units: Percentage %				
median (confidence interval 95%)				
Event-free rate estimate (%) 24 Weeks	95.11 (92.03 to 97.03)			
Event-free rate estimate (%) 48 Weeks	83.50 (78.81 to 87.24)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to onset of 24 weeks Confirmed Disability Improvement (CDI) during the Year 2 treatment period

End point title	Time to onset of 24 weeks Confirmed Disability Improvement (CDI) during the Year 2 treatment period[24]

End point description:

End point type	Primary

End point timeframe:

Year 2

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	252			
Units: Percentage %				
median (confidence interval 95%)				
Event-free rate Estimate % Week 48	100.0 (100.00 to 100.00)			
Event-free rate Estimate % Week 72	97.20 (94.22 to 98.66)			
Event-free rate Estimate % Week 96	90.29 (85.71 to 93.46)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Have Improved, Stable, or Worsened Disability at Year 3, As Measured Using EDSS

End point title	Percentage of Participants Who Have Improved, Stable, or Worsened Disability at Year 3, As Measured Using EDSS[25]

End point description:

End point type	Primary

End point timeframe:

Year 3

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Percentage of Participants				
number (not applicable)				
Worsened (>0.5)	9.3			
Stable (Change <= 0.5 and >= -0.5)	81.5			
Improved (<-0.5)	9.2			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Have Improved, Stable, or Worsened Disability at Year 4, As Measured Using EDSS

End point title	Percentage of Participants Who Have Improved, Stable, or Worsened Disability at Year 4, As Measured Using EDSS[26]

End point description:

End point type	Primary

End point timeframe:

Year 4

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Data is being provided for each stage of this study rather than all arms in the baseline period at once

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Percentage of Participants				
number (not applicable)				
Worsened (>0.5)	18.0			
Stable (Change <= 0.5 and >= -0.5)	59.3			
Improved (<-0.5)	22.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With No Evidence of Protocol Defined Disease Activity

End point title	Percentage of Participants With No Evidence of Protocol Defined Disease Activity

End point description:

Protocol-defined disease activity is defined as having at least one of the following: (1). protocol defined relapse (occurrence of new or worsening neurological symptoms attributable to Multiple Sclerosis [MS], as determined using EDSS/Functional Systems Score [FSS] assessment). (2). CDP, as determined using EDSS. (3). a T1 Gd-enhanced lesion after Week 8. (4). a new and/or enlarging T2 hyperintense lesion on magnetic resonance imaging (MRI) after Week 8 compared to the Week 8 MRI scan. Event-free rate

End point type	Secondary

End point timeframe:

Weeks 96, 144, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: event free rate estimate				
median (confidence interval 95%)				
Week 96	80.38 (77.14 to 83.21)			
Week 144	75.76 (72.28 to 78.86)			
Week 192	70.67 (66.97 to 74.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With no Evidence of Progression Sustained for At Least 24 Weeks and no Active Disease (NEPAD)

End point title	Percentage of Participants With no Evidence of Progression Sustained for At Least 24 Weeks and no Active Disease (NEPAD)

End point description:

NEPAD is defined as no progression on all of the three components of NEP (CDP, T25FWT, 9HPT), no new relapse and no enlarging or new T2 or T1 Gd-enhancing lesion. CDP will be assessed using EDSS. Relapse is defined as occurrence of new or worsening neurological symptoms attributable to MS, as determined using EDSS/FSS assessment.

End point type	Secondary

End point timeframe:

Weeks 96, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: event free rate estimate				
median (confidence interval 95%)				
Week 96	70.29 (66.65 to 73.62)			
Week 192	58.89 (54.96 to 62.60)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Are Relapse Free

End point title	Percentage of Participants Who Are Relapse Free

End point description:

Relapse is defined as occurrence of new or worsening neurological symptoms attributable to MS, as determined using EDSS/FSS assessment.

End point type	Secondary

End point timeframe:

Week 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	624			
Units: Percentage of Participants				
median (confidence interval 95%)	92.00 (89.7 to 94.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in MSFC Composite Timed 25 Foot Walk Test (T25FW) Score.

End point title	Change from Baseline in MSFC Composite Timed 25 Foot Walk Test (T25FW) Score.

