



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 Participants | | | | |
| 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 (\pm 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 (\pm 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 (\pm 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 (\pm 9.26) | | | |
| Week 48 | 5.40 (\pm 9.52) | | | |
| Week 72 | 6.33 (\pm 11.59) | | | |
| Week 96 | 7.66 (\pm 10.93) | | | |
| Week 120 | 7.69 (\pm 12.95) | | | |
| Week 144 | 8.45 (\pm 10.02) | | | |
| Week 168 | 8.47 (\pm 11.79) | | | |
| Week 192 | 9.64 (\pm 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 (\pm 708.07) | | | |
| Week 96 | -405.61 (\pm 755.99) | | | |
| Week 144 | -359.76 (\pm 761.84) | | | |
| Week 192 | -307.64 (\pm 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 (\pm 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 (\pm 12.13) | | | |
| Week 48 | -2.15 (\pm 13.04) | | | |
| Week 96 | -1.26 (\pm 14.31) | | | |
| Week 144 | -0.73 (\pm 14.83) | | | |
| Week 192 | -0.63 (\pm 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 (\pm 0.9) | | | |
| Week 48 | -0.1 (\pm 1.0) | | | |
| Week 96 | 0.0 (\pm 1.1) | | | |
| Week 144 | 0.0 (\pm 1.1) | | | |
| Week 192 | 0.0 (\pm 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 (\pm 0.56) | | | |
| Week 192 | 0.19 (\pm 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 JIROVECI 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