End point description:

T25FW-Composite Timed 25 Foot Walk Test (T25FW) Scores reported below. Higher scores indicate more severity.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24, 48, 72, 96, 120, 144, 168, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Change in T25FW Score				
arithmetic mean (standard deviation)				
Week 24	-0.31 (± 6.62)			
Week 48	-0.49 (± 6.88)			
Week 72	-0.56 (± 6.99)			
Week 96	-0.62 (± 6.95)			
Week 120	-0.44 (± 7.94)			
Week 144	-0.97 (± 6.25)			
Week 168	-0.83 (± 6.64)			
Week 192	0.09 (± 9.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in MSFC Composite 9 Hole Peg Test (9HPT) Score

End point title	Change from Baseline in MSFC Composite 9 Hole Peg Test (9HPT) Score
End point description:	
Composite 9 Hole Peg Test (9HPT) Scores are reported, higher score values indicate more severity.	
End point type	Secondary
End point timeframe:	
Weeks 24, 48, 72, 96, 120, 144, 168, 192	

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Change in 9HPT Score				
arithmetic mean (standard deviation)				
Week 24	-0.47 (± 14.44)			
Week 48	-1.22 (± 11.54)			
Week 72	-1.78 (± 8.09)			
Week 96	-1.67 (± 10.91)			
Week 120	-0.87 (± 15.21)			
Week 144	-1.91 (± 8.70)			
Week 168	-1.84 (± 10.68)			

Week 192	-0.73 (± 17.55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in MSFC Composite (Paced Auditory Serial Addition Test [PASAT]) Score

End point title	Change from Baseline in MSFC Composite (Paced Auditory Serial Addition Test [PASAT]) Score

End point description:

Paced Auditory Serial Addition Test [PASAT] total scores are reported. The higher scores indicate more severity.

End point type	Secondary

End point timeframe:

Weeks 24, 48, 72, 96, 120, 144, 168, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Change in PASAT Total Score				
arithmetic mean (standard deviation)				
Week 24	4.18 (± 9.26)			
Week 48	5.40 (± 9.52)			
Week 72	6.33 (± 11.59)			
Week 96	7.66 (± 10.93)			
Week 120	7.69 (± 12.95)			
Week 144	8.45 (± 10.02)			
Week 168	8.47 (± 11.79)			
Week 192	9.64 (± 11.56)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in cognitive performance as measured by Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS)

End point title	Change from baseline in cognitive performance as measured by Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS)

End point description:

Cognitive status of the participants are evaluated using BICAMS.

End point type	Secondary

End point timeframe:
Baseline, Weeks 48, 96, 144, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Change in BICAMS Score				
arithmetic mean (standard deviation)				
Week 48	2.48 (± 10.12)			
Week 96	1.89 (± 9.98)			
Week 144	3.33 (± 9.31)			
Week 192	4.38 (± 10.38)			

Statistical analyses

No statistical analyses for this end point

Secondary: Total Number of T1 Gd-Enhancing Lesions as Detected by Brain MRI

End point title	Total Number of T1 Gd-Enhancing Lesions as Detected by Brain MRI

End point description:
Number of Lesions are categorized as followed: 1, 2, 3, >1, >3

End point type	Secondary

End point timeframe:
Weeks 24, 48, 96, 144, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Number of Lesions				
Week 24 Number of Lesions 0	659			
Week 24 Number of Lesions 1	6			
Week 24 Number of Lesions 2	2			
Week 24 Number of Lesions >1	2			
Week 48 Number of Lesions 0	650			
Week 48 Number of Lesions 1	7			
Week 96 Number of Lesions 0	629			
Week 96 Number of Lesions 1	1			
Week 144 Number of Lesions 0	567			
Week 144 Number of Lesions 1	1			
Week 144 Number of Lesions 3	1			
Week 144 Number of Lesions >1	1			
Week 192 Number of Lesions 0	545			

Week 192 Number of Lesions 1	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Total Number of New and/or Enlarging T2 Lesion as Detected by Brain MRI

End point title	Total Number of New and/or Enlarging T2 Lesion as Detected by Brain MRI
End point description: Number of Lesions are categorized as followed: 1, 2, 3, >1, >3	
End point type	Secondary
End point timeframe: Baseline, Weeks 24, 48, 96, 144, 192	

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Number of Lesions				
Week 24 Number of Lesions 0	651			
Week 24 Number of Lesions 1	13			
Week 24 Number of Lesions 2	3			
Week 24 Number of Lesions >1	3			
Week 48 Number of Lesions 0	644			
Week 48 Number of Lesions 1	11			
Week 48 Number of Lesions 2	3			
Week 48 Number of Lesions 3	2			
Week 48 Number of Lesions >1	5			
Week 96 Number of Lesions 0	624			
Week 96 Number of Lesions 1	8			
Week 96 Number of Lesions 2	1			
Week 96 Number of Lesions >1	1			
Week 144 Number of Lesions 0	564			
Week 144 Number of Lesions 1	6			
Week 144 Number of Lesions 2	1			
Week 144 Number of Lesions 3	1			
Week 144 Number of Lesions >1	2			
Week 192 Number of Lesions 0	546			
Week 192 Number of Lesions 1	4			
Week 192 Number of Lesions 2	1			
Week 192 Number of Lesions >1	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in total T1 hypointense lesion volume as Detected by Brain MRI

End point title	Change from baseline in total T1 hypointense lesion volume as Detected by Brain MRI

End point description:

End point type	Secondary

End point timeframe:

Baseline, Weeks 48, 96, 144, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Change in Volume				
arithmetic mean (standard deviation)				
Week 48	-310.63 (± 708.07)			
Week 96	-405.61 (± 755.99)			
Week 144	-359.76 (± 761.84)			
Week 192	-307.64 (± 797.87)			

Statistical analyses

No statistical analyses for this end point

Secondary: Total Number of Fluid-Attenuated Inversion-Recovery (FLAIR) Lesion as Detected by Brain MRI

End point title	Total Number of Fluid-Attenuated Inversion-Recovery (FLAIR) Lesion as Detected by Brain MRI

End point description:

End point type	Secondary

End point timeframe:

Baseline, Weeks 8, 24, 48, 96, 144, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Number of Lesions				
Baseline Week 8 0	633			
Baseline Week 8 1	6			
Week 24 0	635			
Week 24 1	6			
Week 48 0	631			
Week 48 1	6			
Week 96 0	611			
Week 96 1	7			
Week 144 0	550			
Week 144 1	5			
Week 192 0	530			
Week 192 1	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Brain Volume as Detected by Brain MRI

End point title	Change From Baseline in Brain Volume as Detected by Brain MRI

End point description:

Percentage change from Normalized brain volume in cm3 (cubic centimeter)values are reported

End point type	Secondary

End point timeframe:

From Baseline to Weeks 24, 48, 96, 144, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Percentage Change in Volume (cm3)				
arithmetic mean (standard deviation)				
Week 24	-0.189 (± 0.564)			
Week 48	-0.479 (± 0.733)			
Week 96	-0.909 (± 0.930)			
Week 144	-1.283 (± 1.156)			

Week 192	-1.535 (± 1.311)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Treatment Discontinuation

End point title	Time to Treatment Discontinuation

End point description:

End point type	Secondary

End point timeframe:

Baseline up to 4 years

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Event-free Rate Estimate %				
number (confidence interval 95%)				
Week 24	98.97 (97.85 to 99.51)			
Week 48	97.49 (96.00 to 98.45)			
Week 72	96.02 (94.25 to 97.25)			
Week 96	93.51 (91.38 to 95.13)			
Week 120	92.04 (89.73 to 93.84)			
Week 144	89.23 (86.65 to 91.34)			
Week 168	87.17 (84.41 to 89.47)			
Week 192	83.85 (80.85 to 86.42)			

Statistical analyses

No statistical analyses for this end point

Secondary: Employment Status: Work Productivity and Activity Impairment Questionnaire (WAPI) Score

End point title	Employment Status: Work Productivity and Activity Impairment Questionnaire (WAPI) Score

End point description:

Work productivity and Activity Impairment Scores are reported.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24, 48, 96, 120, 144, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: WAPI Sub-Score				
arithmetic mean (standard deviation)				
Work productivity Baseline	26.33 (± 31.84)			
Work productivity Week 24	17.65 (± 25.04)			
Work productivity Week 48	18.83 (± 25.92)			
Work productivity Week 96	16.46 (± 23.10)			
Work productivity Week 144	16.78 (± 23.85)			
Work productivity Week 192	15.80 (± 22.25)			
Activity Impairment Baseline	23.23 (± 24.79)			
Activity Impairment Week 24	18.09 (± 22.15)			
Presenteeism Week 48	18.85 (± 23.37)			
Activity Impairment Week 96	17.79 (± 22.92)			
Activity Impairment Week 144	17.80 (± 23.74)			
Activity Impairment Week 192	18.18 (± 23.25)			
Presenteeism Week 144	17.80 (± 23.74)			
Presenteeism Week 192	18.18 (± 23.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life: Multiple Sclerosis Impact Scale (MSIS)-29 Questionnaire Score

End point title	Quality of Life: Multiple Sclerosis Impact Scale (MSIS)-29 Questionnaire Score

End point description:

End point type	Secondary

End point timeframe:
Baseline, Weeks 24, 48, 96, 144, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Change in MSIS-29 Score				
arithmetic mean (standard deviation)				
Week 24	-2.43 (± 12.13)			
Week 48	-2.15 (± 13.04)			
Week 96	-1.26 (± 14.31)			
Week 144	-0.73 (± 14.83)			
Week 192	-0.63 (± 16.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: SymptoMScreen Composite Score

End point title	SymptoMScreen Composite Score

End point description:

End point type	Secondary

End point timeframe:
Baseline, Weeks 24, 48, 96, 144, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Change in SymptoMScreen Composite Score				
arithmetic mean (standard deviation)				
Week 24	-0.1 (± 0.9)			
Week 48	-0.1 (± 1.0)			
Week 96	0.0 (± 1.1)			
Week 144	0.0 (± 1.1)			
Week 192	0.0 (± 1.1)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

End point type	Secondary

End point timeframe:

Baseline up to 4 years

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	1225			
Units: Percentage of Participants				
number (not applicable)				
Adverse Events	95.8			
Serious Adverse Events	15.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants with IRRs Leading to Treatment Discontinuation in the Shorter Infusion Substudy. This outcome was not measured, therefore no data to report.

End point title	Proportion of Participants with IRRs Leading to Treatment Discontinuation in the Shorter Infusion Substudy. This outcome was not measured, therefore no data to report.

End point description:

There were no participants observed with Infusion-Related Reaction Symptoms Leading To Discontinuation of Ocrelizumab Infusion by Randomized Dose.

End point type	Secondary

End point timeframe:

From Week 24 through Week 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	0[27]			
Units: Participants				

Notes:

[27] - There were no participants observed

Statistical analyses

No statistical analyses for this end point

Secondary: Short term safety related to the infusion (infusion-related reactions [IRRs], during infusion and up to 24h after) the overall safety is measured continuously at clinical visits and including every 8 week telephone visits up to 48 weeks post study.

End point title	Short term safety related to the infusion (infusion-related reactions [IRRs], during infusion and up to 24h after) the overall safety is measured continuously at clinical visits and including every 8 week telephone visits up to 48 weeks post study.

End point description:

Infusion Related Reactions in a Short-term safety population were counted.

End point type	Secondary

End point timeframe:

Up to 4 Years

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	372			
Units: Participants				
Number of Patients with an Infusion, Overall	372			
Overall Number of Patients with an Infusion	107			
Number of pts with AE during the infusion	65			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first protocol-defined event of Evidence of Progression (NEP)

End point title	Time to first protocol-defined event of Evidence of Progression (NEP)

End point description:

NEP is defined as no progression sustained for at least 24 weeks on all of the following three components (CDP; 20 percent [%] increase from baseline in timed 25 Foot Walk Test [T25FWT]; 20% increase from baseline in timed 9 hole peg test [9HPT]). CDP will be assessed using EDSS.

End point type	Secondary

End point timeframe:

Weeks 96, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Event-free rate Estimate %				
median (confidence interval 95%)				
Week 96	79.60 (76.33 to 82.48)			
Week 192	69.16 (65.40 to 72.60)			

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary: Change from Baseline in Multiple Sclerosis Functional Composite Score (MSFC) Total

End point title	Secondary: Change from Baseline in Multiple Sclerosis Functional Composite Score (MSFC) Total

End point description:

The MSFC score combines a measure of lower limb function (T25FWT), upper limb function (9HPT) and cognitive function (PASAT) and used to detect disability progression in MS. Total MSFC scores reported, higher scores indicate progression of MS.

End point type	Secondary

End point timeframe:

Weeks 24, 48, 72, 96, 120, 144, 168, 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	678			
Units: Change in MSFC Score				
arithmetic mean (standard deviation)				
Week 24	0.09 (± 0.67)			
Week 48	0.11 (± 0.54)			
Week 78	0.12 (± 0.45)			
Week 96	0.14 (± 0.53)			
Week 120	0.16 (± 0.61)			
Week 144	0.16 (± 0.48)			

Week 168	0.18 (± 0.56)			
Week 192	0.19 (± 0.72)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants with IRR By Dose at Randomization in the Shorter Infusion Substudy.

End point title	Proportion of Participants with IRR By Dose at Randomization in the Shorter Infusion Substudy.

End point description:

End point type	Secondary

End point timeframe:

From Week 24 through Week 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	372			
Units: Percentage of Participants %				
number (not applicable)				
1st randomized dose Overall Participants with IRR	28.80			
2nd randomized dose Overall Participant% with IRR	27.0			
3rd randomized dose Overall Participants with IRR	27.3			
4th randomized dose Overall Participant% with IRR	12.50			
5th randomized dose Overall Participant% with IRR	14.30			
6th randomized dose Overall Participant% with IRR	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants with IRR (overall) in the Shorter Infusion Substudy.

End point title	Proportion of Participants with IRR (overall) in the Shorter Infusion Substudy.

End point description:

End point type	Secondary

End point timeframe:

From Week 24 through Week 192

End point values	Ocrelizumab			
Subject group type	Reporting group			
Number of subjects analysed	372			
Units: Participants				
Number of Participants with an Infusion, Overall	372			
Overall Number of Participants with any IRR	172			
Overall Number of IRR Symptoms	458			
Overall Number of Participants with Serious IRR	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 4 Years	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0
Reporting groups	
Reporting group title	Ocrelizumab
Reporting group description:	
First Enrollment Cohort. Ocrelizumab was administered intravenously (IV) as two 300-milligram (mg) infusions on Days 1 and 15, followed by one 600-mg infusion dose every 24 weeks (+/- 14 days) for a maximum of 8 doses throughout the 192 weeks treatment period	

Serious adverse events	Ocrelizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	184 / 1225 (15.02%)		
number of deaths (all causes)	13		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
INVASIVE DUCTAL BREAST CARCINOMA			
subjects affected / exposed	3 / 1225 (0.24%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
INTRADUCTAL PAPILLOMA OF BREAST			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RENAL CELL CARCINOMA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BENIGN BREAST NEOPLASM			

subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PAPILLARY THYROID CANCER			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
NEOPLASM PROGRESSION			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
UTERINE LEIOMYOMA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MALIGNANT MELANOMA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
PHLEBITIS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HYPOTENSION			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
ABORTION INDUCED			
subjects affected / exposed	4 / 1225 (0.33%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal			

conditions				
ABORTION SPONTANEOUS				
subjects affected / exposed	7 / 1225 (0.57%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
ECTOPIC PREGNANCY				
subjects affected / exposed	1 / 1225 (0.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HAEMORRHAGE IN PREGNANCY				
subjects affected / exposed	1 / 1225 (0.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ABORTION				
subjects affected / exposed	3 / 1225 (0.24%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
PAIN				
subjects affected / exposed	1 / 1225 (0.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CHEST PAIN				
subjects affected / exposed	1 / 1225 (0.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
OEDEMA PERIPHERAL				
subjects affected / exposed	1 / 1225 (0.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME				

subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
UTERINE POLYP			
subjects affected / exposed	2 / 1225 (0.16%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
CERVICAL DYSPLASIA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
VULVOVAGINAL PAIN			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ENDOMETRIOSIS			
subjects affected / exposed	2 / 1225 (0.16%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
OVARIAN CYST			
subjects affected / exposed	2 / 1225 (0.16%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	2 / 1225 (0.16%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
NASAL SEPTUM DEVIATION			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

NASAL TURBINATE HYPERTROPHY				
subjects affected / exposed	1 / 1225 (0.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMOTHORAX				
subjects affected / exposed	1 / 1225 (0.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PULMONARY EMBOLISM				
subjects affected / exposed	2 / 1225 (0.16%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
DEPRESSION				
subjects affected / exposed	2 / 1225 (0.16%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
SUICIDE ATTEMPT				
subjects affected / exposed	2 / 1225 (0.16%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
ANXIETY				
subjects affected / exposed	1 / 1225 (0.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
COMPLETED SUICIDE				
subjects affected / exposed	1 / 1225 (0.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
POST-TRAUMATIC STRESS DISORDER				
subjects affected / exposed	1 / 1225 (0.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

SUICIDAL IDEATION			
subjects affected / exposed	2 / 1225 (0.16%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
SOMATIC SYMPTOM DISORDER			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MAJOR DEPRESSION			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BIPOLAR DISORDER			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DEPRESSIVE SYMPTOM			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
MENTAL STATUS CHANGES			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Investigations			
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
TRANSAMINASES INCREASED			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CAPILLARY PERMEABILITY			

INCREASED			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
LIGAMENT SPRAIN			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MULTIPLE INJURIES			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OVERDOSE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
TENDON RUPTURE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RADIUS FRACTURE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LOWER LIMB FRACTURE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LIGAMENT RUPTURE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

FIBULA FRACTURE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SKIN LACERATION			
subjects affected / exposed	2 / 1225 (0.16%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
FRACTURE DISPLACEMENT			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
WRIST FRACTURE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ANKLE FRACTURE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INFUSION RELATED REACTION			
subjects affected / exposed	6 / 1225 (0.49%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
CONCUSSION			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FEMUR FRACTURE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			

CRI DU CHAT SYNDROME			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
PALPITATIONS			
subjects affected / exposed	2 / 1225 (0.16%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
PERICARDITIS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
NEURALGIA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RADICULOPATHY			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CERVICOBRACHIAL SYNDROME			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEADACHE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MULTIPLE SCLEROSIS RELAPSE			
subjects affected / exposed	9 / 1225 (0.73%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		

SYNCOPE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SEIZURE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PRESYNCOPE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
TRIGEMINAL NEURALGIA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DYSTONIA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MIGRAINE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
TOXIC ENCEPHALOPATHY			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
NEUTROPENIA			

subjects affected / exposed	2 / 1225 (0.16%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
VISUAL IMPAIRMENT			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
SMALL INTESTINAL PERFORATION			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OESOPHAGEAL SPASM			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ABDOMINAL PAIN			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ANAL FISTULA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COLITIS ULCERATIVE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INGUINAL HERNIA			

subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VOMITING			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
BILE DUCT STONE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CHOLELITHIASIS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CHOLECYSTITIS ACUTE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
ERYTHEMA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
NEPHROLITHIASIS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
URINARY RETENTION			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Endocrine disorders			
THYROID CYST			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
ARTHRITIS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OSTEOARTHRITIS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BACK PAIN			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
PNEUMONIA			
subjects affected / exposed	8 / 1225 (0.65%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
GASTROENTERITIS VIRAL			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BRONCHITIS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
NEUTROPENIC SEPSIS			

subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
INFLUENZA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OTITIS MEDIA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GASTROENTERITIS			
subjects affected / exposed	3 / 1225 (0.24%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SUBACUTE ENDOCARDITIS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	23 / 1225 (1.88%)		
occurrences causally related to treatment / all	0 / 23		
deaths causally related to treatment / all	0 / 0		
HEPATITIS A			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MENINGITIS VIRAL			

subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA MYCOPLASMAL			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 PNEUMONIA			
subjects affected / exposed	17 / 1225 (1.39%)		
occurrences causally related to treatment / all	0 / 18		
deaths causally related to treatment / all	0 / 0		
PYELONEPHRITIS			
subjects affected / exposed	4 / 1225 (0.33%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
FALLOPIAN TUBE ABSCESS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PERITONSILLAR ABSCESS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
APPENDICITIS			
subjects affected / exposed	5 / 1225 (0.41%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
GENITAL HERPES			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
URINARY TRACT INFECTION			

subjects affected / exposed	5 / 1225 (0.41%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
EPIDIDYMITIS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
TYPHOID FEVER			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MENINGITIS BACTERIAL			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
UROSEPSIS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VAGINAL INFECTION			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CELLULITIS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RENAL ABSCESS			

subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ORCHITIS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VARICELLA			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VIRAL INFECTION			
subjects affected / exposed	2 / 1225 (0.16%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
PENILE ABSCESS			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
DIABETES MELLITUS INADEQUATE CONTROL			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DECREASED APPETITE			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DEHYDRATION			
subjects affected / exposed	1 / 1225 (0.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Ocrelizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1110 / 1225 (90.61%)		
Injury, poisoning and procedural complications			
INFUSION RELATED REACTION			
subjects affected / exposed	674 / 1225 (55.02%)		
occurrences (all)	1930		
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	88 / 1225 (7.18%)		
occurrences (all)	102		
HYPOAESTHESIA			
subjects affected / exposed	91 / 1225 (7.43%)		
occurrences (all)	113		
PARAESTHESIA			
subjects affected / exposed	98 / 1225 (8.00%)		
occurrences (all)	124		
HEADACHE			
subjects affected / exposed	295 / 1225 (24.08%)		
occurrences (all)	639		
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	201 / 1225 (16.41%)		
occurrences (all)	274		
PYREXIA			
subjects affected / exposed	98 / 1225 (8.00%)		
occurrences (all)	139		
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	91 / 1225 (7.43%)		
occurrences (all)	116		
NAUSEA			

subjects affected / exposed	87 / 1225 (7.10%)		
occurrences (all)	109		
Respiratory, thoracic and mediastinal disorders			
OROPHARYNGEAL PAIN			
subjects affected / exposed	113 / 1225 (9.22%)		
occurrences (all)	156		
COUGH			
subjects affected / exposed	126 / 1225 (10.29%)		
occurrences (all)	160		
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	84 / 1225 (6.86%)		
occurrences (all)	109		
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	75 / 1225 (6.12%)		
occurrences (all)	88		
ANXIETY			
subjects affected / exposed	62 / 1225 (5.06%)		
occurrences (all)	69		
INSOMNIA			
subjects affected / exposed	81 / 1225 (6.61%)		
occurrences (all)	85		
Musculoskeletal and connective tissue disorders			
MUSCLE SPASMS			
subjects affected / exposed	68 / 1225 (5.55%)		
occurrences (all)	76		
BACK PAIN			
subjects affected / exposed	115 / 1225 (9.39%)		
occurrences (all)	147		
ARTHRALGIA			
subjects affected / exposed	132 / 1225 (10.78%)		
occurrences (all)	169		
PAIN IN EXTREMITY			

subjects affected / exposed	133 / 1225 (10.86%)		
occurrences (all)	172		
Infections and infestations			
SINUSITIS			
subjects affected / exposed	109 / 1225 (8.90%)		
occurrences (all)	144		
COVID-19			
subjects affected / exposed	291 / 1225 (23.76%)		
occurrences (all)	344		
URINARY TRACT INFECTION			
subjects affected / exposed	184 / 1225 (15.02%)		
occurrences (all)	319		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	196 / 1225 (16.00%)		
occurrences (all)	301		
INFLUENZA			
subjects affected / exposed	96 / 1225 (7.84%)		
occurrences (all)	119		
BRONCHITIS			
subjects affected / exposed	62 / 1225 (5.06%)		
occurrences (all)	84		
PHARYNGITIS			
subjects affected / exposed	63 / 1225 (5.14%)		
occurrences (all)	81		
ORAL HERPES			
subjects affected / exposed	63 / 1225 (5.14%)		
occurrences (all)	142		
NASOPHARYNGITIS			
subjects affected / exposed	320 / 1225 (26.12%)		
occurrences (all)	646		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 November 2016	V2
28 March 2017	V3
27 July 2018	V4
30 July 2018	V5
30 December 2018	V6
23 April 2019	V7
28 April 2020	V8
17 September 2020	V9
23 March 2021	V10

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported